From Conception to Connection: A Systematic Approach to Integrating Remote Patient Monitoring in Fertility Management

by

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Abstract

The fertility journey, spanning preconception to postpartum, is critically underserved by traditional healthcare systems, which often fail to provide continuous, personalized care. This deficiency is particularly acute for individuals facing infertility, who must navigate a labyrinth of physiological and emotional challenges at each stage. The need for timely interventions and access to sustained, individualized care is central to addressing these issues.

Amid these challenges, remote patient monitoring (RPM) systems are emerging as a transformative approach in healthcare, facilitating continuous patient care and monitoring beyond the conventional settings of clinics and hospitals. Despite the increased adoption of RPM and telemedicine, a gap persists in integrating such systems within the domain of fertility care.

This thesis undertakes a comprehensive and systemic evaluation of the fertility landscape, examining barriers to effective treatments and outcomes and identifying key health metrics for each phase of the journey. Moreover, the work analyzes existing devices and technologies to determine their ability to measure these metrics and their technological readiness for remote monitoring. The work includes a review of RPM frameworks using system architecture methodologies, analyzing their architectures, technologies, and ecosystems to adapt them for fertility applications. Although numerous devices for remote testing are now available, their full potential in fertility care still needs to be explored, necessitating further development, clinical validation, and resolution of interoperability issues.

A patient-centered, customizable fertility-RPM framework is proposed,

integrating the health metrics with essential architectural decisions aligned with stakeholder needs. This thesis offers foundational insights and operational guidelines for fertility institutions considering adopting RPM services, advocating for a holistic, connected, and continuous care model throughout the fertility journey. This work underscores the transformative potential of RPM in enhancing fertility care, paving the way for more integrated and effective fertility treatment solutions.

Thesis Supervisor: Joan Rubin
Title: Executive Director, MIT System Design and Management Program

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Acronyms, Terms, and Definitions

(In Alphabetical Order)

Acronym	Description
ACOG	American College of Obstetricians and Gynecologists
AD	Architectural decision
AFAB	Assigned female at birth
AI	Artificial intelligence
AMAB	Assigned male at birth
AMH	Anti-Mullerian hormone
API	Application programming interfaces
ART	Assistive reproductive therapy
ASRM	American Society for Reproductive Medicine
BBT	Basal body temperature
BMI	Body mass index
CDC	Centers for Disease Control
CGM	Continuous glucose monitoring
COPD	Chronic obstructive pulmonary disease
cxn.	Connection (abbreviation)
DMS	Data management system
DSM	Design structure matrix
E1G	Estrone-1-glucuronide
E3G	Estrone-3-glucuronide
EHR	Electronic health record
EMR	Electronic medical record
FDA	Food and Drug Administration
FHIR	Fast Healthcare Interoperability Resources
FSH	Follicular stimulating hormone
GDPR	General Data Protection Regulation

GIFT	Gamete intrafallopian transfer
GnRH	Gonadotropin-releasing hormone
hCG	Human chorionic gonadotropin
HCP	Healthcare provider
HIPAA	Health Insurance Portability and Accountability Act of 1996
HL7	Health level seven
ICI	Intracervical insemination
ICMART	International Committee for Monitoring Assisted Reproductive Technologies
ICSI	Intracytoplasmic sperm injection
IT	Information technology
IUD	Intrauterine device
IUI	Intrauterine insemination
IVF	*in-vitro* fertilization
LH	Luteinizing hormone
MA	Medical assistants
MAR	Medically assisted reproduction
NASA	National Aeronautics and Space Administration
NPS	Net promoter score
OB-GYN	Obstetrician-gynecologist
OHSS	Ovarian hyperstimulation syndrome
OS	Ovarian stimulation
OS-IUI	Ovarian stimulation-intrauterine insemination
PCOS	Polycystic ovary syndrome
PGT	Preimplantation genetic treatment
PID	Pelvic inflammatory disease
PPD	Postpartum depression
QR	Quick response (QR code)

REI	Reproductive endocrinologist
RHM	Remote health monitoring
ROI	Return on investment
RPM	Remote patient monitoring
STI	Sexually transmitted infection
TRL	Technology readiness level
US(A)	United States (of America)
vs.	Versus
WHO	World Health Organization
ZIFT	Zygote intrafallopian transfer

Chapter 1

Introduction

Infertility is estimated to affect approximately one in every six people of reproductive age, or around 17.5% of the adult population globally, according to the estimates that the World Health Organization (WHO) published in 2022 [1].

In general, the medical term “infertility” is defined as a disease or condition of the male or female reproductive system characterized by the failure to achieve a pregnancy after 12 months or more of regular unprotected sexual intercourse when the female partner is under 35 years old and after six months when the female partner is 35 years of age or older [2]. Many individuals may not even be aware of their infertility until they attempt to conceive, which can lead to significant emotional distress upon discovering fertility issues. The journey to parenthood is often fraught with challenges and setbacks, intensifying feelings of frustration and inadequacy for many couples.

For individuals or couples desiring to conceive, access to fertility services is a tremendous barrier in getting timely information for diagnosis and treatment of the disease. The accessibility issue is hypothesized to be an indirect causal effect of the lack of personal health information available throughout the various stages of the reproductive process leading to conception. The limited access to health information regarding fertility exacerbates the issue of frustration when the desired outcome is not achieved.

Furthermore, numerous fertility services were delayed during the outbreak of the novel coronavirus disease 2019 (COVID-19) pandemic to alleviate pressures and burdens on the healthcare system. In certain instances, virtual consultations augmented and replaced some fertility care, especially for postpartum individuals who faced a heightened risk of hypertension from the infection [3].

The promise of telemedicine via remote patient monitoring (RPM) presents an innovative approach to addressing the challenges and barriers associated with infertility. RPM can significantly enhance the accessibility and efficiency of fertility services, providing continuous and comprehensive health monitoring directly to patients, irrespective of their

geographic location or mobility.

RPM systems utilize devices like wearable and standalone sensors and smartphone applications to collect vital health data in real time. For individuals facing infertility, these technologies can monitor crucial reproductive health metrics, including menstrual cycle patterns, hormonal fluctuations, and other physiological data relevant to fertility. Leveraging RPM technologies enables regular communication with healthcare providers, allowing for the early detection of potential issues that might affect a person's ability to conceive and deliver timely medical interventions to achieve a positive fertility outcome.

Furthermore, RPM empowers patients by giving them access to their health information, which can enhance their understanding of their reproductive health and foster greater involvement in their treatment processes. This increased patient engagement is crucial in fertility treatments, where the complexity of care can lead to emotional strain and fatigue.

The integration of RPM into fertility care holds the potential to transform how services are delivered, making them more accessible, efficient, and patient-centered. This technology could lead to better health outcomes, reduced healthcare costs, and an overall improvement in the quality of care for individuals struggling with infertility.

While digital health continues to be invaluable in keeping patients connected with their care teams, the adoption and implementation of remote patient monitoring in fertility care are not widespread, and evidence is still limited.

Note: In this work, patients desiring pregnancy who were assigned female at birth (AFAB) are referred to as "women" or "female." The author acknowledges these terms might not fully represent the gender identities of many individuals.

1.1 Research Questions

This thesis aims to explore the current landscape of infertility, evaluate current practices for addressing the issue, and assess the potential for integrating remote patient monitoring for fertility applications.

To effectively address the overarching problem at hand, this work seeks to answer the following research questions:

a. What are the prevalent causes of infertility, and how are they diagnosed using

current medical practices?

b. What are the barriers to accessing fertility treatments, and how might RPM systems mitigate these barriers?
c. How can RPM technology be incorporated into existing fertility protocols, and what are the potential benefits and drawbacks?
d. What are the technological and clinical challenges in developing RPM devices that track fertility-related metrics accurately?

1.2 Research Methodologies

The thesis undertakes a comprehensive literature review to map out the landscape of infertility, focusing on its causes, current treatments, and the technologies used in its management. It delves into various sources to construct a well-rounded view of infertility, detailing the biological, psychological, and social factors that contribute to it.

In addition to the literature review, the research includes interviews with key stakeholders in the fertility field—focusing on patients and healthcare providers. These interviews are essential for acquiring direct insights into the real-world challenges and gaps in current fertility treatments. The perspectives obtained from these discussions enrich the understanding of both obstacles and aid in existing fertility practices, helping to define the specific needs of these stakeholders better.

The thesis employs various system architecture principles to comprehensively analyze both primary data (from interviews) and secondary data (from literature). This analytical approach aids in identifying the functional requirements and potential constraints in designing an effective remote patient monitoring system for fertility applications. By integrating system architecture with empirical data, the thesis aims to outline a blueprint for how RPM technology could be designed and implemented to improve the management of fertility treatments.

1.3 Thesis Structure

The research and findings are presented in this thesis as follows:

Chapter 2 offers an overview of the current infertility landscape relevant to this study. It includes a literature review regarding the etiologies, current diagnosis practices, and available technologies available for treatment. This chapter also introduces and

defines the concept of the fertility journey that delineates the boundary of care discussed in this thesis.

Chapter 3 describes remote patient monitoring technology and its current applications. Additionally, a systematic breakdown is provided to define critical components and functions of the system.

Chapter 4 evaluates the concept of remote patient monitoring within the context of fertility. This chapter conducts a comprehensive analysis of a fertility RPM system, emphasizing stakeholders, their requirements, and architectural considerations crucial for system design.

Chapter 5 examines the current devices and technologies available for fertility testing and their readiness for fertility RPM implementation. The chapter also provides use-case examples to demonstrate how the system can be used in scenarios inspired by interviews with stakeholders.

Chapter 6 concludes the research, offering insights, recommendations, and suggestions for future studies in the field.

Chapter 2

Understanding Infertility

This chapter provides a comprehensive overview of infertility, its classifications, causes, and approaches to treatment.

2.1 Infertility Definitions and Etiologies

Various definitions of infertility exist between clinical and demographic approaches. The World Health Organization (WHO) and the International Committee for Monitoring Assisted Reproductive Technology (ICMART) define *infertility* as a disease or condition of the male or female reproductive system characterized by the failure to achieve a pregnancy after 12 months or more of regular unprotected sexual intercourse when the female partner is under 35 years old and after six months when the female partner is 35 years of age or older [4]. Demographers, or population specialists, generally align more closely with the public definition and refer to infertility as the condition where birth, rather than conception, is not achieved [5]. In the context of this thesis, the clinical definition of infertility is utilized.

Globally, infertility is estimated to affect approximately one in six individuals of reproductive age, corresponding to about 17.5% of the adult population [1]. The WHO classifies the condition as a disease that can impact both male and female reproductive systems.

Additionally, infertility is associated with impaired fecundity, but the two factors are distinguished measures for fertility problems. While infertility focuses on the difficulty of conception, *impaired fecundity* is defined as the physical difficulty in getting pregnant or carrying a pregnancy to term [6].

Infertility is classified into primary and secondary infertility. The primary categorization applies to infertility cases where an individual has never achieved the ability to conceive or carry a pregnancy to term. In contrast, secondary infertility occurs in individuals who have previously conceived and carried a pregnancy to term but have difficulties conceiving

again [7]. The prevalence of primary and secondary infertility has been reported to differ between different regions, but global prevalence is estimated to be between 0.6-3.4% and 8.7-32.6%, respectively [8].

The etiologies of infertility can be attributed to different factors, including lifestyle, genetics, and other pre-existing conditions. Primary infertility commonly arises from the latter two factors that prevent conception from occurring. Generally, these causes are dysfunctions or abnormalities that affect reproductive functions. Common infertility causes in female reproductive systems may include [2]:

- Ovulatory disorders, such as polycystic ovary syndrome (PCOS)
- Pelvic infections, such as pelvic inflammatory disease or PID (infection of female reproductive organs)
- Tubal abnormalities, such as fallopian tube blockages or structural defects
- Uterine abnormalities, such as endometriosis, septate uterus, or uterine fibroids or polyps
- Reproductive hormones or endocrine system imbalance, such as hypothalamus and pituitary gland disorders
- Genetic disorders, such as chromosomal abnormalities or single gene mutations, that impact the proper development of reproductive systems.

Infertility in males may be caused by similar disorders but specific to the male reproductive system and involves sperm-related issues. These factors include:

- Obstructions in the reproductive tract, including tubal blockages that prevent sperm motility
- Abnormal sperm morphology
- Reproductive hormone imbalance, particularly issues with testosterone regulation for sperm production or disorders of the hypothalamus and pituitary glands.

Secondary infertility slightly differs from the etiologies of primary infertility due to age-related and lifestyle factors that impact reproductive health. Secondary infertility tends to be attributed to multiple factors:

- Females over 35 years old tend to be at higher risk of secondary infertility due to a decrease in ovarian reserves and egg quality [9]
- Males over 50 years tend to produce lower semen quality [10]
- Complications from a previous pregnancy or surgery, including abdominal or pelvic

surgeries or unsafe abortions [11]
- Lifestyle factors, including medications, alcohol consumption, body weight increase, and less active lifestyle that impact the body's ability to produce reproductive hormones
- Sexually transmitted infections (STIs), which may lead to tubal disorders or PID.

In addition to the medical conditions outlined above, individuals diagnosed with other underlying adverse health conditions, including cancer, diabetes, thyroid disease, and autoimmune diseases, tend to have a higher risk of infertility. Aggressive treatments, including chemotherapy, radiation, and certain surgeries, can also damage reproductive organs, further increasing the likelihood of infertility [12].

While many causes of infertility are identifiable, there are cases where the underlying cause remains unknown. It is estimated that about 30% of couples seeking fertility evaluations and treatments are diagnosed with unexplained infertility [13].

2.1.1 Recognition as a disease

Despite the prevalence of infertility in many couples, the designation of infertility as a disease is a topic of debate among health organizations and critics from societal and philosophical groups. The debate sparks several healthcare policy implications, including funding for research, treatments, and insurance coverage. One of the primary considerations for determining the disease status of infertility is the complexity of etiology, which is often associated with numerous conditions. Some of these conditions are categorized as diseases independently, while others are not. For example, pelvic inflammatory disease (PID) is an infection often caused by STIs that lead to damage to female reproductive organs and cause infertility. PID is considered a disease and is usually covered by most insurance for treatment. On the contrary, medical coverage for fertility treatment due to advanced age, weight issues, or environmental factors that can impact hormone levels is much more complex to determine medical necessity.

The American Society for Reproductive Medicine (ASRM) aligns with the WHO's definition and recognition of infertility as a disease [14] and continues to advocate for addressing infertility as a public health priority.

2.1.2 Emotional impact

For many couples, the path to pregnancy can bring emotional distress, especially when

confronted with the consequences and impact of the inability to conceive. While medications and assistive reproductive technologies are available, access to these treatments is limited by other socio-economic factors. The stigma of infertility and failure to conceive is even more significant for the female partner due to cultural norms and perpetuated societal views tied to traditional child-rearing and work pressures [15]. Hence, the impact of infertility goes beyond physical distress but also psychological, which leads to a decreased quality of life [16].

When infertility is treated and results in pregnancy, the emotional challenges may persist even after the baby is born as the woman adjusts to motherhood. The childbirth experience often brings intense emotions of joy, excitement, and love for the newborn. However, these feelings can be mixed with anxiety, sadness, and uncertainty. Factors like hormonal changes, lack of sleep, physical discomfort, and the demands of newborn care can contribute to postpartum mood disorders, including depression and anxiety. It is estimated that 1 in 7 mothers develop postpartum depression (PPD) [17], which can last anywhere from weeks to years [18].

2.2 Current Approach to Infertility Diagnosis

The American College of Obstetricians and Gynecologists (ACOG) and the American Society for Reproductive Medicine (ASRM) recommend an infertility evaluation for individuals desiring to have children but having difficulty with achieving pregnancy after 12 months of unprotected intercourse. For women over 35, an expedited evaluation is recommended after just six months, while those over 40 are advised to seek immediate evaluation without the waiting period [19]. Obstetrician-gynecologists (OB-GYNs) often serve as the first point of contact for females seeking fertility evaluations. Other healthcare specialists, including reproductive endocrinologists, infertility specialists, and male reproductive specialists, may be referred during the initial consultations.

A typical infertility evaluation or workup includes obtaining a medical history from the individual with or without their partner, a physical examination, and any additional fertility tests deemed necessary by the healthcare professional.

Medical History. For females, information about menstrual history, coital frequency, methods of contraception, and other relevant factors are captured during the infertility evaluation. History with previous surgeries, illnesses, infections, and genetic and familial infertility predispositions are also typically reviewed. For males assigned at birth (AMAB), lifestyle factors (e.g., smoking, alcohol, and drug use) are considered in addition

to family history, surgeries, and pre-existing health issues [19].

Physical Examination. A physical pelvic exam is considered a standard procedure to inspect the state of reproductive organs, focusing on the presence of inflammations, infections, or masses that may exist. A manual examination to palpate the size, shape, and position of the uterus and ovaries is also routinely performed for females to check for any masses, tenderness, or pain that could indicate conditions affecting fertility, such as endometriosis, fibroids, or ovarian cysts. Genital inspection of the penis, scrotum, and testicles may be performed on male partners to assess for similar symptoms [19].

Additional diagnostics. Results from medical history and physical exams may recommend laboratory and medical imaging to complement the evaluation.

For females, hormonal tests to measure levels of reproductive markers include:

- Follicle-stimulating hormone (FSH): a hormone that regulates the production and maturation of eggs in the ovaries
- Luteinizing hormone (LH): a hormone produced by the pituitary gland that triggers ovulation
- Anti-Mullerian hormone (AMH): a hormone produced by the follicles in the ovaries that is typically correlated with egg count. Females who have reached menopause do not secret AMH and indicate lower egg yield
- Estradiol: a primary hormone in the estrogen group responsible for ovarian function
- Progesterone: produced in the ovaries during ovulation to help prepare the uterus for egg fertilization. Some females do not release an egg every cycle; a rise in progesterone confirms ovulation.
- Prolactin: a hormone that inhibits the secretion of FSH. High levels of prolactin interfere with ovulation and may prevent proper egg production.

Testosterone imbalance, low or high, can indicate some fertility issues in males. FSH levels may also be measured as the hormone regulates the production and transportation of sperm, indirectly measuring sperm count. In addition to count and concentration, sperm may be examined for motility and morphology to gain insight into male fertility status. **Figure 1** illustrates the various hormones working in concert to regulate reproductive functions.

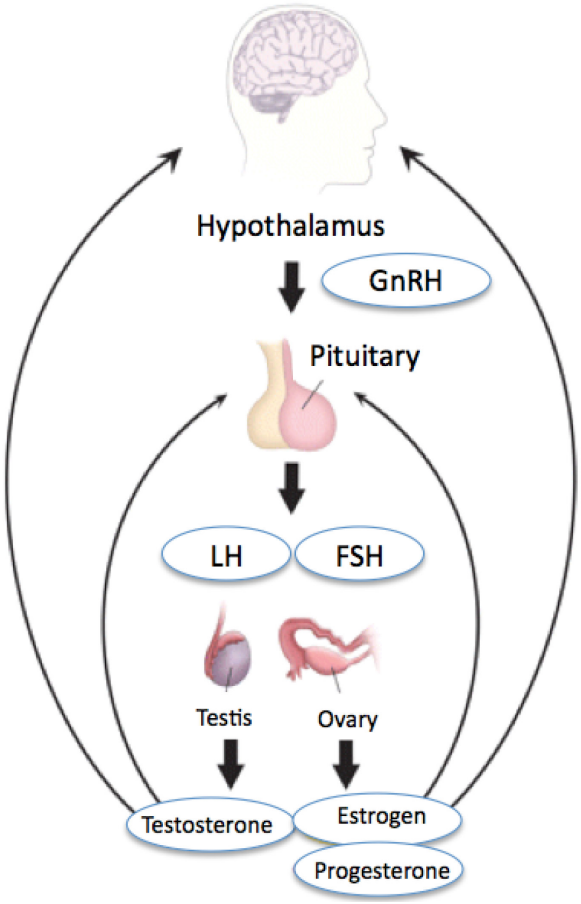

Figure 1. Hypothalamic-pituitary-gonadal axis [20]

Physical examination may be complemented with medical imaging via ultrasound or X-ray. Transvaginal ultrasound is used to visualize the ovaries, uterus, and other female reproductive organs for the presence of cysts, fibroids, and other physical abnormalities that could impact fertility. Scrotal and transrectal imaging may be ordered for males to evaluate the physical condition of the scrotum and testicles that affect sperm production and ejaculation.

2.3 Infertility Treatment and Reproductive Medicine

When infertility is suspected or when primary evaluation leads to a diagnosis of infertility for either the male or female partner, infertility services may be offered as an option for treatment. Medically assisted reproduction (MAR) may be through pharmacological interventions, surgery, or assistive reproductive therapy and is generally determined based on infertility etiology, age of the female partner, insurance coverage, and patient gender. The most common type of treatment options currently available include ovulation induction, assistance via timed intercourse, artificial insemination, and *in vitro*

fertilization (IVF).

2.3.1. Fertility Medications and Timed Intercourse [2], [21], [22]

Pharmacological treatments primarily target ovulatory dysfunctions, which constitute a significant portion of female infertility cases. These medications are often the first-line therapy for females with anovulation or ovulatory disorders. Clomiphene Citrate is an example of a commonly used oral medication that impacts the balance of vital reproductive hormones, GnRH, FSH, and LH, which are responsible for promoting ovarian follicular growth. Other ovarian stimulation medications include aromatase inhibitors, gonadotropins, and different combinations of these agents, all sharing the same goal of hormone balancing for proper follicular development and ovulation functions. Proper medication should be selected based on the evaluation with healthcare providers and the cause of anovulation.

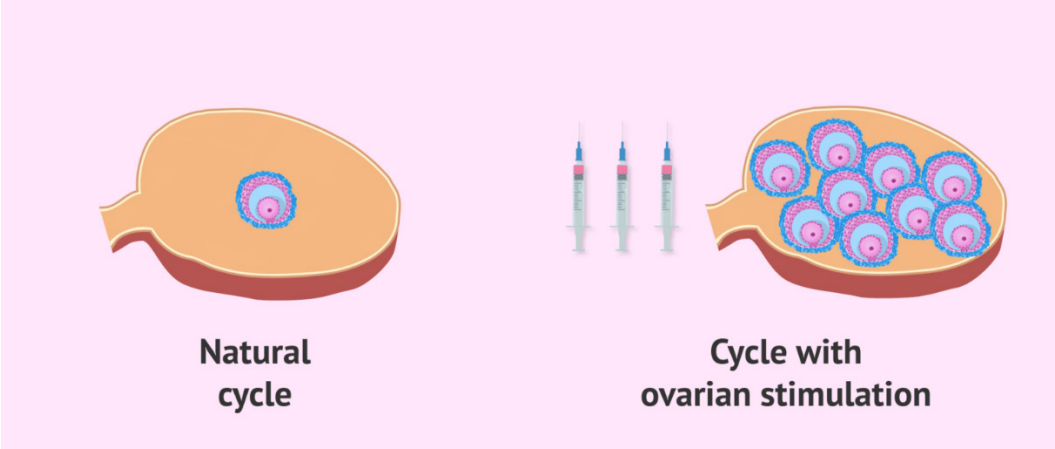

Figure 2. Representation of a typical vs. stimulated ovary with ovarian stimulation [23]

Stimulation and induction treatments of the ovaries bear the risk of multiple gestations and the potential for ovarian hyperstimulation syndrome (OHSS). The condition occurs in approximately 1.4% of females [24] receiving ovarian induction and can be life-threatening, requiring hospitalization [25]. Therefore, it is crucial to meticulously assess the risks associated with these treatments and closely monitor how patients react to the medications being administered.

It is also important to note that limitations exist with pharmacological treatment. Females with known limited ovarian reserve or low egg count due to age, hormone imbalances, genetic abnormalities, or other environmental or medical factors may not significantly benefit from ovarian stimulation. Alternative treatments suitable for their conditions

should be explored [26].

Timed intercourse is often recommended alongside ovulation induction, leveraging the natural window of fertility and precise timing of ovulation to enhance the likelihood of conception. This approach relies heavily on accurate ovulation prediction and may be less effective for couples with non-ovulatory infertility factors.

2.3.2. Artificial Insemination

Artificial insemination serves as a bridge between pharmacological treatment and more invasive reproductive technologies. Two primary artificial insemination approaches are intrauterine insemination (IUI) and intracervical insemination (ICI), with the main difference being the location of insemination, either directly into the female's uterus or cervix, respectively (refer to **Figure 3**). Artificial insemination is particularly suitable for couples with unexplained infertility, mild endometriosis, or minor male factor infertility. This approach may also be used for females receiving donor sperm in cases of poor sperm quality, same-sex relationships, or females without male partners. Pregnancy rates for ICI and IUI range between 37.8% to 40.5% after six treatments [27]; however, ICI is considered more straightforward and a lower-risk procedure than IUI as the latter involves placing washed versus unwashed sperm [28]. The procedures place the concentrated sperm directly into the cervix or uterus through a catheter, thereby reducing the travel distance to the fallopian tubes where fertilization occurs. This direct approach can circumvent issues like hostile cervical mucus or slight motility problems in sperm and increases pregnancy rates from 33% to 51% compared to those not receiving active treatment [29]. Despite its advantages and relative simplicity, the success rates of IUI can be influenced by factors such as the female partner's age and the underlying cause of infertility, making it less effective for more severe infertility issues.

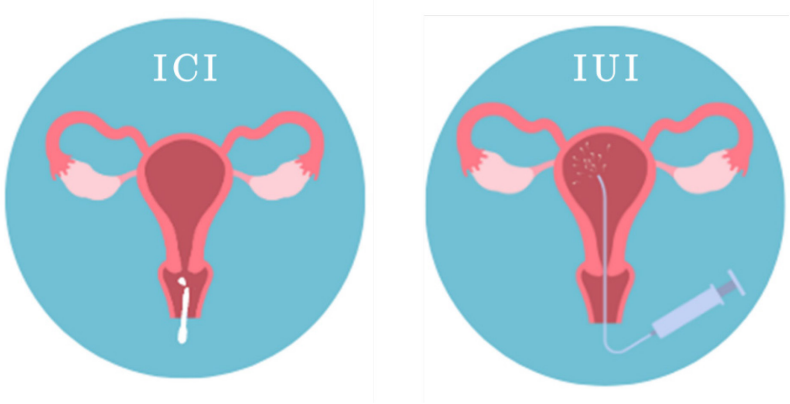

Figure 3. IUI vs. ICI sperm deposition.
This diagram illustrates the differences in sperm deposition techniques between Intracervical Insemination (ICI) and Intrauterine Insemination (IUI). In ICI, sperm is deposited at the cervix, whereas in IUI, sperm is directly injected into the uterus, closer to the fallopian tubes, enhancing the chances of fertilization. Adapted from [30]

Combining ovulation stimulation or other ovulatory medications with artificial insemination increases live birth rates in couples with unexplained infertility [31]. Successful artificial insemination is highly dependent on the timing of the procedure and must be carried out during the ovulatory period of the female patient. Ovulation tracking using hormone measurements for FSH, AMH, and LH indicates the correct timing that highly influences the procedure's outcome.

Medications and timed intercourse tend to be considered less invasive than other forms of treatment. The ASRM recommends 3 or 4 cycles of ovarian stimulation and artificial insemination before proceeding with more invasive assisted reproductive procedures [32].

2.3.3. Assisted Reproductive Technology (ART)

The Centers for Disease Control (CDC) defines *Assisted Reproductive Technology* as any fertility-related interventions or procedures that handle eggs or embryos. By this definition, IUI and ICI are not considered ART techniques. The CDC 2021 Fertility Clinic Success Rates report that 238,126 patients received ART treatments (40% from egg or embryo banks) over multiple cycles, resulting in over 91,000 live births. Additionally, it is estimated that approximately 2.3% of all infants born in the United States are conceived using ART [33].

The most common ART procedure is *in-vitro* fertilization (IVF), which involves fertilizing extracted eggs outside the body in a laboratory setting [34]. The resulting one (or more) embryo is transferred into the female uterus to establish pregnancy. This approach is

particularly beneficial for severe infertility cases, including tubal factor infertility, severe male factor infertility, and older maternal age. IVF also allows for surrogacy or partners at risk of passing on a genetic disorder to screen embryos through preimplantation genetic treatment (PGT) or for individuals with underlying health conditions (e.g., cancer) with exposure to radiation or chemotherapy treatments. Despite its higher success rates, IVF is also the most invasive and costly option, with considerations such as the emotional and physical toll on patients and the ethical implications of such advanced reproductive technologies. **Figure 4** and **Figure 5** provide estimated costs for fertility treatments, including IUI and IVF.

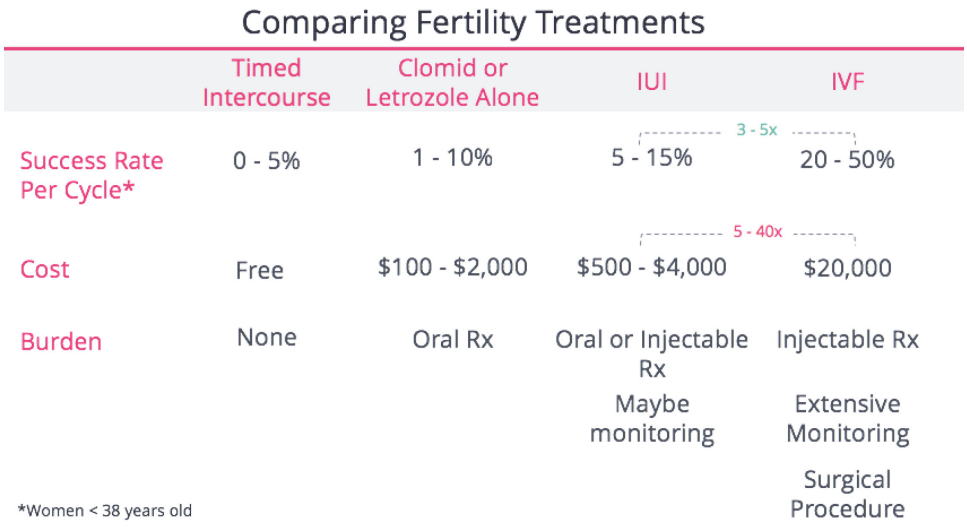

Figure 4. Fertility treatment costs comparisons [35]

Itemized IVF Costs by U.S. City and Region

	SF	LA	NYC	NJ	Chicago	Boston	Seattle	Atlanta
IVF	$12,246	$13,325	$9,705	$10,866	$11,666	$8,267	$12,450	$11,363
Medication	$5,000	$5,000	$5,000	$5,000	$5,000	$5,000	$5,000	$5,000
Consultation	$410	$320	$408	$408	$438	$352	$312	$282
ICSI	$1,891	$1,763	$2,500	$1,725	$1,750	$1,280	$900	$1,687
PGT-A	$5,202	$5,475	$5,881	$5,000	$5,425	$5,111	$4,700	$4,800
Total	$24,749	$25,883	$23,494	$22,999	$24,279	$20,010	$23,362	$23,132

Figure 5. IVF costs by U.S. city and region [35]

Variations to IVF have also been developed to address specific challenges and optimize the success of fertility treatment. Intracytoplasmic sperm injection (ICSI) has emerged as a vital adjunct to IVF, particularly in cases of male infertility, where a single sperm is directly injected into an egg to facilitate fertilization [22], [36]. In contrast to conventional IVF, where the sperm penetrates the egg naturally, the sperm is directly inserted and bypasses natural fertilization in cases of ICSI intervention. This approach overcomes low sperm count, poor sperm motility, or abnormal sperm morphology.

Furthermore, techniques such as gamete intrafallopian transfer (GIFT) and zygote intrafallopian transfer (ZIFT) offer alternative approaches to optimize the natural fertilization process within the fallopian tubes. These techniques mimic the natural fertilization process and early embryo development more closely [37]. GIFT involves transferring eggs and sperm into the fallopian tubes, where fertilization occurs naturally. However, ZIFT involves transferring fertilized embryos into the fallopian tubes at the zygote (fertilized egg) stage [38]. These methods are particularly beneficial for patients with patent fallopian tubes and can offer higher success rates compared to traditional IVF [39].

Regardless of the technique performed, the process of IVF is complex and involves a multi-step procedure to prepare the female body for egg retrieval and receiving the embryo. The risk, complexity, cost, and invasive nature of this procedure excludes IVF as the recommended first-line of infertility treatment, except for critical factors such as maternal

age and preferences.

The IVF journey begins with ovarian stimulation using a series of fertility medications to induce the development of multiple ovarian follicles. This pharmacological intervention, typically administered as injectables, is tailored to each individual, with dosages adjusted based on factors like age, ovarian reserve, and previous responses to fertility drugs. The aim is to produce a cohort of oocytes, thereby maximizing the number of mature eggs retrieved during the egg retrieval process. Additionally, birth control or estrogen may be prescribed before stimulation to synchronize follicle development and allow healthcare providers to control the timing of follicle growth and coordinate it with the maturation of eggs within the ovaries.

Once the eggs are mature, they are extracted directly from the ovaries through an invasive process involving an ultrasound-guided needle and aspiration of follicular fluids. The retrieved eggs are then exposed to sperm in a controlled laboratory environment, facilitating fertilization. The sperm may be introduced through conventional IVF, where multiple sperm are placed with the oocyte in culture media or directly injected via ICSI. Post-fertilization, the embryos are cultured in the laboratory for a period ranging from 3 to 5 days, during which time they are closely monitored for growth and development. This stage is crucial for selecting the most viable embryos for transfer, with the option of employing genetic abnormality screening (i.e., PGT).

In some cases, IVF can result in multiple embryos and recommendations for embryo cryopreservation (freezing embryos) may be considered, especially for future family planning. This technique also minimizes the IVF cycle repetition, which can be costly and invasive, and avoids risks of OHSS, which is higher after IVF than ovarian induction alone [24]. Cryopreservation is often an option adopted by individuals undergoing medical treatments that impact fertility, such as cancer radiotherapy or hormone therapy [40].

The final step in the IVF process is the transfer of embryos into the uterus. This procedure is typically performed using a catheter inserted through the cervix under ultrasound guidance, ensuring precise placement of the embryos within the uterine cavity. The number of embryos transferred is carefully considered, balancing the desire for a successful pregnancy against the risks of multiple gestations. Post-transfer, patients usually continue with progesterone support to enhance the uterine lining and promote implantation.

In comparing these treatments, the choice of intervention must be tailored to the specific causes of infertility and the circumstances faced by individuals or couples. Ovulation

induction and timed intercourse offer less invasive options for ovulatory disorders, while IUI provides a middle ground for cases where direct sperm placement may overcome the barriers to fertilization. IVF, with its broad applicability and high success rates, remains the definitive treatment for more challenging infertility diagnoses, albeit with significant financial, emotional, and ethical considerations.

2.4 The Fertility Journey

As infertility diagnosis can occur not only to individuals who have never achieved a pregnancy previously but also to those who may have had a successful pregnancy before, it is essential to consider fertility in the entire landscape from preconception to postpartum. This "fertility journey," as referred to in this thesis, represents the process that an individual of reproductive age goes through, starting from desiring to have children to achieving pregnancy and motherhood, either through natural or assisted efforts.

To discuss the fertility journey, one can consider a map (**Figure 6**) that consists of four stages: preconception, conception, pregnancy, and postpartum.

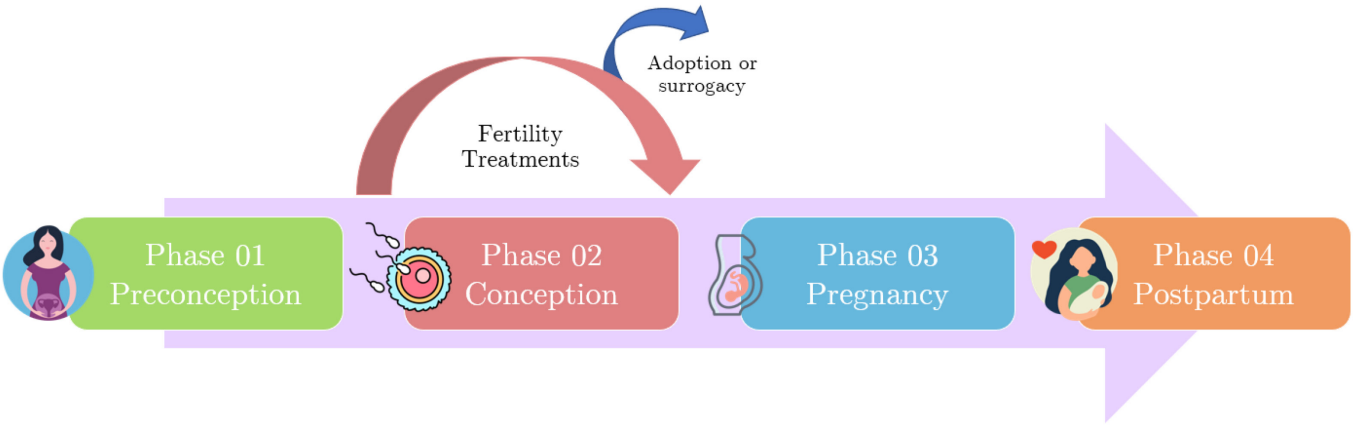

Figure 6. The fertility journey

Phase 1: Preconception

The preconception phase is typically defined in the context of the female and refers to the reproductive period before the female becomes pregnant. In this context, the male perspective is also considered, emphasizing both partners' health and wellness before conception and increasing pregnancy chances. The preconception stage begins with the decision for family planning, whether for pregnancy prevention or preparing for pregnancy. The scope of this thesis focuses on the latter.

At this stage, females may already know a little about their fertility status, primarily through their menstrual cycles. Females who experience "regular" periods are considered healthy and typically do not suspect any infertility issues. The typical adult menstrual cycle length varies from 21 to 34 days, with an average of 3-7 days of bleeding [41]. Young females who experience cycle irregularity (e.g., lack of menses, bleeding between cycles, or cycles <21 days) or pain during their cycles are generally advised to consult with their primary care physician or ob-gyn and receive guidance for treatments or other therapies. Sixty-five percent of females (aged 15-49 years old) in the United States, regardless of cycle regularity, may seek or receive birth control medication (oral contraceptive pills) or implantable contraception to prevent unintended pregnancy or induce hormone balance [42]. During these consultations, it is not uncommon for females to also receive a physical evaluation or laboratory testing as part of cancer prevention, pap smears, or hormonal treatments.

With the decision to start planning to conceive, the importance of preconception care is emphasized to increase the chances of a healthy pregnancy. Preconception care typically comprises of risk assessment, health promotion, and medical and psychosocial interventions [43]. Specifically, risk assessments involve evaluating the likelihood of successful conception and pregnancy based on the medical history and lifestyle behaviors of both partners, along with physical examinations and laboratory tests that might reveal potential concerns. Preconception care encourages behaviors to achieve a healthy pre-pregnancy weight through nutrition and exercise and receive the necessary immunizations against infections while advising against smoking, alcohol, and substance consumption and exposure to environmental factors that would disrupt the proper function of the endocrine system responsible for hormone production. The overarching goal of preconception care is to identify and address any factors that could affect pregnancy outcomes, focusing on health and lifestyle changes to support reproductive and general well-being.

Phase 2: Conception

Conception is the process where a sperm fertilizes an egg, leading to the formation of a zygote (a fertilized egg). Conception is highly dependent on the timing of this fertilization. This stage of fertility begins with ovulation, the midpoint phase in a female menstrual cycle, when an egg is released from the ovary and travels into the fallopian tube. As the viability of ejaculated sperm can last up to five days, sperm already present in the fallopian tube can fertilize the released egg. If sperm is introduced within 12-24 hours after the egg is released, fertilization and conception can also occur [44].

Upon conception, the fertilized egg or zygote travels to the uterus and divides to create a blastocyst. This cluster of cells then implants onto the lining of the female's uterine wall, where it will continue to develop into the embryo and the placenta. Failure to implant in the uterus will lead to shedding of the fertilized egg and will not lead to pregnancy. In 1.2-1.4% of cases [45], implantation in the wrong location (outside the uterus) may occur and present a complication known as ectopic pregnancy. This condition is life-threatening for the female and requires prompt medical intervention to stop embryonic growth or remove the embryo.

The problem of infertility is most often determined at this stage, where couples desiring pregnancy are unable to conceive successfully, and additional sub-steps within the conception phases are taken to accommodate infertility evaluations and treatments.

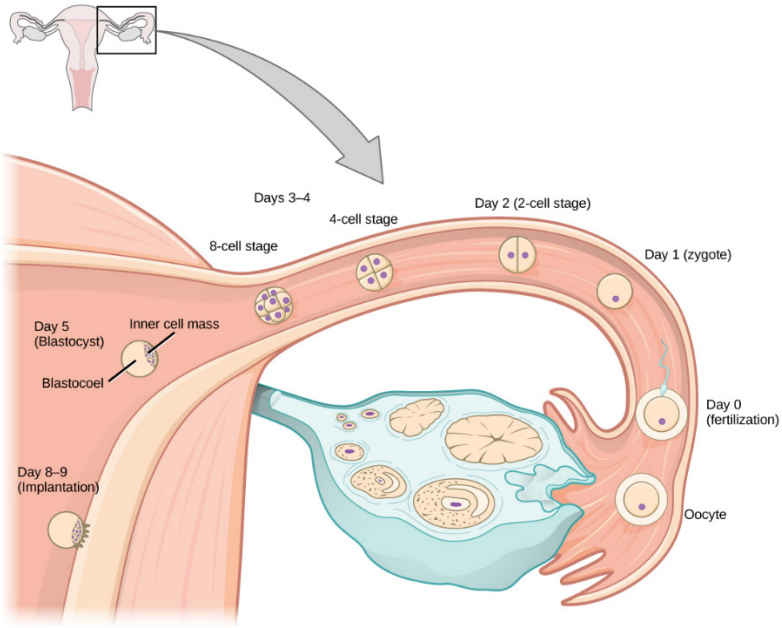

Figure 7. Conception process, from egg fertilization to implantation [46]

Phase 3. Achieving Pregnancy

Pregnancy is established once fertilized egg implantation is complete. Successful blastocyst implantation onto the uterine lining also triggers hormone releases, including hCG, estrogen, and progesterone, that work together to support the establishment and maintenance of pregnancy following implantation. These hormones play a crucial role in creating a favorable environment for the developing embryo and fetus and regulate various physiological changes in the mother's body to support pregnancy. The embryonic period concludes after week nine post-conception, marking the end of the first trimester of

pregnancy and the beginning of the fetal stage [47]. This transition from an embryo to a fetus marks a shift in the developmental milestone; it is considered a center of debate for ethical and legal implications regarding the onset of human life.

The fetus goes through a significant growth stage for the remainder of the pregnancy. The second trimester of fetal development involves the differentiation of organs, and fetal movements become more pronounced as the muscular and nervous systems mature. Maternal estrogen and progesterone levels continue to rise [48]. Fetal brain development extends into the third trimester, along with lung maturation. At this stage of pregnancy, increased levels of oxytocin increase to prepare the mother for labor and childbirth.

Phase 4. Postpartum

Colloquially referred to as the "fourth trimester," the postpartum phase begins after the delivery of the baby and lasts up to six to eight weeks. Most commonly, postpartum is associated with postpartum depression, but this phase of the journey encompasses far more than the emotional and mental health. During this time, the mother's body undergoes physical changes to return to its pre-pregnant state.

Physiologically, the postpartum period involves expulsing leftover placental tissue, initiating lactation, dramatic hormone shifts, and gradual weight loss [49] [50]. The uterus shrinks back to its original size through a process known as involution, helping to expel any remaining placental fragments and minimize the risk of postpartum hemorrhage. Mothers also experience vaginal discharge called lochia, which consists of blood, mucus, and uterine tissue, for several weeks following childbirth. Additionally, the breasts prepare for breastfeeding, becoming larger, swollen, and tender as they produce milk. Hormone levels, especially estrogen and progesterone, fluctuate significantly during this period. The timing of the first menstrual period after delivery can vary, influenced by breastfeeding and the normalization of reproductive hormones.

This postpartum period is a critical time for maternal and newborn health, with most maternal and newborn deaths occurring during these weeks. Mothers may face complications such as hemorrhage, sepsis, hypertension, and diabetes, highlighting the importance of medical care and monitoring during the postpartum phase.

Deviations to the Fertility Journey

Deviations and interventions due to infertility issues may occur at any time during these stages in the fertility journey. While infertility treatments exist, generally involving medications or ART therapies, some outcomes do not include successful pregnancy and

childbirth. In such cases, alternative options to build families may be explored, including surrogacy and adoption.

2.5 Addressing Infertility

The CDC developed a public health plan focusing on three strategies to promote healthy outcomes and address the concerns associated with the rise in infertility. The plan, known as the National Public Health Action Plan for the Detection, Prevention, and Management of Infertility [6], highlights three strategies for collaboration between key stakeholders from academia, healthcare community, organizations, and federal agencies:

1. Promoting healthy behaviors that can help maintain and preserve fertility.
2. Promoting prevention, early detection, and treatment of medical conditions that can threaten fertility.
3. Reducing exposures to environmental, occupational, infectious, and iatrogenic agents that can threaten fertility.

This thesis focuses on addressing infertility through the second strategy, targeting the detection and treatment of infertility. With the complexity of infertility workup that has been explored and summarized in the previous chapter, management of relevant clinical information regarding fertility requires timeliness and accessibility to support individuals and healthcare professionals with making informed medical decisions regarding fertility health, regardless of where they are in their fertility journey.

2.5.1 Timing

The importance of timing is rooted in the biological constraints of human reproduction and the progressive nature of many conditions affecting fertility. The term "biological clock" extends beyond the female reproductive years but also refers to the time orchestration of biological processes required to achieve pregnancy. By prioritizing timely interventions, healthcare providers can significantly enhance fertility outcomes for individuals and couples.

Fertility Window. The timing of the menstrual cycle is crucial for understanding fertility, as it dictates the brief window during which conception is possible. The cycle is characterized by distinct phases, each integral to preparing the body for ovulation and potential pregnancy.

The cycle starts with the menstruation phase, during which the uterine lining is shed—evidenced by menstrual bleeding—if the egg from the previous cycle was not fertilized. This phase typically lasts 3 to 7 days, followed by the proliferative phase. During the proliferative phase, FSH is secreted to stimulate the development of follicles to house the oocytes. Of these, usually one follicle will mature fully into an egg. Concurrently, estrogen produced by the follicles rises as the follicles mature, preparing the uterine lining for implantation.

The end of the proliferative phase marks the midpoint of the menstrual cycle and when ovulation occurs. Peak estrogen levels cause a surge in LH and lead to the release of a mature egg from one of the ovarian follicles. This released egg is available for fertilization for about 12-24 hours, indicating the fertility window. However, since sperm viability in the female reproductive tract can last up to five days, the overall fertile window extends from about five days before ovulation to one day after [51], [52]. Despite the precise fertile windows delineated in clinical guidelines, only about 30% align with the specified days [52]. As a result, hormone tracking can provide more accurate predictions of the true fertile window.

The second half of the menstrual cycle is the luteal or secretory phase, dominated by LH and progesterone to prepare the uterine lining for potential implantation of a fertilized egg. If fertilization does not occur, hormone levels decline, leading to the shedding of the uterine lining and the start of a new menstrual cycle.

Understanding the timing of these phases is essential for those trying to conceive, as it highlights the limited fertile window and the importance of timing intercourse or insemination accordingly to increase the chances of successful conception.

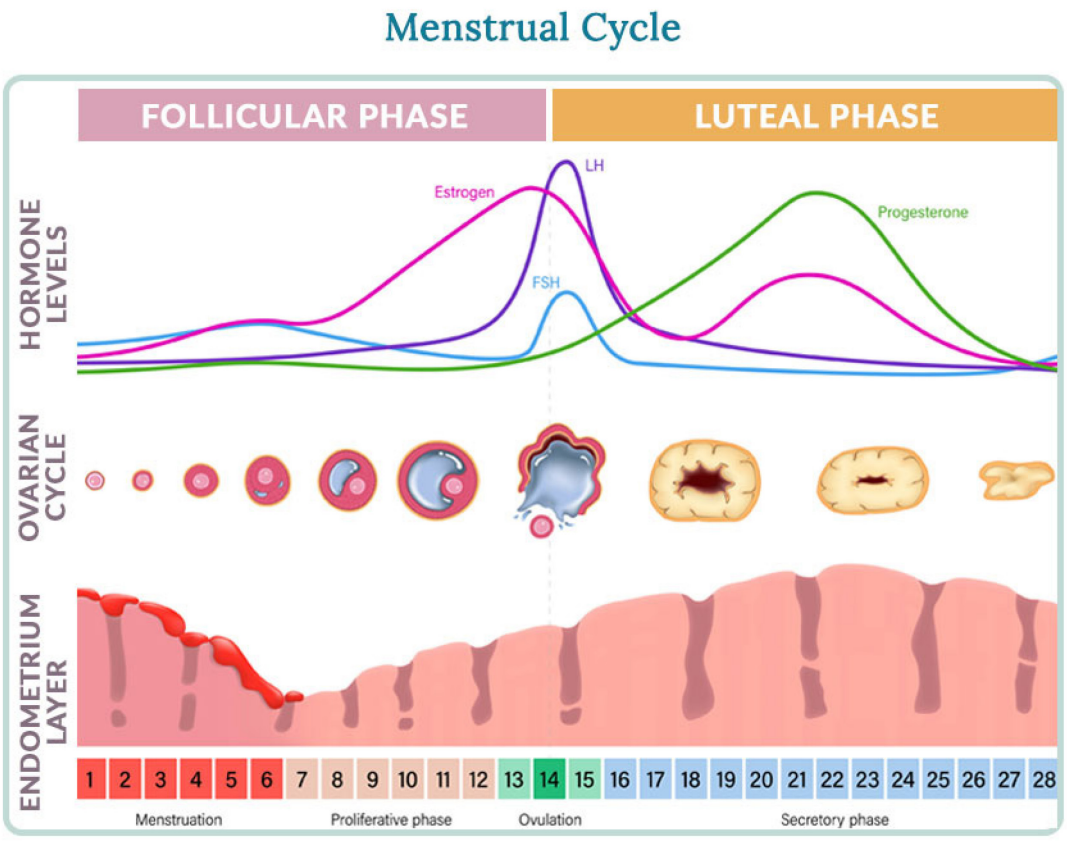

Figure 8. Phases and hormone levels of the menstrual cycle [53]

Treatments. Additionally, early detection of fertility-threatening conditions can vastly improve the prognosis for fertility preservation. Conditions such as PCOS, endometriosis, and certain sexually transmitted infections (STIs) can lead to reduced fertility if not promptly identified and managed [54]. Furthermore, early detection of cancer and prompt fertility preservation measures can be pivotal for individuals of reproductive age diagnosed with cancer.

Most diagnostic tests are dependent on menstrual cycles, a cyclical nature that is also reflected when it comes to infertility treatment. Infertility services, such as IVF and artificial insemination, have varying success rates significantly influenced by the timing of these procedures, starting from the initial decision to seek treatment to the precise scheduling of each step of the process. For IVF cycles, the timing of medication administration, egg retrieval, and embryo transfer is meticulously scheduled to coincide with the natural cycle and optimize embryo implantation chances.

Before starting IVF treatment, medication is administered to help regulate and predict

the menstrual cycle more accurately. This initial step is crucial as it sets the schedule for the entire IVF process. Ovarian stimulation then follows, lasting about 10-14 days, during which the development of ovarian follicles is closely monitored at 1-3 day intervals using transvaginal ultrasound and hormone level assessments [55]. A strict daily regimen of medications is maintained to ensure optimal follicular development while minimizing the risk of OHSS. When the eggs are ready, a crucial timing element involves the administration of a trigger shot, typically an hCG injection, which is given to finalize the maturation of the eggs. This shot is precisely timed to occur about 34 to 36 hours before the scheduled egg retrieval. This narrow window is critical as it prepares the eggs for fertilization, ensuring they do not ovulate naturally. Finally, the embryo transfer to the uterus is also carefully timed to coincide with the phase of the menstrual cycle when the uterine lining is most receptive to implantation. Accurate hormone testing is vital to determine the optimal timing for this phase, ensuring the best possible conditions for the embryo to implant and develop. **Figure 9** illustrates a representative timeline of the IVF steps; blood work and ultrasounds are conducted regularly from stimulation to ovulation trigger and resume post-embryo transfer.

Similar to artificial insemination, the procedure's success hinges on inseminating during the female's fertile window, just before or during ovulation, to maximize the chances of sperm meeting the ovum. Misalignment in the timing of either procedure can significantly reduce the likelihood of a successful pregnancy.

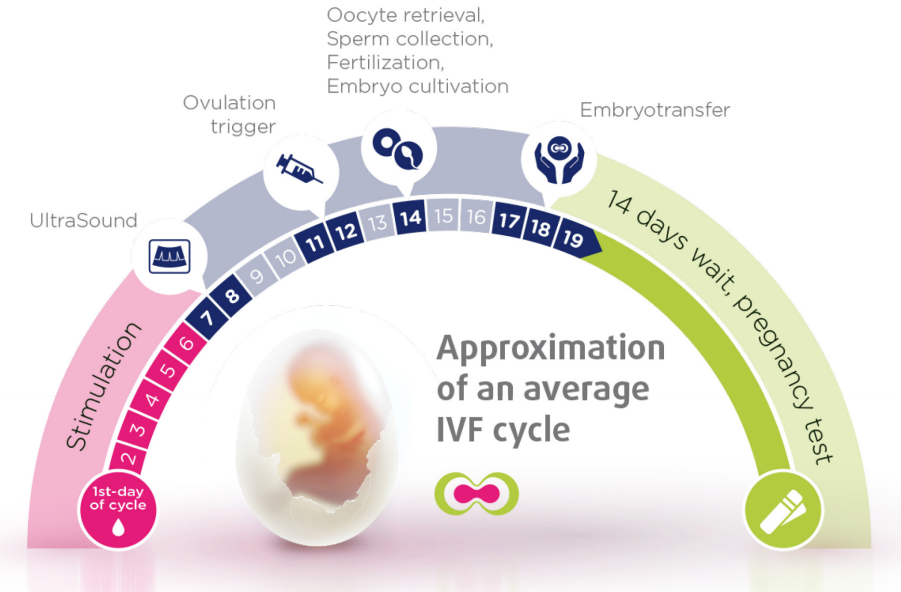

Figure 9. Average timeline of an IVF cycle [56]

Pregnancy and postpartum interventions. Collecting data on blood pressure, blood sugar levels, fetal heart rate, and other vital parameters at the correct times is crucial for the early detection of issues that could affect the health of both the mother and the developing fetus. Monitoring these indicators is critical to identifying and managing conditions like preeclampsia or gestational diabetes early on. Timely intervention can help prevent complications, leading to safer pregnancies and deliveries. Pregnancies affected by hypertension or diabetes are categorized as high-risk and necessitate more frequent monitoring to facilitate rapid adjustments and responses.

After childbirth, it remains critical to maintain timely care as the mother begins her recovery. Monitoring for hypertension, depression, and infections during this period is essential to ensure proper recover. Timely identification and management of these conditions help provide the necessary support and make necessary adjustments during the recovery process.

2.5.2 Accessibility

Ensuring broad and equitable access to healthcare resources and services is crucial in overcoming barriers to fertility care and improving outcomes for individuals and couples facing infertility challenges. Access to such care significantly increases pregnancy rates; couples receiving fertility treatments like IUI and IVF have seen cumulative pregnancy rates rise to 50%-70% and 35%-60%, respectively, compared to 28% without any treatment [57]. Access to preventive healthcare services, such as regular gynecological and urological exams for early identification, management, and treatment of infertility conditions, is critical to benefit from these treatments. Factors influencing access include the geographical distribution of clinics, cost, and insurance coverage.

Many individuals encounter barriers due to the high cost of treatments (e.g., IUI, ICSI, IVF) and the lack of comprehensive insurance coverage, which is not universally available. While many private insurance plans generally cover diagnostic testing, including blood work, imaging, and other non-invasive tests, coverage for infertility treatments is limited and often not deemed "medically necessary" [58]. As of 2023, only 21 states, plus Washington DC, in the United States have implemented infertility insurance mandates requiring insurance companies to offer coverage for infertility treatments [59]. These mandates detail covered treatments, eligibility criteria, and any limitations or exclusions. The interpretation of these mandates varies and may not apply to specific health plans, such as self-funded plans or Medicaid. State laws can significantly impact the extent of insurance coverage for infertility. Only 15 of the 21 states include treatment coverage for

IVF, and coverage for male infertility evaluations is often excluded (18-27%) [60] despite the need for both sperm and eggs for conception [61]. Even states with laws mandating infertility coverage have varying requirements for services to be received.

Furthermore, access to healthcare during pregnancy and the postpartum periods poses significant challenges, particularly for mothers living in rural or underserved areas. Geographic isolation limits access to regular medical check-ups, which are necessary and increase in frequency as pregnancy advances. Typically, the schedule includes one visit every four weeks for the first 28 weeks, then biweekly visits, and finally, weekly check-ups in the last month of pregnancy [61]. For a healthy pregnancy, this timetable results in around 15 in-person visits, with high-risk pregnancies needing even more monitoring or possible hospitalization. The lack of nearby healthcare facilities often forces pregnant females to either travel long distances for prenatal appointments, which can be both physically taxing and financially burdensome, or forego the visits altogether. As of 2023, such disparities in access to maternal care are leading causes of preterm birth and maternal mortality [62]. Additionally, the scarcity of specialized maternal healthcare providers in these areas can complicate the management of pregnancy-related conditions such as gestational diabetes or hypertension.

In the postpartum period, close monitoring is crucial to identify signs of complications such as infections, postpartum depression, and other health issues that may arise. However, the traditional healthcare model frequently fails to provide adequate support during this essential time, particularly in remote areas where resources and continuous care are scarce. The necessity for frequent travel to healthcare facilities can be especially burdensome during the postpartum period when mothers are recovering from childbirth and caring for a newborn. These barriers to access emphasize disparities in maternal and infant health outcomes, highlighting the urgent need for improved healthcare delivery systems during these critical stages of the fertility journey.

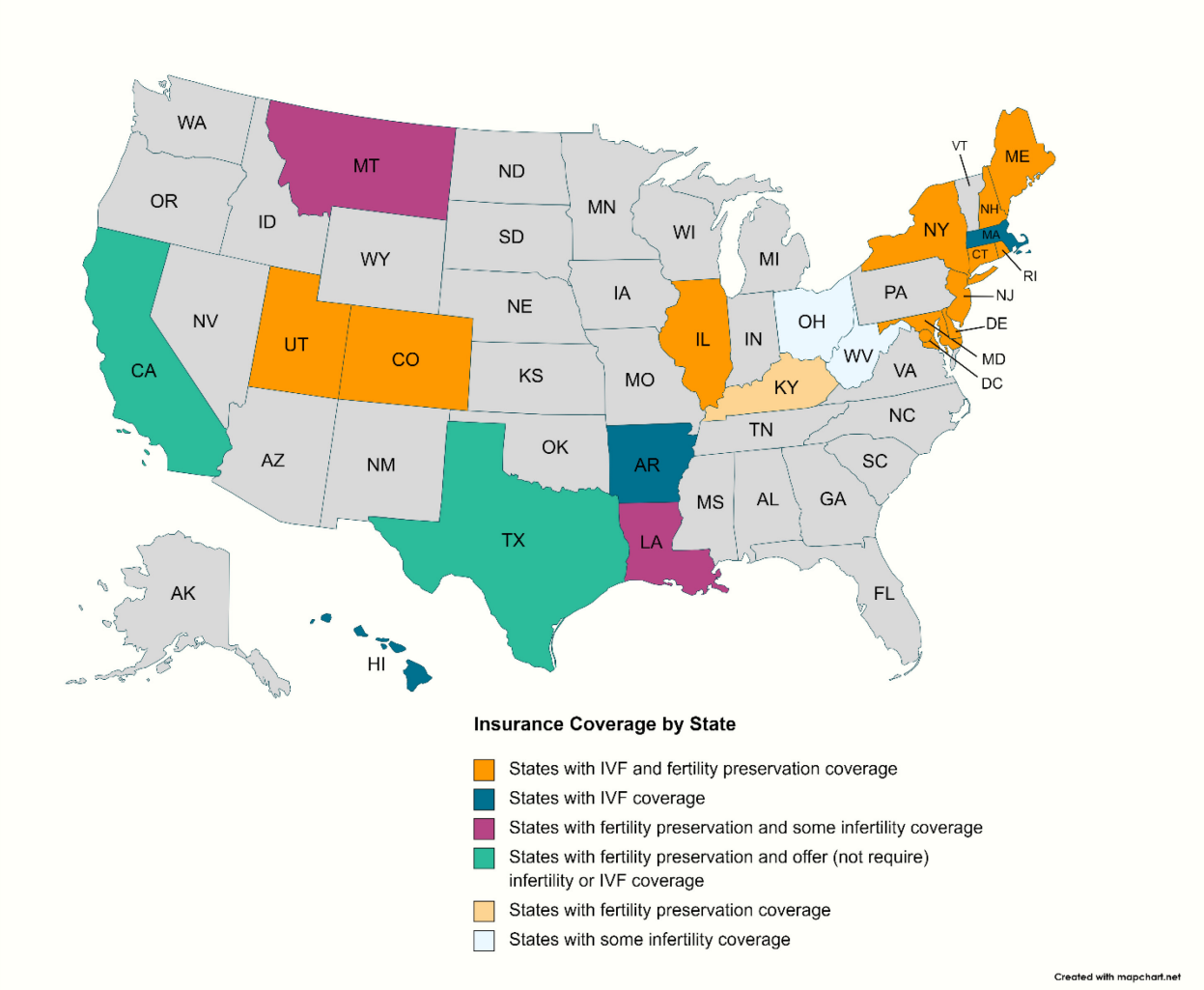

Figure 10. Fertility insurance coverage by U.S. state [59]

The complexities of insurance coverage, in combination with the multifaceted nature of infertility diagnosis, mean patients and healthcare providers often are constrained by coverage limits rather than considering what treatment would be most suitable. In addition to the financial barrier introduced by the cost of medical services, studies have shown that cultural and socio-economic backgrounds create disparities between individuals who seek and receive access to infertility care [63]. Geographic distributions of fertility clinics embody the disparity, with fertility clinics predominantly located and concentrated in urban centers, making access challenging for those in rural areas. As of 2010, only 51% of US counties had access to obstetrician-gynecologists nearby [64]. With approximately 1,500 reproductive endocrinologists (REIs) [65], the ratio of specialists who can perform and administer IVF to infertile females is roughly 1:5300. It is estimated that more than 25 million reproductive-age females have limited or no access to ART clinics, and lack of accessibility can delay treatment initiation [66], which in turn also impacts

the timing aspect.

Throughout the fertility journey, fertility services can require frequent visits with healthcare professionals, specifically in the cases of infertility treatments. Medication delivery and response monitoring become critical, starting with menstrual cycle regulation to prepare for ovarian stimulation. Controlled stimulation of the ovaries is highly monitored to prevent overstimulation, requiring, on average, 5 to 7 office visits for approximately two weeks [67]. Traditional in-person visits to fertility clinics are often scheduled based on standard protocols rather than individual patient needs, potentially leading to either excessive or insufficient monitoring. Excessive visits can impose significant time, financial, and emotional burdens on individuals, while insufficient monitoring might lead to missed opportunities and timely interventions or adjustments in treatment plans. Fertility services and treatments like IVF hinge upon these in-person clinic visits, posing another barrier associated with non-medical costs.

Chapter 3

Remote Patient Monitoring

This work explores how remote patient monitoring can address the timing and accessibility challenges associated with infertility services. In the evolving landscape of reproductive healthcare, the integration of remote fertility monitoring technologies holds the promise of significantly enhancing the personalization and efficacy of fertility treatments. The promise of digital tools and remote solutions can complement or even replace some of the in-person visits and reduce the medical and non-medical costs that would be incurred from fertility care.

3.1 An Introduction to Remote Patient Monitoring

Remote healthcare has emerged with the advancement and increased capability of telecommunications technology, enabling access and convenience to medical consultations, diagnosis, treatment, and monitoring to be delivered from a distance. This approach utilizes video conferencing, secure messaging platforms, and remote monitoring devices to connect patients with healthcare providers, facilitating timely and efficient healthcare delivery. As technology advances, telehealth is poised to play an increasingly significant role in healthcare delivery, offering a scalable and sustainable solution to many of the challenges traditional healthcare systems face [68].

Remote patient monitoring is a component of telehealth that facilitates the collection and transmission of patient health data from a remote location (e.g., a patient's home) to healthcare providers through digital technology. The term remote patient monitoring is often used interchangeably with *remote health monitoring* (RHM), which refers to a broader healthcare delivery method for general wellness management in the telehealth domain. Specifically, the RPM system enables healthcare professionals to monitor patients' health in real time, making it an invaluable tool for managing health conditions through early and real-time detection of illnesses, continual monitoring, and timely interventions.

3.1.1 Advantages of RPM

Remote patient monitoring offers extensive benefits to patients and clinicians that overcome the limitations of traditional patient monitoring without sacrificing, and in some cases improving, quality of care [69]. These benefits include [70]:

(A) Early detection. RPM allows healthcare providers to monitor patients' vital signs, symptoms, and health data in real time or regularly from a distance. By continuously monitoring patients remotely, healthcare providers can detect changes or abnormalities early, even before symptoms become apparent to the patient. When patients' vital signs are reviewed and monitored, acute care hospitalization rates and emergency department visits are significantly lower than when patients are not enrolled in a telemonitoring program [71]. Early detection enables prompt intervention, potentially preventing the progression of health issues or complications.

(B) Timely intervention. With RPM, healthcare providers can promptly intervene when patients' health data indicate a need for action. This action could involve adjusting medications, recommending lifestyle modifications, or scheduling follow-up appointments. Timely intervention can help stabilize patients' conditions and prevent exacerbations; RPM was reported to reduce hospital admissions, length of stay, and emergency room visits by 49%, 49%, and 41%, respectively [72].

(C) Access. One of the most salient benefits of RPM is its ability to extend healthcare access to remote and underserved populations, mitigating geographic barriers that have traditionally limited patient access to quality care. This aspect of RPM is particularly crucial in rural or resource-limited settings, where healthcare facilities may be sparse.

(D) Patient-centered. By providing patients with real-time data about their health status, RPM empowers them to take an active role in their healthcare journey. This empowerment is associated with improved adherence to medication and treatment regimens and lifestyle changes through reminders, educational resources, and feedback to patients and healthcare providers, leading to better health outcomes [73].

(E) Cost. RPM also offers the advantage of reducing healthcare costs by minimizing the need for in-person consultations and hospital readmissions. The continuous monitoring capability of RPM allows for early detection of potential health issues, enabling timely interventions that can prevent costly emergency room visits and hospitalizations. A

review of the economic impact of telehealth has shown cost reduction of up to 53% [74], particularly when the use of secondary care (i.e., healthcare services provided by specialists and emergency departments) is avoided. The cost of illness extends beyond the direct medical costs (see **Figure 11**), and remote monitoring offers the opportunity to reduce non-medical costs incurred from travel to and from in-person consultations.

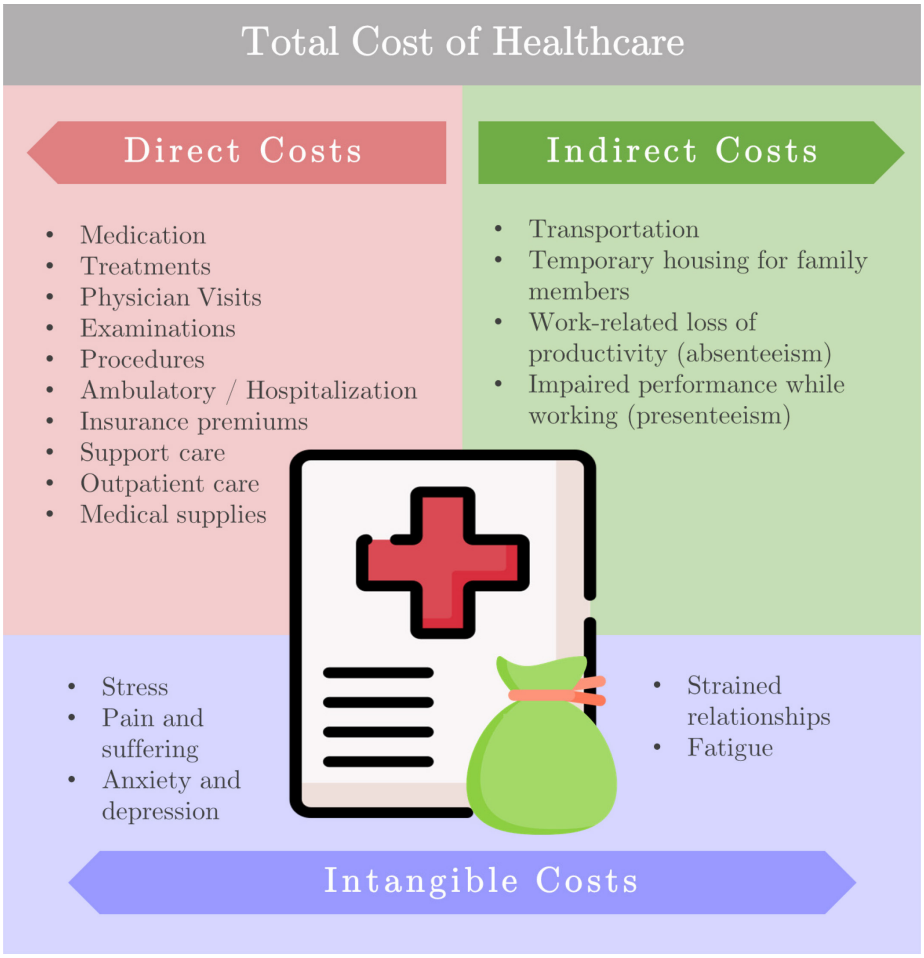

Figure 11. Total cost of healthcare

3.1.2 Challenges of RPM

Despite these advantages, RPM is not devoid of challenges, which causes hesitancy in its dissemination and implementation [70].

(A) Security and privacy. One of the primary concerns with RPM is data security and patient privacy. The transmission of sensitive health information over digital networks introduces vulnerabilities that could potentially be exploited, risking patient confidentiality. A robust implementation of remote patient monitoring requires

cybersecurity safeguards and encryption to protect patient data.

(B) Data overload. With an increased stream of clinical data, data fatigue is a potential side effect of RPM. The vast amount of data streaming in from multiple patients necessitates continuous review and analysis. Providers must sift through this data to identify significant trends, anomalies, or acute issues that require intervention. The sheer volume of information can be daunting, potentially leading to overlooked critical information or delayed responses to patient needs. The challenge is exacerbated in settings where healthcare professionals are already stretched thin, adding another layer of complexity to their workload. From the patient's perspective, there is also a similar concern about data interpretation and constant data reminders or messages that may exacerbate anxiety levels.

(C) Technology reliability. Ensuring the reliability and accuracy of RPM devices is paramount to reduce risks of technical failures and inaccuracies in health data collection, which could lead to misdiagnoses or inappropriate interventions from false positives.

(D) Access and training. Access to the necessary technology, internet connectivity, and digital literacy are prerequisites for the effective use of RPM, and lack of equitable access to these resources can pose barriers to the group that could benefit the most (e.g., socio-economically disadvantaged groups).

3.2 Remote Patient Monitoring System Breakdown

A formal and functional decomposition of an RPM system breaks the complex system into its core elements and functions. This analysis divides the system into its constituent parts, detailing each component's specific functions, from data collection and analysis to communication and user interaction.

3.1.3 Formal Decomposition

At its core, remote patient monitoring involves several key components, as depicted in **Figure 12**. First, it employs a range of medical devices and sensors that are easy for patients to either use at home or wear on their person. These devices are designed to measure various health indicators dependent on the condition. Typical measurements include blood pressure, heart rate, glucose levels, and oxygen saturation. The sophistication of these devices can vary, from simple wearable sensors to more complex

home monitoring systems that can also prompt patients to take their medication.

A critical aspect of RPM to connect the data between end-users is its communication infrastructure, which securely transmits the collected data from the patient to healthcare providers and vice versa. The infrastructure typically involves the use of the Internet, cellular networks, or other forms of wireless communication, with strong encryption to protect patient confidentiality and ensure compliance with health information privacy regulations.

Another integral component of the system is the data management system (DMS), where the transmitted data is stored, analyzed, and presented in a user-friendly format for patients and healthcare providers. A comprehensive data management system for remote patient monitoring ideally integrates with Electronic Medical Records (EMR) or Electronic Health Records (EHR) systems, which serve as digital repositories for patients' medical histories, diagnoses, medications, and treatment plans, among other essential healthcare information.

The user interface represents the final significant component of an RPM system, acting as the medium through which end-users engage with the monitoring technology. For patients, this may involve a straightforward app on a smartphone or tablet that displays health data, sends reminders, and offers health tips. For healthcare providers, it typically involves a more detailed dashboard that provides in-depth views into each patient's health, issues alert about abnormalities, and facilitates the efficient oversight of multiple patients simultaneously. Often, RPM systems incorporate a feedback loop, where healthcare providers can directly communicate adjustments to treatment plans, advice, or encouragement to patients through the interface, enhancing ongoing interaction and support.

The integration of these components creates a holistic remote health monitoring system that enhances healthcare delivery by making it more accessible, timely, and tailored to individual needs. This approach has the potential to improve health outcomes and patient satisfaction and reduce healthcare costs by minimizing the need for in-person visits and hospital readmissions.

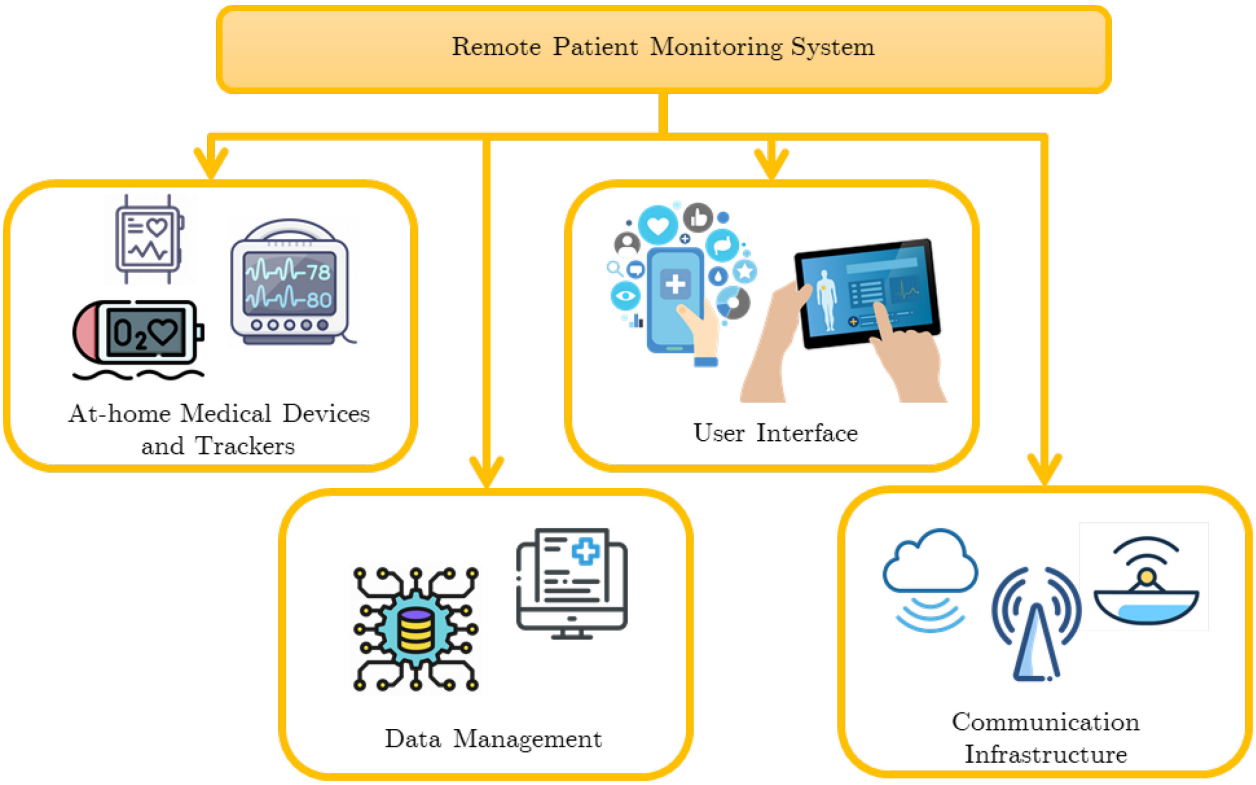

Figure 12. Remote Patient Monitoring (RPM) formal decomposition

3.1.4 Functional Decomposition

The operations of a remote patient monitoring system can be distilled into three essential functions: monitoring, analyzing, and communicating. An RPM functional architecture is illustrated in **Figure 13**, including primary and secondary functions.

Monitoring is the fundamental function of an RPM system, which involves continuously tracking vital health metrics relevant to the patient's specific conditions. This function enables data collection remotely, so patients do not need to visit a healthcare facility. The gathered data is then processed through a data management system, where it is analyzed to predict health trends and determine necessary adjustments or interventions in the patient's care plan.

Remote communication serves as the link between patients and healthcare providers within an RPM system. This communication function involves securely transmitting vital health information directly from the patient's location to their healthcare providers. Effective communication is essential, ensuring that insights, reminders, and alerts generated by the RPM system are quickly relayed to both patients and their care teams. Additionally, communication within RPM also involves user interactions with the system

itself, which includes operating the user interface and connecting to data management systems for comprehensive health management.

Together, these three functions—monitoring, analyzing, and communicating—create a dynamic system that enhances patient care by making it more continuous, data-driven, and responsive to changes in patient health.

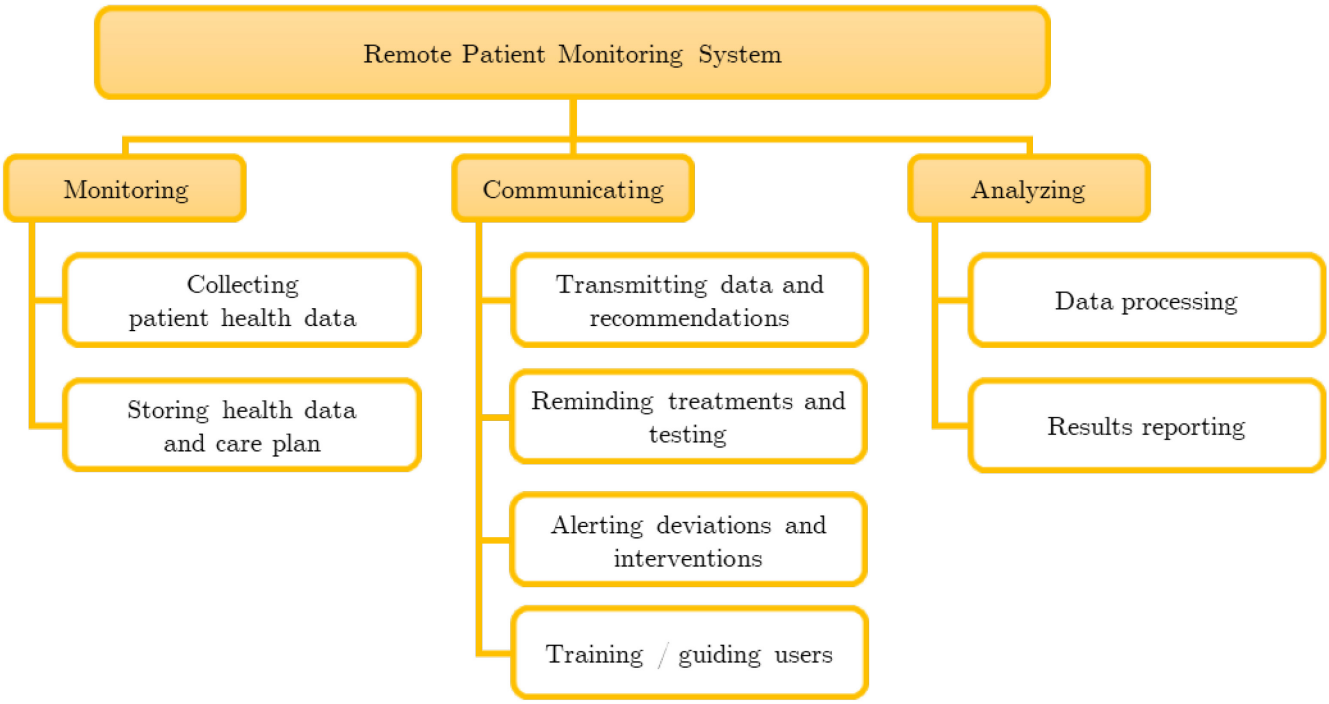

Figure 13. Remote Patient Monitoring (RPM) functional decomposition

3.3 Remote Patient Monitoring Pathologies

The use of remote monitoring systems in clinical applications and patient care has been increasing over the past decade [75]. RPM is most widely adopted in the management of chronic conditions [76], post-operative care [77], and elderly health management [78], where constant monitoring is essential. Diseases include asthma, chronic obstructive pulmonary disease (COPD), diabetes, heart failure, and hypertension [79]. Most recently, RPM systems have been deployed to monitor patients with COVID-19 infections who were required to isolate and reduce in-person visits [80] [81]. **Figure 14** shows the distribution of the most prevalent conditions managed through remote patient monitoring.

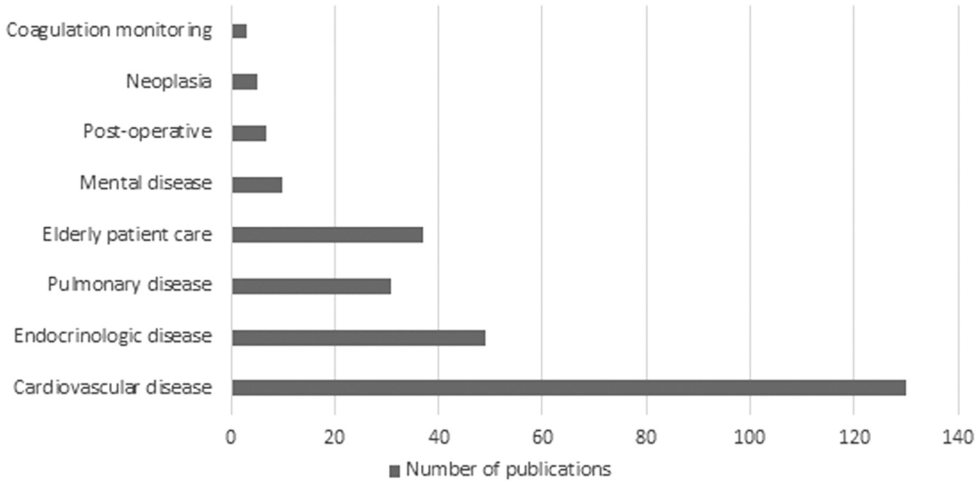

Figure 14. Most prevalent applications for remote patient monitoring systems based on publications [75]

The successful deployment of RPM systems centers significantly on their ability to be customized to the specific medical conditions they are designed to monitor. For example, heart disease monitoring might involve devices like heart rate monitors and blood pressure cuffs to detect real-time cardiac irregularities. In contrast, diabetes management often employs continuous glucose monitors to track blood sugar levels and alert patients to critical changes, while RPM for respiratory conditions like COPD could include pulse oximeters and spirometers to measure oxygen saturation and lung function. For RPM systems to be effective, these systems must align closely with each condition's unique demands and characteristics, considering the type of data to be collected, devices and sensors to be used, and user profiles who will directly interface with the system.

Chapter 4

Remote Patient Monitoring for Fertility Applications

Remote patient monitoring can transform the fertility care landscape, offering new opportunities to healthcare providers and patients navigating the complex nature of conception. The unique challenge of precise timing in fertility treatments, as discussed in **Section 2.5.1**, demands meticulous tracking to enhance the chances of successful conception. Traditionally, this monitoring requires frequent clinic visits for check-ups and assessments, which can be time-consuming and emotionally taxing. RPM can address these challenges by using available advanced technologies to track these critical parameters in real-time, enabling quicker feedback and adjustments.

The potential benefits of RPM in fertility care extend beyond those actively undergoing treatments. It offers substantial support to individuals attempting to conceive naturally by offering valuable insights into their fertility windows and optimal timing for conception. Furthermore, the benefits of RPM can persist into the post-conception phase. For those who have successfully conceived, RPM continues to be valuable by monitoring the health of the pregnancy from its earliest stages, providing reassurance and early detection of potential issues. This level of ongoing engagement and support helps to reduce anxiety and ensures that both the patient and healthcare providers are promptly informed about any health changes, which can be crucial for maintaining pregnancy health.

The following sections will provide a holistic evaluation of an RPM system designed explicitly for fertility care, exploring its components and functionality in depth.

4.1 Fertility RPM Ecosystem

The ecosystem of an RPM system involves the various components of the system working together within the operation environment, with constant interactions between the components and stakeholders of the system. **Figure 15** depicts the RPM system ecosystem.

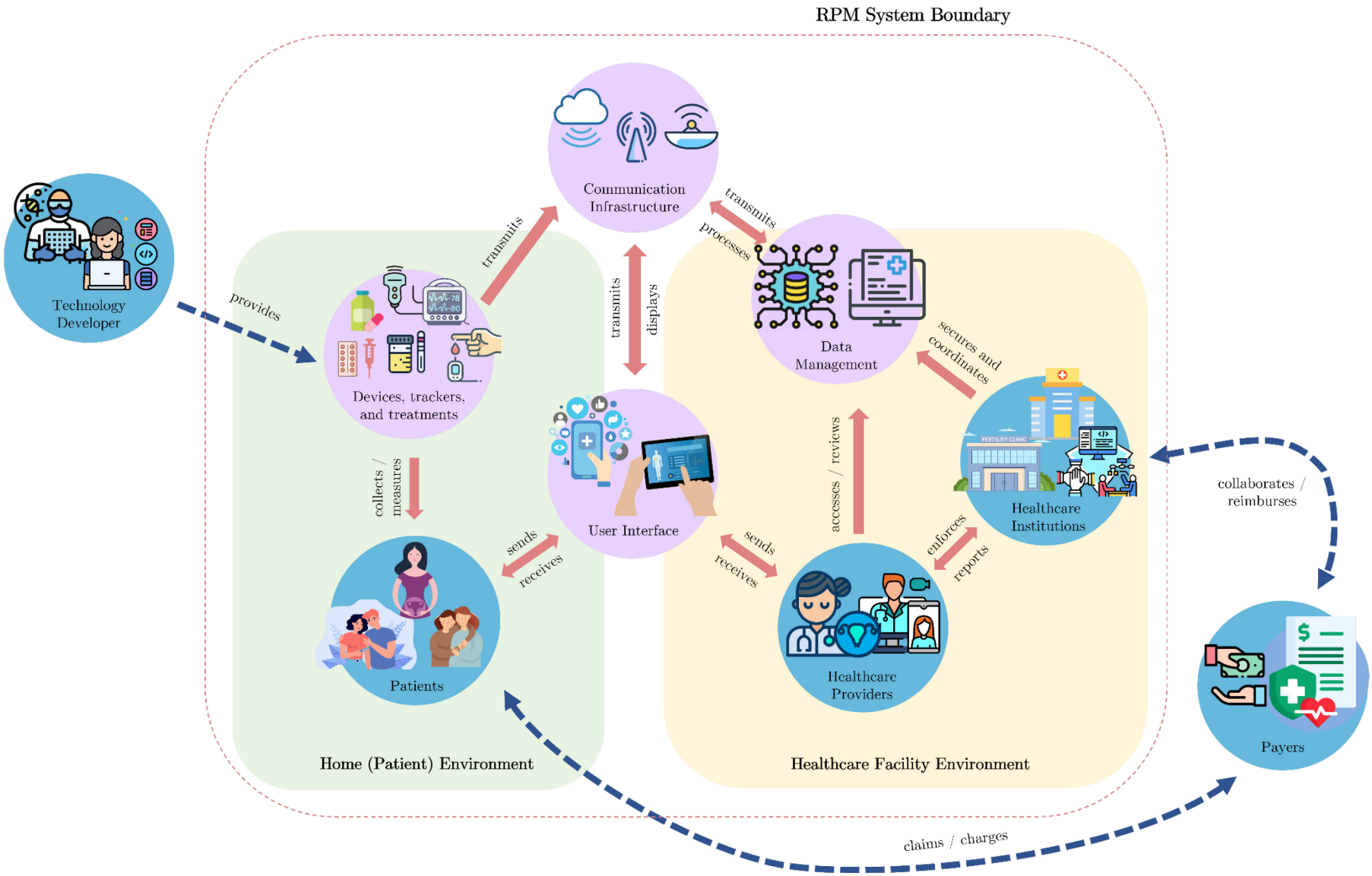

Figure 15. Fertility RPM System stakeholder and component interaction ecosystem

4.1.1 Fertility RPM System Operational Environments

Remote patient monitoring in fertility care is primarily centered around the patient's home and healthcare facilities. These settings provide the foundational environments for continuous health monitoring and data analysis. However, the deployment of RPM can extend into various other settings, tailored according to specific medical situations and risk factors that necessitate closer or specialized monitoring.

In the primary setting of a patient's home, RPM devices are to be used in places that facilitate easy and private collection of health data. Bathrooms often serve as a practical space for tests requiring biological samples such as urine, blood, or vaginal swabs due to the privacy and hygienic conditions they offer. Patients find these areas convenient for handling sensitive procedures discreetly and cleanly. Other places in the home, such as living areas and bedrooms, are crucial spots for non-invasive monitoring, medical administration, and general engagement with user interfaces for logging and communicating with health providers.

Connectivity within the home is a foundational element that supports the functionality of RPM devices. Reliable internet access is crucial for the real-time transmission of collected data to healthcare providers, ensuring that any necessary adjustments to treatment plans can be made swiftly and based on the latest information. The design of RPM equipment considers the diversity of home environments, ensuring ease of use regardless of the space limitations or configurations of different homes.

Complementing the home setup, healthcare facilities like hospitals and clinics provide a controlled environment equipped with advanced technology for more complex or sensitive aspects of fertility care. These facilities typically offer telehealth capabilities that allow virtual consultations and IT infrastructure to securely manage sensitive health data, including data received from home RPM systems. Many healthcare settings are inundated with specialized medical equipment and other devices that may have competing alarms and notifications, requiring active prioritization by the clinical staff.

Considerations for remote patient monitoring environments consider patients' varied lifestyles and daily routines, which is particularly important for those who spend significant time at work or who travel frequently. In such cases, portable RPM devices are essential for continuous monitoring to ensure patient care remains consistent and uninterrupted, no matter the location. In the context of fertility care, using portable RPM devices allows for continuous data collection and health monitoring, which is crucial for

timely medical responses and adjustments to treatment plans. However, portability can also present inevitable trade-offs. While most RPM technologies, such as wearable devices and mobile apps, are designed to be easily transportable, managing medications often requires more stationary conditions to ensure proper storage and handling. For instance, some fertility medications need refrigeration or specific storage conditions that need to be more easily managed on the go. This limitation underscores the need to carefully balance the convenience of portability with the practical requirements of specific treatments in fertility care.

4.1.2 Fertility RPM System Stakeholders

Stakeholder analysis is crucial for evaluating an RPM system as it ensures the system meets the diverse needs and expectations of all parties involved. In the context of fertility care, the stakeholders of a remote patient monitoring solution can be broadly categorized into three main groups based on their primary needs and interactions with the system. The three categories are (1) end-user - patient, (2) end-user – healthcare professionals, and (3) healthcare institutions. To understand how a remote patient monitoring system may fit in fertility care, a series of interviews were conducted to gather inputs and needs from two major stakeholder groups: patients and healthcare providers. No interviews were conducted with representative healthcare institutions or technology developers; their needs are based on general assumptions and secondary research through literature assessed from the business perspective.

(A) End-users: Patients

In the context of fertility care, patients encompass individuals seeking assistance with fertility concerns, irrespective of their stage in the fertility journey. This group includes those in good health and individuals with a heightened risk of infertility, such as those undergoing treatments that may affect fertility. While the typical demographic comprises females of reproductive age (15-49 years old), remote patient monitoring systems are adaptable to individuals of all genders and tailored to their unique health requirements. However, it is noteworthy that males assigned at birth or male partners are not conventional end-users of remote patient monitoring due to the absence of clinical parameters associated with remote monitoring in fertility care.

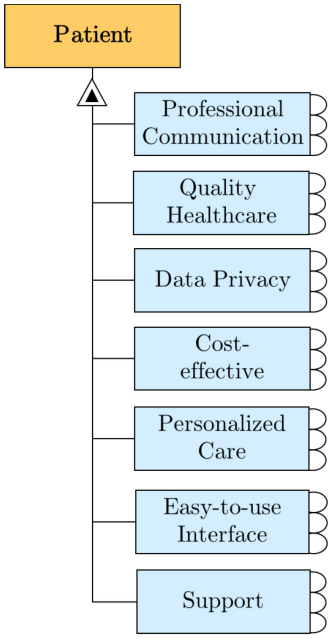

Figure 16. Patient priorities for RPM

Patients are the primary contributors of data within the RPM system, utilizing associated devices to provide essential health information. Their active engagement and compliance with the RPM process, as outlined in their monitoring plan, are imperative for effectively utilizing the system.

For patients, fundamental needs include ensuring privacy, ease of use, quality of care, and cost-effectiveness. These needs entail personalized care plans, real-time communication channels with healthcare providers, and resources for emotional support. Moreover, a comprehensive understanding of the fertility treatment process and the ability to monitor progress are essential (see **Figure 16** for a summary of patient needs).

Stakeholder Needs

a. *Privacy and Confidentiality:* Patients expect assurance that their health data remains confidential, especially when discussing sensitive fertility-related topics. They require secure communication channels to share updates, concerns, and questions with healthcare providers, including obstetricians, midwives, and fertility specialists.
b. *Quality Healthcare:* Patients anticipate that remote delivery of healthcare services does not compromise the quality of care received. They expect the same level of professionalism and quality of care as they would receive from traditional in-person visits. RPM solutions should include appropriate resources to maintain the compassionate "bedside manner" typically experienced during face-to-face interactions.
c. *Cost-effectiveness:* Patients seek cost-sensitive remote patient monitoring solutions, minimizing out-of-pocket expenses and financial barriers to access. The cost should not exceed what patients would expect to pay for traditional care unless improved outcomes are part of the proposed value. Patients may rely on health insurance coverage to offset such costs, emphasizing the need for clear reimbursement policies and support from payers to ensure coverage eligibility and affordability.
d. *Ease-of-use:* Remote patient monitoring systems should be user-friendly, with clear guidance on usage. Patients expect easy access to comprehensive educational materials and resources about the RPM system, regardless of their familiarity with digital solutions. This feature ensures patients can navigate the system effectively and maximize its benefits.

(B) End-users: Healthcare providers (HCPs)

The receiving end of the data is the users of RPM from the healthcare provider

perspective, ranging from physicians, physician assistants, nurses, and medical assistants. According to a systematic review of RPM systems, approximately 47% of RPM-collected data recipients are physicians or nurses, and 18% are patients [82]. This group may also include counselors, pharmacists, and researchers in limited cases. Generally, these stakeholders refer to any healthcare workers who consult with and provide care to monitored patients. For fertility-specific RPMs, HCPs may include obstetricians, gynecologists, urologists, reproductive endocrinologists, and other fertility specialists. This user group reviews the patient data and makes required clinical decisions based on the information received. Refer to **Figure 17** for a summary of HCP needs.

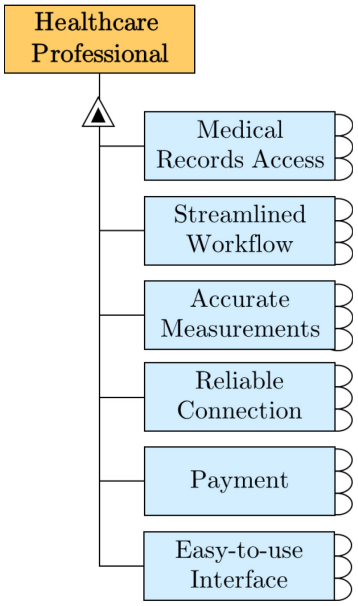

Figure 17. HCP priorities for RPM

Stakeholder Needs

a. *Reliable and connected solution:* Healthcare professionals rely on RPM systems for timely updates and alerts on critical parameters, enabling proactive patient care management. They require a dependable and integrated solution that seamlessly integrates with existing electronic health records (EHRs) to streamline data management. Additionally, since multiple care providers may need access to the system, customizable settings empower the team to prioritize and respond promptly to urgent patient needs, improving overall continuity and patient care delivery.
b. *Accurate devices:* HCPs require RPM devices that deliver diagnostic accuracy equivalent to or surpassing those available in clinical settings. These devices should provide measurements conducive to diagnostics and complement the established care plans for patients.
c. *Easy-to-use and scalable:* HCPs often manage multiple patients concurrently. Therefore, the RPM system must be user-friendly and scalable, allowing for efficient management of multiple cases without imposing additional burdens on healthcare workforce resources or organizational efforts.
d. *Privacy:* privacy is paramount for HCPs, mirroring patient needs. They require secure platforms that enable coordination with care teams and facilitate the confidential exchange of sensitive patient data, ensuring compliance with privacy regulations and maintaining the integrity of patient-provider communications.

(C) Healthcare Institutions

Healthcare institutions serve as vital stakeholders in implementing and utilizing RPM systems. Their central role lies in effectively integrating RPM technologies into the established workflows of hospitals and clinics, guaranteeing a seamless, secure, and efficient connection to clinical practices. Healthcare administration and information technology teams play instrumental roles and collaborate with healthcare providers to enable and integrate RPM workflows.

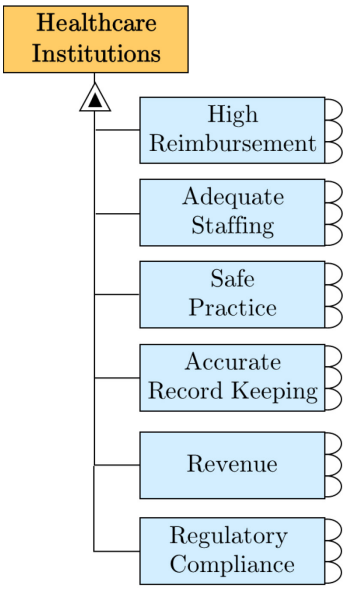

Figure 18. Healthcare institution priorities for RPM

Furthermore, healthcare institutions bear significant responsibility for managing external interfaces related to RPM systems, which includes rigorously vetting RPM solutions to ensure compliance with regulatory standards, such as those set by HIPAA and the FDA. Additionally, institutions take the lead in collaborating with healthcare payers to establish reimbursement policies that support the adoption and sustainability of RPM within the organization. Thus, healthcare institutions actively shape the landscape of RPM implementation, both internally within their facilities and externally within the broader healthcare ecosystem.

The needs of healthcare institutions encompass business-focused targets, including financial viability, staff well-being, and regulatory compliance and compatibility. Refer to **Figure 18** for a summary of healthcare institution needs.

Stakeholder Needs

a. *Financial viability:* RPM systems must demonstrate a return on investment (ROI) that aligns with targeted revenue margins to justify their implementation within these institutions. However, beyond financial considerations, the value proposition of RPM systems lies in enhancing the quality of care provided, which ultimately leads to increased revenue streams. Improved financial outcomes can be achieved by seeing more patients, made possible by the time saved from not needing to conduct in-office visits and perform measurements in the clinic. The investment in RPM systems should be robust and compatible with the institution's existing infrastructure. The solution necessitates minimal downtime during implementation and ongoing operations to prevent disruptions to patient care and administrative processes, which have indirect calculations that impact the institution's operational expenses.

b. *Staff support:* Ensuring the well-being of staff members is paramount. Integrating RPM systems into existing workflows should be seamless to minimize disruption and prevent staff from feeling overwhelmed. RPM systems should offer tailored training programs for staff members, equipping them with the necessary skills to effectively utilize the system. Furthermore, the systems should be intuitively designed and user-friendly, allowing staff to navigate them effortlessly without adding unnecessary stress or burden to their workload.
c. *Compliance:* Compliance with healthcare regulations is non-negotiable to uphold patient safety and mitigate liability risks, which includes adhering to government policies and regulations governing healthcare data privacy and security. In the fertility ecosystems, compliance also involves maintaining relationships with external stakeholders such as regulatory bodies, fertility clinics, and insurance providers. Adherence to these regulations and standards ensures the accuracy of results and the integrity of patient care practices within healthcare institutions.

Other stakeholders beyond these three categories exist but are not analyzed in detail as they are secondary stakeholders and do not directly interact with the daily utilization of RPM. Two of these secondary stakeholders (payers and technology developers) interface with the RPM ecosystem and have essential roles and influences on the development and implementation of remote patient monitoring systems.

(D) Technology Developers

The Technology Developers group consists of device manufacturers and software developers responsible for creating and refining RPM technologies. Manufacturers and developers are at the forefront of creating and refining RPM technologies and are typically third-party entities that provide the devices and software platforms used in remote patient monitoring systems. For devices and software applications that provide diagnoses and analyses of clinical data, this group is also responsible for validating the technology to ensure safety and efficacy.

(E) Payers

Payers, such as insurance companies and government healthcare agencies, are interested stakeholders and are influential in adopting remote patient monitoring. They establish coverage and reimbursement policies for RPM and fertility services, assessing medical necessities and the cost-effectiveness of medical treatments. Payers work closely with the primary stakeholders (patients, healthcare providers, and healthcare institutions) to facilitate healthcare services, negotiate costs, process claims, and contribute to healthcare policies and regulations. Although they indirectly interface with remote

patient monitoring systems, the payers' broad reach and involvement with the rest of the system are important inputs to consider in designing a robust and effective RPM for fertility applications.

Figure 19 presents the value exchange among stakeholders of the fertility RPM system. Stakeholders within the dashed box are directly within the system's boundary (primary stakeholders), while those outside interact with the system more indirectly (secondary stakeholders).

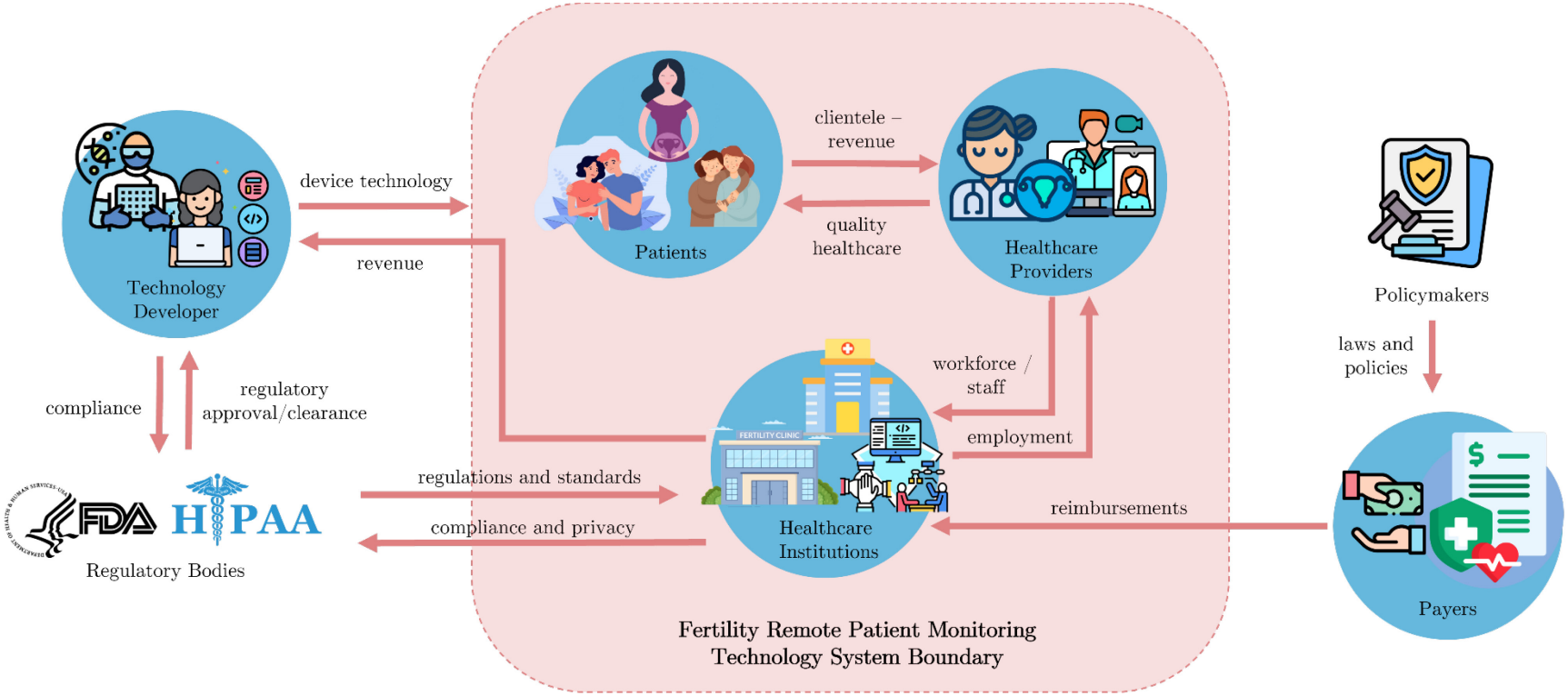

Figure 19. Fertility remote patient monitoring (RPM) stakeholder value exchange

4.2 Fertility RPM System Requirements

Developing a fertility RPM system requires a comprehensive evaluation of the combined needs of all stakeholders, including patients, healthcare professionals, and healthcare institutions. This collaborative assessment leads to identifying key qualities that are essential for the system's effectiveness and efficiency. These prioritized qualities form the foundation for the primary requirements of the system. The core attributes highlighted are customizability, accuracy, confidentiality, usability, and cost-effectiveness. Each of these qualities addresses specific aspects of stakeholder expectations and operational demands, ensuring the RPM system is functional and practical in a real-world setting.

(A) **Customizability**. *The system must provide flexible configuration options for healthcare providers to tailor treatment plans and monitor parameters according to individual patient needs.*

Customization is a key component in designing a fertility RPM, ensuring that the technology aligns precisely with the specific requirements of patients and healthcare providers. The architecture of an RPM system involves making strategic decisions about its design and functionalities, tailored to accommodate the diverse needs encountered at various stages of a patient's fertility journey. Aspects of customization include monitoring parameters and devices based on the specific fertility need. For example, someone trying to conceive naturally may need to track hormone levels that would inform them of their ovulation and fertile window. In contrast, those undergoing IVF may need to monitor additional hormone markers and vital responses to medication, including the need for an imaging device. For an illustration of assessing risks associated with different monitoring levels, see **Figure 20**. Furthermore, customization extends to the frequency and timing of monitoring. Patients may have different treatment protocols or fertility windows, necessitating personalized monitoring schedules. For example, individuals with irregular menstrual cycles may require more frequent monitoring to identify ovulation accurately, while others may benefit from targeted monitoring during specific phases of their treatment cycle.

From the perspective of the care team and healthcare institution, the choice of a remote patient monitoring system should align with the patient population they serve. Specialty fertility clinics focus on providing care to individuals requiring treatments and interventions. In comparison, general OB-GYN clinics cater to a broader range of reproductive health needs, including preconception, pregnancy, and postpartum care. Specialty clinics may have the resources to dedicate specific staff and targeted

communications, whereas larger clinics may need more generalized monitoring approaches to accommodate their diverse patient base.

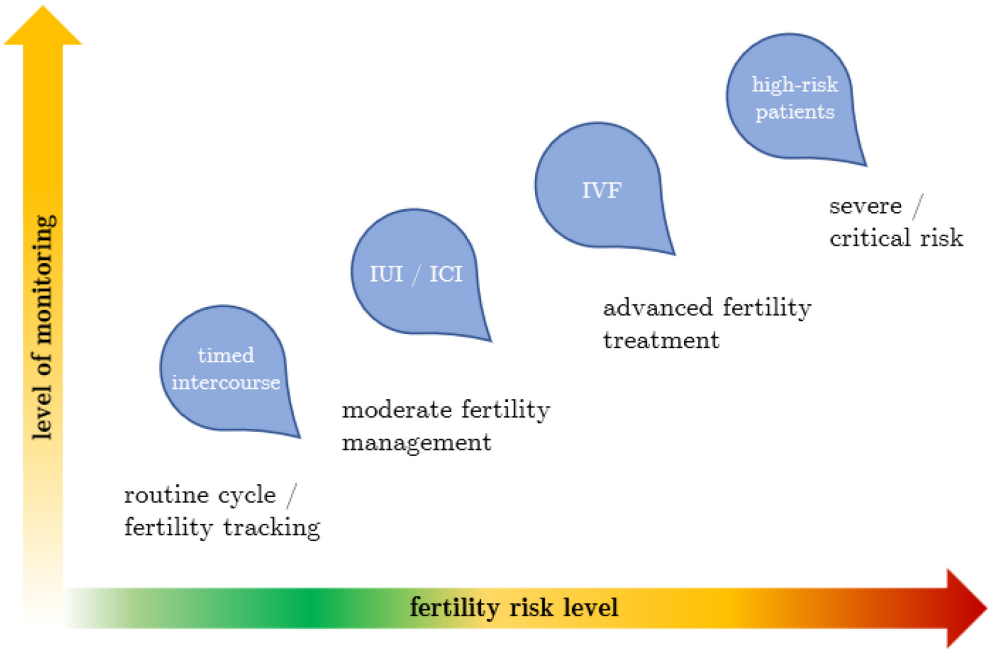

Figure 20. Customizability of monitoring levels based on risk

(B) **Accuracy**. *The system must maintain high data accuracy across all fertility monitoring functionalities.*

The proposed value of an RPM system in fertility applications hinges upon the accuracy and precision of data collected and transmitted to support medical decision-making. Measurements from a chosen RPM device should be reliable and appropriate, reflecting the actual physiological status of the patient. High accuracy in these devices enables care teams to make adjustments necessary to treatment medications, procedures, and timing of procedures. Deploying an RPM system that does not meet accuracy requirements can lead to safety concerns for the patient or ineffective interventions that do not translate into improved fertility outcomes.

Choosing the right metrics to measure and monitor contributes to the usefulness of RPM systems. Tracking LH, PdG, and FSH levels for natural conception efforts is critical for optimizing peak fertility timing. However, these metrics are not insightful for situations where women are already pregnant or are not monitored for any postpartum issues.

Several factors contribute to the accuracy requirement in RPM for fertility applications.

These include the quality and calibration of the sensors used in monitoring devices, the reliability of data transmission and storage systems, and the accuracy of algorithms used for data analysis and interpretation. Device developers must undergo rigorous testing and validation processes to ensure performance against clinical and regulatory standards.

(C) Privacy. *The system must comply with all applicable privacy laws and regulations.*

Many of the devices and test kits available for fertility have associated mobile health applications used for data collection, storage, and transmission to HCPs. These mobile health apps are critical in delivering a connected care solution in remote patient monitoring. However, an assessment of over 24,000 health-related apps revealed that 95.6% of the applications show potential risks of privacy infringements, and 11.7% are highly vulnerable to attacks [83].

For fertility applications, patient confidentiality is essential in RPM to uphold trust between patients and healthcare providers. Patients must feel confident that their reproductive health data will be kept confidential and only accessed by authorized individuals involved in their care. RPM solutions operate within a medical environment and are subject to privacy laws, such as HIPAA in the United States or GDPR in Europe. The goal is to protect sensitive patient data by implementing end-to-end data transmission encryption and preventing unauthorized access and breaches. Concerns exist about the potential for leveraging this sensitive information to shape policies without patients' consent and being subject to digital surveillance [84].

Privacy enforcement is an expectation for technology developers developing medical devices as they become more contributors to digital health solutions. Implementing robust security measures from the devices to RPM communication platforms is critical in meeting the needs of RPM.

(D) Usability. *The system must be user-friendly to accommodate users of varying technical skill levels.*

To ensure broad accessibility among users needing remote monitoring solutions, an RPM system should prioritize the clarity and intuitiveness of its components. Despite the prevalence of mobile phones and computers, many users may find digital health applications unfamiliar, potentially leading to disengagement if technological literacy or training levels are not considered. Additionally, prioritizing usability is crucial for

ensuring patient safety [85]. In contrast to hospital settings, where tests are administered by trained healthcare professionals, the home environment presents fewer controls and variations [86]. Factors such as user compliance, device placement, and environmental conditions can also affect the accuracy of RPM measurements; therefore, RPM systems should be compatible with home environments, featuring devices that are easy to store and operate without requiring resources uncommon to home use.

The interface platform, devices, and communication methods should offer intuitive usability or be accompanied by training, clear instructions, or aids for setup and use. Customizable and localized features should be incorporated into RPM designs to cater to a diverse user base, considering factors such as language, device handling, display, and messaging preferences. Given that fertility RPM users span a range of backgrounds and familiarity with medical devices, these factors are particularly important in promoting engagement and adherence.

Furthermore, data handling and interpretation should be intuitive, with guided workflows implemented if manual user input is necessary. Given the complexity of fertility markers and metrics, providing users with insights into their measurements and guidance on interpreting results can foster a sense of ownership over their reproductive health. Reports, alerts, and reminders should have clear recommendations based on the data collected and avoid technical jargon or complex terminology that may lead to confusion.

Device and technology developers are responsible for many of these usability aspects, but healthcare institutions should evaluate the devices and ensure proper training to empower users to use the system effectively.

(E) Cost-effectiveness. *The system's initial investment cost is offset by the overall expenses incurred by end-users for fertility care.*

Ensuring the cost-effectiveness of implementing an RPM system for fertility is crucial for its long-term viability and acceptance in healthcare settings. A significant challenge in accessing fertility care is the financial strain on patients, so the RPM system must not add significant financial burdens without corresponding benefits. Evaluating cost-effectiveness involves comparing the expenses of setting up and running the RPM system with its improvements to patient outcomes and healthcare efficiency. RPM aims to reduce patient costs by cutting indirect healthcare expenses like frequent clinic visits or hospital stays; thus, the costs of implementing and maintaining the system should ideally

replace or minimize these expenses. Factors such as increased pregnancy rates, decreased healthcare utilization, and enhanced patient satisfaction and quality of life are considered in assessing cost-effectiveness in fertility care. An RPM system demonstrating cost-effectiveness is more likely to garner support from healthcare providers, payers, and policymakers.

From the perspective of healthcare institutions, initial expenses for establishing an RPM system may include acquiring hardware and software, training staff and patients, and integrating the system with existing healthcare infrastructure. These costs vary based on factors like technological complexity and the scope of implementation. Moreover, ongoing system maintenance and operation expenses, such as device upkeep, software updates, data management, and user support, must also be factored in. Proper budgeting for these costs is essential to ensure the RPM system's sustainability over time.

These system requirements are essential guidelines for designing an effective remote patient monitoring system. They outline the key factors that must be prioritized to ensure the system's form and functions align with the performance metrics needed to meet stakeholders' needs. Specific metrics for each requirement may vary depending on the application, particularly in fertility settings, where different uses may necessitate tailored approaches.

4.3 System Architectural Choices and Concepts

In designing an RPM system for fertility applications, the approach involves decomposing a generic monitoring system (**Section 3.2**) and assessing various mutually exclusive architectural options. Each architectural decision is informed by the forms and functions inherent to a remote monitoring system. These decisions are organized based on the three primary functional components of a remote patient monitoring system. Various architectural options are then generated and must be assessed to create unique concepts. By combining these decisions, distinct concepts for remote monitoring systems can be created, each tailored to meet the specific requirements of fertility monitoring.

4.3.1 Architectural Decisions

The architectural decisions are derived from the primary functions described in the functional architecture found in **Section 3.1.4** (monitoring, communicating, and analyzing). **Table 1** summarizes the various architectural decisions (ADs) and corresponding options for remote patient monitoring in the context of fertility.

Function 1: Monitoring – related architecture decisions

Monitoring Frequency: This decision determines how often patient data is collected, ranging from scheduled periodic measurements (daily, hourly) to intermittent or real-time continuous monitoring, depending on the parameters monitored throughout the fertility journey.

Kit Contents: This decision specifies the components in the monitoring kit provided to patients, including sensors, devices, instructions, and medications tailored to their needs.

Device Type(s): This decision in architecture determines if the monitoring device will be a wearable sensor or a standalone system, such as a hormone test kit. A mobile application may be considered for symptom recording in cases where the monitoring kit does not include any physical devices.

Data Storage: The storage infrastructure and protocols for securely storing patient data, ensuring compliance with regulatory requirements, and safeguarding sensitive health information must be determined. Data storage options include local storage, where patients provide information to the doctor during consultations or visits, or cloud-based storage and EMR/EHR systems. The devices and platforms used may connect directly to electronic health records and medical records, or healthcare providers may need to transfer the information using alternative methods.

Function 2: Communicating – related architecture decisions

Interaction Platform: This decision defines the digital platform or interface through which patients interact with the monitoring system, including mobile apps, web portals, or dedicated devices, ensuring accessibility and ease of use.

Interaction with HCP: Another decision concerns how patients communicate and share data with their healthcare providers. This interaction can take two forms: a two-way communication allowing patients and the care team to interact directly or an indirect option where only the care team communicates with patients. Additionally, there is the option of no interaction via RPM, where patients can only communicate with their care team during in-person visits.

Notifications: This architectural decision determines if end-users receive reminders, updates, messages, and alerts, with the frequency ranging from passive notifications for medication timing to active alerts for emergencies or critical readings.

Training Availability: This decision addresses providing user training resources using the monitoring system. If the kit includes medical devices, manufacturers are required by regulations to include documentation and instructions for using the device.

Device to Device Monitoring System (DMS) Connection: This decision outlines how monitoring devices connect to the DMS, utilizing methods like Bluetooth, Wi-Fi, or cellular networks to ensure reliable data transmission. In cases where devices do not connect to the system, manual information entry is necessary.

Function 3: Analyzing – related architectural decisions:

Information Entry: RPMs may offer manual or automatic data entry options. With manual entry, patients (and healthcare providers) input information into the system, whereas automatic entry involves devices transmitting data directly.

Data Push Frequency: The entered data can be transmitted to the healthcare provider (HCP) team periodically or continuously, enabling real-time monitoring. This frequency may vary in cases where no device is included to connect with the system and information is reviewed indirectly (through in-person visits or messaging).

Results Interpretation: The RPM system might utilize an AI-driven mechanism to interpret and analyze collected data or assist HCPs to make actionable patient recommendations. While HCPs are ultimately responsible for patient care, AI may support care teams in decision-making. In certain instances, such as with the standard calendar method for timed intercourse, patients may be the sole stakeholders involved in the data interpretation.

Table 1. RPM architectural decisions

		Architectural Decisions	Option 1	Option 2	Option 3	Option 4	Classification
Primary RPM Functions	Monitoring	**Monitoring frequency**	Periodic (Prompted)	Continuous (Active)			Function
		Kit contents	None	Device	Device + Medications		Form
		Device type(s)	No device (symptom tracking only)	Wearables	Stand-alone	Mix	Form
		Data storage	None (local device storage)	EMR/EHR connected	Cloud server (No EMR/EHR connection)	Mix	Form
	Communicating	**Interaction platform**	Phone / mobile app	Web portal	Stand-alone	Mix	Form
		Interaction with HCP	None	Direct (two-way interaction, video calls, messaging)	Indirect (one-way interaction or in-person visits)		Form
		Notifications	None	Passive (regular updates/reminders)	Active (alarms/alerts)		Function
		Training availability	No training provided	Printed / digital manuals	Online videos and guidance	Mix	Form
		Device to DMS connection (cxn.)	None	Bluetooth	Internet, cellular (Wi-Fi, 4G, 5G)	Mix	Form
	Analyzing	**Information entry**	Manual (user-entry)	Automatic (device connection)			Function
		Data push frequency	None	Periodic (set-interval or as entered)	Continuous		Function
		Results interpretation	HCP-driven	HCP-driven, AI-aided	AI-driven	Patient-driven	Form

4.3.2 Architectural Concept Examples

Different combinations of architectural decisions yield RPM system concepts that would be suitable depending on the needs of the stakeholders and the patient's standing in their fertility journey. Specifically, each architectural decision should be chosen to make the solution most compatible with the healthcare system and patient needs. Example concepts are generated and described below and in **Table 2**.

Concept 1: "Self-Management Mobile App Tracking" - Baseline
This RPM concept serves as a baseline and is designed for self-sufficient individuals on their fertility journey, emphasizing a hands-off approach with the convenience of a mobile app. The app facilitates periodic self-monitoring without any devices, requiring manual data entry and local data storage, which is ideal for those in the preconception phase or for those monitoring their general reproductive health without active treatments. There is no direct patient-HCP interaction, enabling users to maintain complete control over their data, with the responsibility for interpreting results lying with the patient.

Concept 2: "Minimal Intervention Mobile App Monitoring"
This concept supports those in the preconception or early conception phases who prefer a less intrusive approach, using a mobile app for intermittent symptom recording and manual data entry for menstrual cycling. It is suitable for individuals managing their fertility journey independently without the need for active medical intervention or constant monitoring while still having the option to share their data with healthcare providers during regular check-ups or consultations.

Concept 3: "Scheduled Monitoring Kit with In-Person HCP Interaction"
Designed for patients who prefer direct healthcare provider interactions, this fertility RPM concept facilitates scheduled measurements using standalone hormone test kits. The focus on in-person visits ensures patients receive personalized guidance and support during critical fertility treatments and pregnancy and postpartum processes. Users may include those less comfortable with high-tech solutions or have easy access to fertility specialists for frequent clinic visits. The patients receive notifications for any medications required and measurement reminders but do not use the complete offering of data management systems.

Concept 4: "Smart Fertility Monitoring Kit"
This concept is an advanced RPM system designed for continuous and comprehensive monitoring throughout the fertility journey. It comprises a mix of wearable devices for

real-time physiological tracking and standalone devices for specific tests, all seamlessly integrated with a phone/mobile app for easy user interaction. Notifications are proactively managed to alert results and reminders to ensure adherence to testing time. Data is automatically captured and continuously pushed to a secure cloud server. The interpretation of results is handled by an AI algorithm, minimizing direct contact with the patient's local care teams. HCP support, however, may be given through online coaching or third-party healthcare providers.

Concept 5: "AI-assisted Comprehensive Continuous Monitoring Kit"

This RPM concept utilizes innovative features from integrated AI algorithms but leaves decision-making and clinical interventions to HCPs. This concept is comprehensive and tailored to patients who require intensive monitoring and therapeutics. It features real-time continuous monitoring through various devices that can be directly reviewed by HCPs through EMR/EHR. The AI's role is to streamline the care process by managing schedules, sending medication reminders, and alerting patients and healthcare providers when clinical readings fall outside of predetermined norms established by the medical team. This system is particularly suitable for those undergoing complex treatment paths, like fertility treatments or managing high-risk pregnancies, where detailed oversight and swift medical action are paramount.

Concept 6: "Advanced Treatment Support"

Similar to **Concept 5**, this RPM system is ideal for detailed tracking across all stages of the fertility journey, including preconception planning, various fertility treatments like IVF or IUI, and pregnancy care. It employs wearable sensors for continuous health monitoring and standalone kits for specific hormone tests. Additionally, it features a web portal that complements the mobile application, providing another avenue for two-way communication with healthcare providers. While this system does not directly integrate with EMR/EHR systems, it actively records and stores data in the cloud, where healthcare providers can access the information as needed.

Table 2. Fertility RPM concept examples

Colored blocks indicate the differences in architectural choices from the baseline concept (**Concept 1**)

	Concept 1	**Concept 2**	**Concept 3**	**Concept 4**	**Concept 5**	**Concept 6**
Monitoring frequency	Periodic	Periodic	Periodic	Continuous	Continuous	Continuous
Kit contents	No devices (mobile app)	No devices (mobile app)	Device and medications	Device	Device and medications	Device and medications
Device type(s)	No devices (mobile app)	No devices (mobile app)	Standalone (e.g., hormone kit)	Mix (standalone and wearables)	Mix	Mix
Data storage	Local	Cloud server	Local (brings results to HCP)	Cloud server	EMR/EHR connected	Cloud server
Interaction platform	Phone / mobile app	Phone / mobile app	Standalone (device only)	Phone / mobile app	Phone / mobile app	Mix (mobile app and web portal)
Interaction with HCP	None	Direct communication	Indirect	None	Direct communication	Direct communication
Notifications	None	Passive notifications	Passive (medication and measurement reminders)	Active (alerts and reminders)	Active (alerts and reminders)	Active (alerts and reminders)
Training availability	No training provided	Online guidance	Printed and digital manuals	Online guidance	Mix	Mix
Device to DMS cxn.	None	Cellular	None	Mix	Mix	Mix
Information entry	Manual data entry	Manual data entry	Manual data entry	Automatic	Automatic	Automatic
Data push frequency	None	Periodic	Periodic	Continuous	Continuous	Continuous
Results interpretation	Patient-driven	HCP-driven, AI-aided	HCP-driven (during visits)	AI-driven	HCP-driven, AI-aided	HCP-driven, AI-aided

4.4 Coupling Analysis

A coupling and connectivity analysis is conducted to prioritize these architectural decisions and identify which decisions strongly influence others. This analysis aims to uncover interdependencies among decisions that may impose constraints or limit the available options for subsequent decisions. For example, selecting the option of no interaction with healthcare providers (architecture decision #5) automatically negates the necessity to push data for review (architecture decision #9). Conversely, the decision regarding the frequency of data pushed to healthcare providers necessitates the existence of the interaction itself and cannot be omitted.

A Design Structure Matrix (DSM) in **Table 3** is constructed to visually represent the relationships between architectural decisions, supplemented by a ranking of their connectivity. This ranking, denoted as weak, medium, or high coupling, delineates the relative degree of interconnection among decisions (1=weak coupling, 2=medium coupling, 3=high coupling). The interaction is determined and organized by looking at the effect of the architectural decisions from columns to rows.

The symmetrical relationships observed among architectural decisions underscore their mutual dependencies, wherein changes in one decision can reverberate across the system, influencing other decisions in return. While not necessarily equal in influence, these reciprocal effects highlight the interconnected nature of architectural choices. As decisions become more refined and specific, asymmetry may emerge, reflecting the nuanced relationships between elements.

Understanding and leveraging these symmetrical relationships can inform decision-making processes and system design efforts, fostering a more cohesive RPM framework. Recognizing the mutual influence of architectural decisions enables stakeholders to navigate trade-offs and constraints inherent to the system, ensuring that changes made to one aspect align with the broader goals and objectives of the RPM system.

This method has been adapted from the works of Crawley, Cameron, and Selva [87].

Table 3. Architectural decisions coupling and connectivity analysis

Combined Coupling Score		Columns to Rows	AD-1	AD-2	AD-3	AD-4	AD-5	AD-6	AD-7	AD-8	AD-9	AD-10	AD-11	AD-12	Total Susceptibility Score
26	**AD-1**	Monitoring frequency		1	3				2		1	3	3		**13**
8	**AD-2**	Kit contents	1		3										**4**
31	**AD-3**	Device type(s)	3	3					2		2	1	3		**14**
6	**AD-4**	Data storage									3				**3**
0	**AD-5**	Interaction platform													**0**
22	**AD-6**	Interaction with HCP							3		3		3	2	**11**
28	**AD-7**	Notifications	2		2			3			3	2	2		**14**
0	**AD-8**	Training availability													**0**
43	**AD-9**	Device to DMS connection	1		3	3		3	3			3	3	3	**22**
26	**AD-10**	Information entry	3		3				2		3		3		**14**
34	**AD-11**	Data push frequency	3		3			3	2		3	3			**17**
10	**AD-12**	Results interpretation						2			3				**5**
		Total Impact Score	**13**	**4**	**17**	**3**	**0**	**11**	**14**	**0**	**21**	**12**	**17**	**5**	

Note: Relationships are determined from column to row (the table should be interpreted such that AD in a column influences the AD in a row). The total susceptibility score is derived by summing the interconnections for each row, indicating the degree to which other architecture decisions impact the architecture decision of interest. Conversely, the total impact score is calculated by summing each column's scores and reflecting how much the architecture decision of interest influences other decisions. The combined coupling score is obtained by adding together the total susceptibility score and the total impact score.

4.5 System Performance Metrics

A spectrum of performance metrics that holistically capture the system's impact on patients, healthcare providers, and the broader healthcare system is considered to fully evaluate the effectiveness of a fertility remote patient monitoring system. Fertility is a deeply personal and often challenging journey, fraught with emotional and financial burdens. An RPM system in this domain must navigate these complexities with sensitivity and demonstrate tangible benefits in patient outcomes and system efficiencies. Setting specific targets and using quantitative methods to track these key performance indicators ensure that the system meets clinical and operational goals and enhances the patient's journey through fertility treatment.

The primary measure of a fertility-focused RPM system's success is its ability to enhance **clinical outcomes and fertility success rates**. These outcomes encompass the ultimate goal of achieving pregnancy, the management of treatment side effects, and the optimization of the overall health of individuals seeking to conceive. For high-risk scenarios, such as patients with a history of miscarriages, PCOS, or those undergoing IVF, an effective RPM system should demonstrate a reduction in adverse outcomes and an increase in successful pregnancies. It is crucial to recognize that while RPM does not directly enhance the efficacy of treatments, it supports better outcomes by providing precise and dependable data that healthcare professionals can act upon. Improvements in fertility outcomes can be quantified by monitoring success rates, such as the percentage of users who achieve pregnancy while using the system compared to a control group not using RPM. For instance, measure the increase in successful pregnancies post-RPM implementation, aiming for a specific target percentage increase.

Additionally, an RPM system should serve as an early-warning mechanism, particularly for high-risk pregnancies where conditions like pre-eclampsia or gestational diabetes may arise. By monitoring vital signs and symptoms, the RPM can enable healthcare providers to intervene preemptively, potentially reducing the **frequency of hospital admissions and the severity of complications**. For IVF patients, monitoring can help manage the risks of OHSS or hypertension, leading to timely and potentially less costly medical interventions. For high-risk pregnancies, the decrease in hospital admissions due to conditions manageable by RPM, such as the incidence of hospital stays for pre-eclampsia, can be a measure of this system performance. Similarly, monitoring emergency visits due to OHSS from IVF treatments can benchmark a reduction rate.

Fertility treatments are notoriously expensive, and costs often escalate due to repeated

unsuccessful treatments or unanticipated complications. A well-designed RPM system could **mitigate the costs** by reducing the need for in-person consultations, minimizing hospital stays, and streamlining the treatment process. The cost-effectiveness metric of an RPM should compare the expenses associated with its use versus traditional care methods, considering both direct medical costs and indirect costs like travel and time off work. The cost-effectiveness of the RPM system can be evaluated by comparing the average cost per fertility treatment cycle with and without RPM over a defined period, such as one year. This comparison should include direct costs, such as medications, procedures, and hospitalization, and indirect costs including travel and time off work. Cost savings can also be indirectly extended to healthcare institutions through improved operational efficiency by freeing time to focus on prioritized patients and enhancing patient capacity.

At such a clinically sensitive time, it is imperative that the RPM system is user-friendly and adds clarity and control to the process without overwhelming the users. **Satisfaction metrics** should reflect the system's usability, clarity value to the fertility process, and impact on reducing anxiety and stress. For healthcare providers, the RPM should seamlessly integrate into existing workflows, enhance patient care without adding to the **workload**, and improve **patient adherence** to treatment plans. User satisfaction can be quantitatively assessed using a standardized survey tool like the Net Promoter Score (NPS), aiming for a score improvement after RPM implementation. User engagement can be measured by monitoring log-in frequency to the RPM platform and adherence rates (in percentage) to prescribed monitoring schedules. For healthcare providers, tracking the reduction in time spent on patient management per case can indicate successful integration and efficiency of the RPM system.

A summary of these metrics is described in **Table 4**.

Table 4. Performance metrics of a fertility RPM system

Metric	Example Performance Metric	Data Source	Stakeholder Need Satisfied
fertility outcomes	Percentage increase in successful pregnancies among patients using RPM compared to a control group not using RPM. This metric could be tracked over a specific period (e.g., a year or a specific number of treatment cycles).	Patient records and RPM system logs	Quality Healthcare
hospitalization rates (for high-risk conditions)	Percentage reduction in the number of hospital admissions for high-risk conditions (like pre-eclampsia or OHSS) before and	Hospital admission records and	Quality Healthcare

	after implementing RPM. Target a specific percentage reduction, such as a 20% decrease within the first year of RPM deployment.	RPM alerts/log entries	
patient medical costs	Average fertility treatment cost per patient before and after RPM introduction, aiming for a quantifiable reduction (e.g., 15% decrease). Include costs associated with hospitalizations, treatments, and medications.	Billing records and insurance claim data	Cost-effectiveness
user satisfaction	Standardized survey tools such as Net Promoter Score (NPS) to measure satisfaction. Aim for a score improvement by a specific number of points (e.g., an increase of 10 points) after implementing RPM.	Surveys conducted periodically among patients and healthcare providers.	Ease-of-use Privacy and confidentiality Reliable and Connected
reduced workload for patients and HCPs	Average time spent per patient visit before and after RPM implementation, targeting a reduction (e.g., decrease time spent by 30%). Aim for a decrease in the number of in-person visits required per treatment cycle.	Time tracking software and patient visit logs	Staff support
patient engagement and adherence	Percentage of patients adhering to their prescribed treatment and monitoring schedules, aiming for an increase (e.g., achieving 80% adherence). Engagement metrics such as frequency of app logins or system interactions can be considered.	RPM software analytics and patient interaction logs	Patients HCPs

4.6 Performance Metric Sensitivity Analysis

Section 4.4 analyzed the impact of architectural decisions on other decisions. Beyond measuring connectivity between them, architectural decisions can also be evaluated against the defined, categorical performance metrics. This systematic exploration of how variations in key design decisions may influence system performance and outcomes enables effective prioritization of architectural decisions based on their ability to deliver impact on meeting stakeholder needs.

The evaluation system employs a scoring method where values of 1, 4, or 9 are assigned

to indicate the degree of impact each decision has on specific system performance metrics. A score of 1 indicates low impact, 4 suggests moderate impact, and 9 signifies a high impact. Refer to **Table 5** for the detailed scoring of each architectural decision against the performance metrics. Sensitivity scores are determined by summing the scores for each architecture decision.

Table 5. Sensitivity analysis of architectural decisions on performance metrics

			Metrics						
			fertility outcomes	hospitalization rates (for high-risk conditions)	patient medical costs	user satisfaction	reduced workload for patients and HCPs	patient engagement and adherence	Sensitivity Score
Architectural Decisions	**AD-1**	Monitoring frequency	9	9	9	4	9	9	**49**
	AD-2	Kit contents	1	1	9	4	1	1	**17**
	AD-3	Device type(s)	9	9	9	9	9	9	**54**
	AD-4	Data storage	1	1	9	4	9	1	**25**
	AD-5	Interaction platform	4	4	4	9	9	9	**39**
	AD-6	Interaction with HCP	9	9	1	9	4	4	**36**
	AD-7	Notifications	4	9	1	9	9	9	**41**
	AD-8	Training availability	1	1	1	9	4	9	**25**
	AD-9	Device to DMS cxn.	4	4	4	9	9	9	**39**
	AD-10	Information entry	4	4	4	9	9	9	**39**
	AD-11	Data push frequency	9	9	4	1	4	1	**28**
	AD-12	Results interpretation	9	9	1	4	4	1	**28**

The performance metrics sensitivity demonstrates the decisions made about how often monitoring will occur (AD-1, sensitivity score = 49), what kind of devices are used (AD-3, sensitivity score = 54), and what platform is used for RPM (AD-4, sensitivity score 39) impose the most significant influence on meeting the specified performance metrics for RPM systems.

Monitoring frequency emerges as an integral architectural decision due to its direct impact

on most of the metrics defined. By tailoring monitoring frequency to align with patients' fertility windows and treatment protocols, healthcare providers can optimize the timing of interventions, thereby enhancing fertility outcomes. This alignment is particularly beneficial for high-risk patients, as it amplifies the effectiveness of timely interventions. However, it is essential to note that while a high score indicates a high degree of impact, it does not guarantee a positive impact in all cases. A well-calibrated monitoring frequency can foster patient engagement by providing timely insights into their reproductive health status, thereby promoting adherence to treatment plans and reducing the likelihood of missed opportunities for conception. Nevertheless, there are potential drawbacks to consider, such as the possibility of inducing fatigue from constant data streams associated with continual monitoring. Moreover, while monitoring frequency may significantly impact costs through improved outcomes in fewer cycles or treatments, this influence does not automatically translate into cost reduction. The need for a continual monitoring system may necessitate additional devices with advanced features, potentially offsetting any cost-saving benefits.

In turn, device types play a crucial role in determining remote monitoring programs' accuracy, reliability, and user experience. Wearable devices, for instance, offer continuous monitoring capabilities, enabling real-time tracking of vital fertility parameters such as ovulation cycles. This continuous monitoring can enhance the precision of fertility predictions and facilitate timely interventions, ultimately contributing to improved fertility outcomes. Although not explicitly listed as individual options within the architectural decisions, selecting the appropriate device that meets the required quality standards is essential to leverage the full value proposition of remote monitoring systems.

Moreover, the selection of interaction platforms significantly influences user satisfaction, workload, and engagement. Digital platforms like mobile applications and web portals provide convenient channels for patients to communicate with their healthcare providers without substantially impacting the overall cost to the patient. However, user satisfaction depends largely on these platforms' implementation and ease of use. Mobile phones are more accessible than web-based systems, while the latter may enable more features than the former. For healthcare providers and institutions, having bug-free and secure mobile or web portals is crucial to avoid additional burdens associated with system usage.

Overall, the analysis underscores the importance of strategic decision-making in selecting architectural elements that align with the overarching goals of remote monitoring programs in fertility applications. By prioritizing architectural decisions related to monitoring frequency, device types, and interaction platforms, RPM system designers can

optimize the delivery of care, improve fertility outcomes, reduce healthcare costs, and enhance patient satisfaction, among other performance indicators.

4.7 Sensitivity vs. Coupling Analysis

To combine the two analyses, a sensitivity versus coupling analysis is conducted, and the prioritization of architectural decisions is determined based on their sensitivity to metrics and interactions with other decisions. The total sensitivity score from **Table 5** is plotted against the total coupling score from **Table 3**.

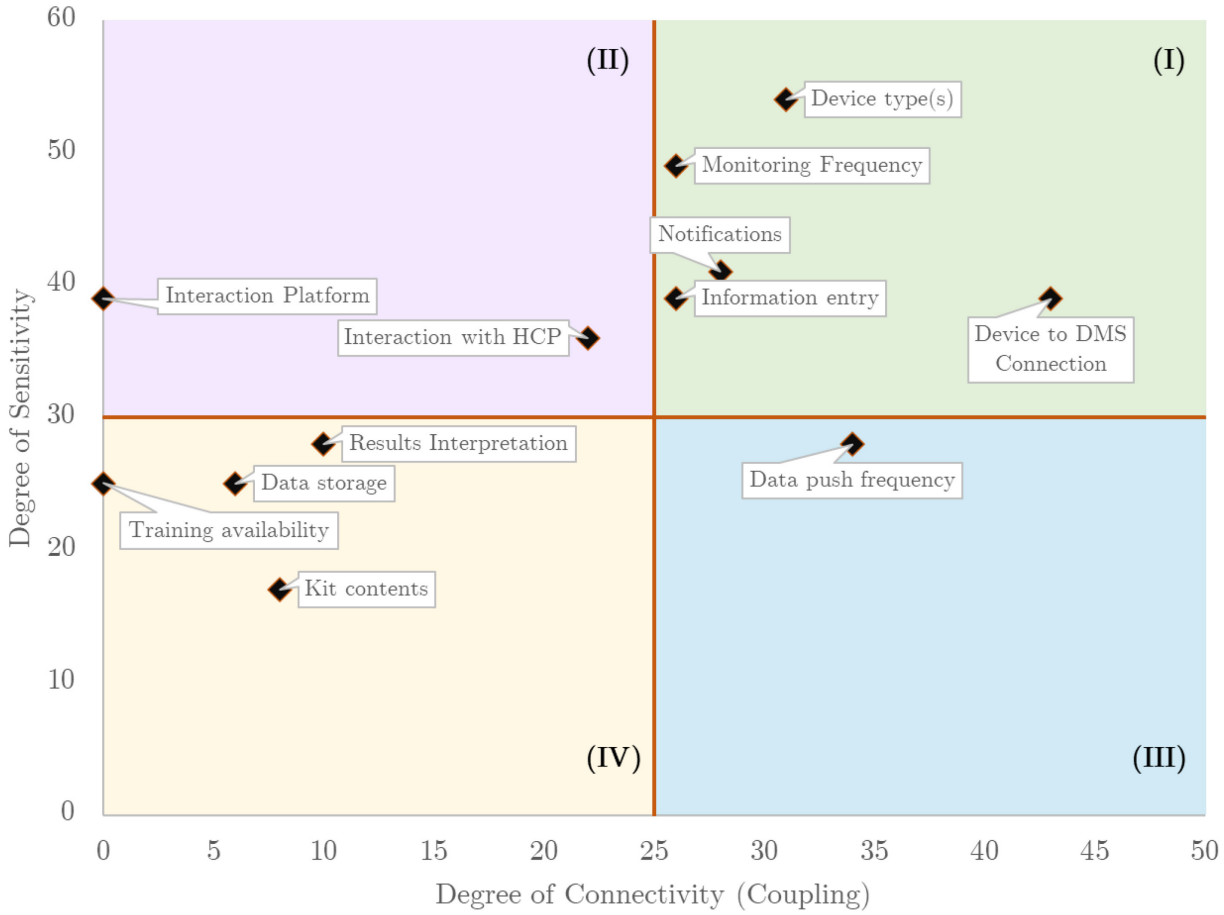

Figure 21. Sensitivity vs. Connectivity mapping of fertility RPM architectural decisions

(I) Highly coupled and highly sensitive

Prioritizing highly coupled and sensitive architectural decisions is crucial for successfully designing and implementing remote patient monitoring systems in fertility applications. These decisions encompass device types, monitoring frequency, information entry methods, and data management connections, all addressing critical design considerations

with significant impacts on performance objectives and stakeholder needs. For instance, the choice of device types directly influences the accuracy and reliability of data collection, affecting the precision of fertility predictions and the effectiveness of interventions. Similarly, tailoring monitoring frequency to align with patients' fertility windows enhances intervention timeliness and improves fertility outcomes. Additionally, the information entry method, whether automated or manual, impacts patient engagement and adherence to treatment plans, thereby influencing patient satisfaction.

(II) Low coupling but highly sensitive

While the interaction platform is not directly connected to other decisions, it substantially influences performance metrics. The value of remote patient monitoring hinges on its ability to connect patients with healthcare providers for better insights into patient health status. Although there is some flexibility in the embodiment of the interaction platform, prioritizing interaction with healthcare providers as a key feature in fertility remote patient monitoring systems is essential.

(III) Highly coupled but low sensitivity

The frequency of data pushing to healthcare providers is closely linked to the interaction with healthcare providers in Quadrant II. Real-time or appropriately timed patient health data is critical for timely interventions, especially in emergencies where healthcare providers rely on immediate measurements rather than AI algorithms. Therefore, this decision is crucial for enabling care teams to respond promptly to adverse measurements and ensure patient safety.

(IV) Low coupling and low sensitivity

Despite falling into the low coupling quadrant, training availability, data storage, and results interpretation decisions are close to the border between low and high sensitivity. While training availability does not directly influence other architectural decisions, it significantly impacts the adaptation of remote patient monitoring systems by providing relevant educational resources on system usage. Similarly, data storage and results interpretation decisions can affect system effectiveness. Establishing a direct connection to electronic medical records delivers substantial value by addressing fragmentation issues associated with storing medical information in multiple locations. Additionally, integrating AI to assist healthcare providers in analyzing monitored data is critical for preventing data fatigue and maximizing the value of remote patient monitoring systems.

Chapter 5

Technological Progress in RPM for Fertility

The growing demand for fertility health information has led to the emergence of innovative solutions that allow individuals to obtain fertility data from the comfort of their own homes. Many system properties outlined in the previous chapter have been implemented in at-home test kits and wearables, offering various options to support individuals and couples along their fertility journey. This chapter explores the range of devices currently available for fertility monitoring and assesses their compatibility with remote patient monitoring systems. Additionally, it discusses the limitations of the current systems, highlighting areas where further technological enhancements are necessary to meet user needs effectively.

5.1 Fertility RPM Device Evaluation

Remote patient monitoring systems depend highly on the devices conducting the medical measurements from afar. These systems enhance the timeliness of clinical decision-making and improve the accuracy of health measurements. For effective patient interaction, the devices are designed to be user-friendly and tailored to the patient's specific needs, which influences their size and design. The functionality and accuracy of these technologies are crucial in determining the reliability of the data when making clinical judgments.

5.1.1 At-Home Fertility Testing

At-home fertility testing allows individuals and couples to assess their reproductive health using simple kits that measure vital fertility indicators. These tests can be administered easily via samples like saliva, urine, or blood; results are typically available promptly or within a few days. The fertility metrics measured by these kits fall into three categories: (a) hormone levels, (b) physiological and metabolic health measures, and (c) reproductive health metrics. This discussion explores the suitability of various fertility metrics for integration into remote patient monitoring systems, considers examples of relevant

devices, and addresses their limitations.

(A) Measures of hormone levels and related devices

At the heart of fertility-related measurements are hormonal levels, which include sex hormones like FSH, LH, estradiol, and progesterone (measured through its metabolite PdG in urine). Tracking the fluctuations of hormone levels is a way to determine the fertility window and responses to fertility medications. Devices like *Clearblue Fertility Monitor* and *Mira Hormone Fertility Kit, Inito, Proov, and Oova* can measure these hormones and use their algorithm to pinpoint the days of high and peak fertility [88]. **Table 6** and **Figure 27** provide a comparison summary of these devices.

Figure 22. *Clearblue Fertility Monitor* [78]

Clearblue Fertility Monitor [89] includes a handheld monitor and urine test sticks to detect estrogen and LH levels for predicting fertile days. The device offers easy-to-read digital results indicating low, high, or peak fertility. Additional features include a calendar to track menstrual cycles, sexual activity, and test days, with the ability to store this data for up to six months. It also provides reminders to take tests at the appropriate times. Although the monitor is portable, it lacks connectivity to smartphones or mobile apps, and the initial purchase price does not cover the ongoing expense of replacement test strips.

Figure 23. *Proov Complete Kit* and associated mobile app. Adapted from [79]

Proov Complete Testing [90] utilizes test strips to measure four hormones, specifically FSH and three others using separate strips for E1G (an estrogen marker), LH, and PdG. Users dip a strip into the urine and either read the results visually like a pregnancy test or use the *Proov* Insight App, which translates these results into numerical data. The app enhances user engagement by notifying users when to collect and test their urine. However, the manual process of photographing and interpreting test strips might lead to issues with user adherence and variability in result interpretation.

Figure 24. *Oova Hormone Kit.* Adapted from [80]

The *Oova Fertility Tracker* [91] innovatively measures LH, PdG, and E3G quantitatively. This system includes test cartridges for E3G (estradiol metabolite), LH, and PdG, each equipped with a QR code for easy scanning via the *Oova* App. The app uses the smartphone's camera to analyze and display results. It also prompts users to perform scans on specific cycle days, offers a calendar to track the fertile window, and provides comprehensive reports summarizing hormone patterns, enhancing user interaction and data accuracy.

Figure 25. *Mira Hormone Monitor* and associated mobile app. Adapted from [81]

The *Mira Hormone Monitor (Clarity Kit)* [92] provides an in-depth hormonal analysis by measuring PdG, FSH, LH, and E3G, suitable for those with conditions like PCOS or irregular menstrual cycles. The kit includes single-use test wands and the *Mira* Monitor, which syncs data to the *Mira* app after the user dips a wand in urine and inserts it into the monitor. Results are displayed as charts, requiring user interpretation, and the app provides a fertility score predicted by AI, though this only predicts rather than confirms ovulation. The kit's cost, including 10 test wands, is about $249, and each cycle may require 10-20 wands.

Figure 26. *Inito Fertility Monitor* and associated mobile app. Adapted from [82]

The *Inito Fertility Monitor* [93] uniquely measures estrogen, LH, PdG, and FSH on a single test strip. The Starter Kit includes 15 test strips—enough for one cycle—and the monitor that attaches to a smartphone using a clip. It utilizes the phone's camera as a sensor, with the *Inito* App providing results and fertility predictions. The app also sends reminders for test timing based on hormone levels, with initial testing recommended on the sixth day of the cycle. However, because *Inito* relies on the phone's camera, compatibility is limited to specific smartphone models.

While these devices are valuable, very few published studies demonstrate these monitors' validity and clinical performance [94]. Their application in RPM would necessitate thorough validation in clinical studies to confirm that they deliver data robust enough for

sound clinical decision-making.

Table 6. At-home hormone fertility kits comparison

	Clearblue Fertility Monitor	Proov Complete Testing	Oova Fertility Tracker	Mira Clarity Kit	Inito Fertility Monitor
LH	✓	✓	✓	✓	✓
Estrogen	✓	✓	✓	✓	✓
FSH	✗	✓	✗	✓	✓
PdG	✗	✓	✓	✓	✓
AMH	✗	✗	✗	✗	✗
Cost (per kit)*	$162*	$99	$159	$259	$159
Sample Type	Urine	Urine	Urine	Urine	Urine
TTR	5 minutes	10 minutes	10 minutes	16 minutes	10 minutes
Interface Platform	Monitor Device	Mobile App	Mobile App	Monitor Device + Mobile App	Monitor Device + Mobile App
Claimed Accuracy	99%	99%	95% correlation to bloodwork	99%	NP*
FDA	Registered	Registered (cleared for PdG)	Registered	Registered	Registered

**Cost of Clearblue Monitor Device ($120) and Test Kits ($42)*

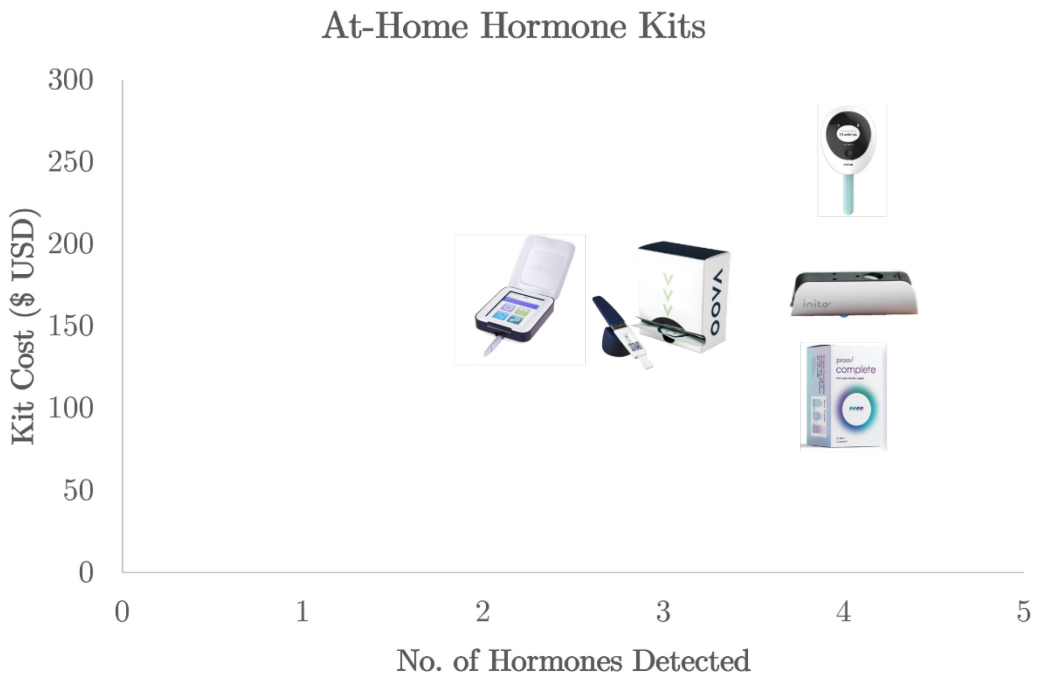

Figure 27. Cost comparison of at-home hormone kits based on the number of hormones detected.

(B) Physiological and metabolic health metrics and related devices

In addition to hormone level tracking, an intricate network of physiological metrics provides crucial insights into reproductive health. Physical measurements such as Basal Body Temperature (BBT), body mass index (BMI), activity level, blood pressure, and glucose levels also play a significant role in overall health and reproductive function. Devices for these metrics are more readily available as they are used more broadly for other applications beyond fertility tracking.

Fertility medications like letrozole, leuprolide, and estradiol can induce hypertension in females undergoing fertility treatments at 3-8% prevalence rates [95]. Preeclampsia is a specific form of hypertension that can cause damage to the mother's organs. Elevated blood pressure occurs in 10% of pregnancy [96] and 2% of postpartum [97] cases. Notably, hypertension contributes to 7% of maternal deaths, with 70% of those deaths occurring postpartum [98].

Additionally, high blood sugar levels can negatively impact reproductive hormones and menstrual cycles, leading to ovulatory dysfunction and decreased fertility [99]. Blood pressure monitors and glucometers are common remote patient monitoring tools for chronic disease management, including cardiovascular conditions and diabetes [100].

Activity and BMI/body weight. Wearables such as those from *Fitbit, Garmin,* and *Apple Watches* can track BMI/body weight and activity levels, providing insights into general health. They often have associated mobile apps for tracking and storing this information. Smart scales are also available as non-wearable options for tracking body weight and BMI.

Blood Pressure. Smart blood pressure monitors like *Omron Evolv* and *Garmin Index* provide convenient and accurate blood pressure monitoring at home and can be connected to patients' smartphones via mobile apps. These apps have built-in analysis and visualization features of results, as well as capabilities to share the data with HCPs. By regularly monitoring blood pressure, early detection and management of hypertension can reduce the risk of complications for both the mother and the developing fetus.

Glucose Levels. Similarly, glucose levels can be tracked using glucometers or continuous glucose monitoring (CGM), helping maintain optimal glucose levels is essential for fertility and pregnancy. For pregnant individuals with pre-existing diabetes or gestational diabetes, monitoring glucose levels is critical for preventing complications such as macrosomia (large birth weight) and birth defects. CGM systems like *Dexcom* [101] and *Freestyle Libre* [102] are sensor-based, wearable devices that can connect to mobile apps for results interpretations and data sharing. Diligently monitoring blood pressure and glucose levels provides valuable insights into glucose trends and enables timely interventions to maintain stable blood sugar levels throughout pregnancy.

Basal Body Temperature. Basal body temperature is more specific to fertility applications. BBT refers to the body's temperature at rest, typically measured immediately after waking up in the morning, before any physical activity. It is usually measured orally with a specialized basal body thermometer. This metric is different from body temperature, which generally refers to the overall temperature of the body and can vary throughout the day. Body temperature readings are commonly used to monitor fever using a regular thermometer (taken orally, rectally, under the arm, inside the ear, or trans-dermally on the forehead). BBT correlates with changes in the menstrual cycle, with a spike in BBT indicating ovulation. BBT can be manually charted, but digital solutions provide convenient data analysis. However, there are downsides to tracking BBT. The metric is susceptible to cycle changes and can fluctuate from stress, medication, and physical activity; therefore, BBT on its own is not typically not sufficient to predict fertility.

Examples of BBT thermometers are *Tempdrop, Femometer, Mira,* and *Natural Cycles*.

Tempdrop [103] is a wearable thermometer worn on the upper arm overnight, allowing for uninterrupted sleep while continuously monitoring BBT. It syncs with a smartphone app, providing comprehensive tracking and analysis tools for fertility patterns. Additionally, Tempdrop allows users to track their symptoms to verify ovulation and the results are provided on the app.

Figure 28. *Tempdrop* arm band. Adapted from [88]

Femometer thermometer (Vinca 2.0) [104], on the other hand, is a standalone BBT thermometer that can connect to the user's phone through the *Femometer* App. Upon waking, users are instructed to measure their temperature by placing the device under the tongue. The app provides visualization of the results and cycle interpretation, but some versions do not include a reminder for when the temperature should be taken.

Figure 29. *Femometer* thermometer [89]

Mira [105] is a digital handheld thermometer requiring manual temperature measurements, similar to *Femometer*. While not offering continuous monitoring like *Tempdrop*, it remains easy to use and portable. It utilizes the *Mira* App for logging and connects the thermometer via Bluetooth.

Figure 30. *Mira* BBT thermometer [90]

Natural Cycles [106] utilizes standalone thermometers like *Mira* and *Femometer* but also works with wearable sensors, specifically *Oura* rings and Apple watches. *Natural Cycles* is the only FDA-cleared birth control app, measuring temperature overnight in cases with Apple Watch and *Oura*, or in the morning using the *Natural Cycle* thermometer. The *Natural Cycles* app allows for finding fertility days using their proprietary algorithm to determine fertility status. It also provides calendar and symptom tracking features similar to other mobile app solutions.

Figure 31. *Natural Cycles* mobile app and associated wearables. Adapted from [91]

The effectiveness of these BBT solutions hinges on consistent user engagement and correct use of the device, factors that can introduce variability and compromise accurate readings, posing one of the key challenges in RPM environments.

Table 7. BBT device comparison

	Tempdrop	Femometer Vinca II	Mira BBT	Natural Cycles
Device Type	Wearable	Standalone	Standalone	Wearable* or Standalone
Data Collection Frequency	Continuous	Periodic	Periodic	Periodic or Continuous
Cost	$215	$59	$35	$119.99 Annual Subscription (with thermometer)
Interface Platform	Monitor Device + Mobile App	Monitor Device + Mobile App	Monitor Device + Mobile App	Monitor Device + Mobile App
Device Type	Wearable	Standalone	Standalone	Wearable or Standalone

*Optional Wearable Devices for Natural Cycles: Oura Ring ($299), Apple Watch ($399)

(C) Reproductive Health Metrics

The final grouping of fertility metrics is reproductive health measures, including AMH, semen analysis for male partners, and cervical mucus.

AMH. While many of the devices measure most reproductive hormones, one key infertility marker, AMH, cannot be directly measured at home with a remote patient monitoring device. AMH levels are typically measured through a blood test performed in a clinical setting, usually in a laboratory or healthcare provider's office. While home-based diagnostic testing solutions are available from companies such as *Modern Fertility* [107] and *Everlywell* [108], which provide kits for collecting finger-prick blood samples at home, these samples must still be sent to a laboratory for analysis. Results are typically provided after 2-3 days, so real-time detection is limited, and the method is unsuitable for on-demand monitoring to deliver timely interventions.

However, there is no consensus on the need for continual testing for AMH levels, with some studies reporting that AMH levels do not change during the cycle while others show

variation. A meta-analysis study to bring consensus concludes that AMH levels do differ between follicular and luteal phases of a cycle, and while AMH may not be required to be tested as part of monitoring, initial collection of samples should be timed appropriately [109].

Sperm Analysis. Other tests that may not be relevant for monitoring include male fertility kits, which are more targeted to analyze sperm in semen samples. While sperm count may fluctuate[110] and is susceptible to several intrinsic and extrinsic factors, periodic testing is generally adequate to assess fertility concerns. However, home kits for sperm analysis offer some level of convenience and privacy. Some examples of such kits include the *Yo Sperm Test [111], SwimCount [112], and* the *Spermcheck Fertility Test* [111], which utilize colorimetry for visual interpretation or smartphone cameras for interpretation via mobile app.

Cervical Mucus. Sperm function and viability for successful transport are dependent on vaginal pH and cervical mucus [112]. Cervical mucus changes throughout the menstrual cycle in response to hormonal fluctuations, becoming thin, clear, and stretchy around ovulation to facilitate sperm survival and transport. While observing cervical mucus can help predict ovulation and optimize timing for conception, it is a subjective and qualitative observation that may vary between individuals. Some devices have been developed that can be used to test cervical mucus at home and assist in identifying fertile windows. One device is *kegg* [113], which involves a device that can be inserted in the vagina and measures electrolyte levels of mucus. The FDA-registered device takes 2 minutes to capture information, which is sent over and analyzed using the companion mobile app.

Figure 32. *kegg* fertility monitor and associated mobile app [99]

5.1.2 Imaging Devices

The use of specialized assessments in fertility monitoring further complicates the technological landscape. Ultrasound technology is required for imaging and monitoring follicular and embryo development and remains largely restricted to clinical environments due to the need for specialized equipment and expertise for precise imaging and analysis

capabilities.

Follicle count, ovarian volume, and endometrial thickness are typically assessed via transvaginal ultrasound, which provides detailed images of the uterus, ovaries, and follicles. The procedure requires sophisticated ultrasound machines operated by trained professionals who can accurately identify and measure the follicles and the overall ovarian structure. The equipment is expensive and requires a controlled environment and technical expertise for accurate operation and data interpretation.

Fetal heart rate monitoring is an essential aspect of prenatal care, typically performed using Doppler fetal monitors or more detailed ultrasound equipment in a clinical setting. While there are home-use Doppler devices available, these are generally recommended for occasional use and do not replace detailed assessments in a clinical environment. These home devices also raise concerns about overuse or misinterpretation of the data by laypersons, potentially leading to unnecessary anxiety or reassurance without proper medical consultation.

While there are ongoing developments in portable ultrasound devices[114], [115], such as handheld ultrasound units that can connect to smartphones, these technologies are still primarily in the prototype stage or are used as an adjunct to clinical care rather than for independent home use. Regulatory approvals, data accuracy, cost, and the need for professional oversight are significant hurdles that prevent these devices from being integrated into remote patient monitoring systems for home use. Therefore, while the technology is advancing, the complexity of these measurements and the critical nature of their accurate interpretation ensure that they remain within the walls of specialized clinics for the foreseeable future.

5.2 Device Readiness

The Technology Readiness Level (TRL) scale is employed to evaluate the overall readiness of these various fertility devices for their potential inclusion in fertility remote patient monitoring systems. The TRL scale, initially developed by NASA and now widely used in various industries, provides a systematic metric to assess the maturity of technologies [116]. The scale ranges from TRL 1 (basic principles observed) to TRL 9 (actual system proven through successful mission operations).

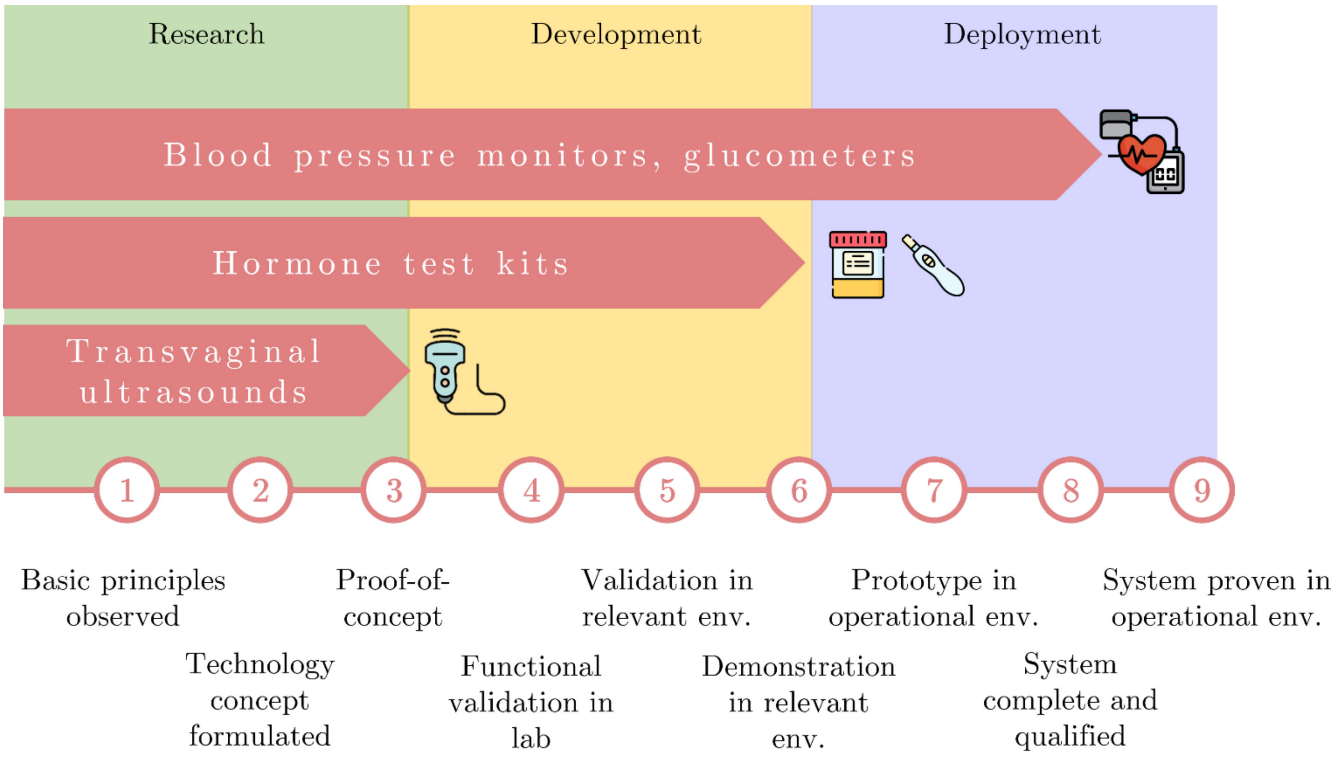

Figure 33. Technology readiness level (TRL) for fertility-related devices in the context of RPM

Figure 33 presents the readiness levels of various medical devices relevant to fertility care, specifically for fertility remote patient monitoring. Blood pressure monitors are at TRL 8 because they are fully developed, have undergone various validations, and are currently used in various real-world RPM environments. Although not specifically validated for fertility applications, their utility in monitoring pregnancy-related conditions like preeclampsia makes them highly relevant and adaptable to fertility-related RPM systems. Similarly, glucometers are technologically mature and widely accepted for their current primary RPM application of diabetes management. Monitoring glucose during pregnancy, especially in high-risk pregnancies, presents a potential for glucometers to be included in fertility RPMs. In the US, both glucometers and blood pressure monitors are regulated as Class II medical devices. To fully integrate these technologies into fertility RPM systems, their corresponding metrics need to be aligned with fertility outcomes that can help HCPs and decision-makers make proper interventions.

Despite their widespread commercial availability and consumer use, hormone tests are rated as TRL 6 for RPM fertility applications. The rating reflects the absence of a proven, dedicated RPM system that integrates these tests for fertility monitoring at this time. The primary barriers to advancing these hormone tests in RPM systems include the need for further validation to ensure their accuracy and reliability in home settings.

Additionally, regulatory approvals specific to their use in RPM need to be addressed, along with ensuring robust data security measures to protect sensitive health information.

The least mature of the discussed technologies for RPM fertility applications are at-home ultrasound and other imaging technologies. Rated at TRL 3, prototypes of such devices offer promising capabilities for monitoring reproductive health but are still in the conceptual phase with little real-world demonstration. The challenges here are considerable and include the need for significant technological advancements to ensure the devices can provide medical-grade imaging. Additionally, extensive clinical validation is required to confirm their efficacy and safety, alongside comprehensive user training programs to ensure accurate and reliable home use.

Despite the significant strides in technology development and the availability of a range of devices designed to measure various fertility metrics, the field still faces substantial challenges in creating a cohesive RPM system. Current solutions tend to be fragmented, requiring the use of multiple devices and the manual integration of data, which is less than ideal for RPM where streamlined operations and minimal patient intervention are preferred. The development of a comprehensive system that integrates hormonal levels, physical measurements, and specialized assessments into a single RPM framework remains an essential goal. Such a system would not only facilitate real-time, holistic monitoring supported by robust data analytics but also transform RPM into an effective tool for managing fertility and pregnancy, thus marking a significant advancement in reproductive health technology.

5.3 Interoperability

In addition to the challenges that exist in device maturity and validation for fertility monitoring, the ability of those different systems and applications to exchange and interpret data seamlessly remains a persistent challenge within the healthcare industry. Despite the availability of health information collected and stored by numerous fertility devices in the cloud, this data often remains locked within proprietary data silos, inaccessible to healthcare professionals. Such lack of interoperability exacerbates the fragmented nature of healthcare information technology, leading to inefficiencies in the healthcare system.

Interoperability among devices, regardless of their source or vendor, is crucial for effective remote patient monitoring systems. When devices used in RPM programs are interoperable, they can communicate not only with each other but also with other

healthcare systems, such as electronic health records, healthcare provider portals, and analytics platforms. While comprehensive discussions and solutions to interoperability issues lie beyond the scope of this research, it is essential to acknowledge its significance in designing end-to-end remote patient monitoring programs utilizing available market devices.

A significant factor contributing to interoperability challenges is the diverse array of healthcare data types, each with its unique characteristics and requirements. These data types encompass a broad spectrum of clinical information, including patient demographics, medical history, diagnoses, treatments, medications, laboratory results, imaging studies, and vital signs. Additionally, data may be structured or unstructured, originating from various sources such as EHRs, laboratory information systems, medical devices, government agencies, and telehealth platforms.

For fertility applications, many devices are integrated with companion mobile applications, necessitating connectivity with EHRs for seamless data access. Such app connections and data exchanges are commonly facilitated through application programming interfaces (APIs). Notably, the 21st Century Cures Act of 2020 has simplified the integration of third-party apps by promoting the use of standards-based APIs, such as those utilizing Health Level Seven (HL7) Fast Healthcare Interoperability Resources (FHIR) data exchange [117]. It's noteworthy that approximately 28% to 35% of patient engagement and care management applications, similar to those required for fertility remote patient monitoring, currently utilize FHIR standards. Companies like Apple have demonstrated the feasibility of remote patient monitoring directly connected to EHRs, including innovative applications in neonatal care at institutions like the University of Virginia[118]. Furthermore, Apple has provided a toolkit [119] for third-party mobile app developers, facilitating compatibility with Apple Health and fostering collaborative efforts to promote the adoption of interoperable health IT solutions.

5.4 Fertility RPM Use Case Examples

This work examines four primary use cases and environments for a fertility RPM system, corresponding to the three main phases of fertility outlined in **Section 2.4**. These examples, inspired by stories from interview participants, serve as representative scenarios. While they illustrate a range of applications, they are only partial of some potential uses and not exhaustive of all situations for fertility RPM solutions. These use cases showcase possible implementations of RPM. Additionally, an example fertility RPM kit is provided to illustrate the customization required for each patient and use case. The RPM kits are

based on available and potential devices, presuming complete validation and integration of RPM systems.

5.4.1 Fertility Use Case #1: Preconception Care

For this use case, the goal of the RPM is to enhance fertility awareness and provide tailored health interventions to improve the likelihood of conception. Successful outcome is early identification and management of potential fertility issues.

Actors and Actor Profiles:

- **Patient ("Jane"):** 30-year-old female planning to conceive with a male partner. Jane has an implanted hormonal intrauterine device (IUD) for over 5 years, which has led to irregular menstrual cycles (a common side effect of this type of birth control). Because of period irregularity, her ovulation patterns are uncertain. While Jane has not been pregnant before, she has no known existing condition that would compromise fertility, except for some family history of infertility. Jane is, otherwise, in good physical health. The male partner does not have known infertility issues. Jane consults with an OB-GYN to remove the birth control and discuss the intention to conceive over the next year. Jane does not have coverage for fertility services and lives in a U.S. state without a fertility care mandate.

- **HCP**: Primary care physician with OB-GYN specialty. HCP's clinic is a medium-sized family clinic in a metropolitan area. HCP consults and provides care to Jane for annual physicals and reviews birth control options. HCP previously performed IUD insertion on Jane and will be removing the IUD in the upcoming appointment. HCP is assisted by the practice's dedicated **nurses** and **medical assistants** (MA's).

Pre-conditions:

- HCP removes Jane's implanted birth control after consultation regarding family planning.
- Jane's age and health status are low risk for infertility, and HCP recommends a natural conception route.
- Familial history and lack of regular menses lead to a need for monitoring, and Jane voluntarily enrolls into an RPM program.
- Jane receives an at-home hormone kit and instructions to connect to the RPM system through a mobile application.
- HCP and supporting staff have access to data reported via the RPM system.

Post-conditions:

- Jane receives regular updates and personalized recommendations based on the monitored data.
- HCP and/or staff reviews collected data periodically over a period of pre-determined time and schedules consultations, as deemed necessary.
- The RPM system for preconception care ends at Jane's discretion and the recommendation of the HCP.

RPM Features:

As Jane does not have insurance coverage, cost is a big factor in the fertility care that is provided to her. Her HCP determines to begin with tracking her hormone levels over two cycles and recommends tracking any menstrual symptoms manually post-IUD removal. HCP also recommends timed intercourse as the initial method for conception.

Figure 34. Potential RPM concept for a preconception use case

- *Menstrual Monitoring:* Since the hormonal IUD has suppressed Jane's menstrual cycle, the RPM system includes features that monitor limited hormonal levels through urine that tracks specific biomarkers. The device included could help predict the return of the patient's natural cycle once the IUD is removed.
- *Health Tracking:* RPM syncs with any wearable device and scale Jane already owns to track health and fitness goals. As hormones fluctuate after an IUD, information to be collected and recorded may include physical activity, heart rate, body weight and BMI, and dietary intake.

- *Conception Planning Tools:* The RPM system includes a menstrual cycle feature to log cycles or symptoms, and data analytics provides feedback to predict fertile windows with increasing accuracy over time.
- *Indirect Communication with Healthcare Providers:* The system facilitates seamless communication with her gynecologist. This implementation includes the possibility of virtual consultations and the ability to send data to her medical team at periodic intervals.
- *Medication and Treatment Tracking:* Post-IUD removal, if hormonal supplements or other treatments are needed to regulate her cycle, the system can track her medication schedule and send reminders, ensuring adherence to treatment protocols designed to optimize her fertility.

5.4.2 Fertility Use Case #2: Conception Care + Fertility Care Treatment

During fertility treatments such as IVF, patients would benefit from features that monitor medication adherence, schedule reminders for treatment milestones (like hormone injections), and provide direct communication channels with their healthcare providers. The goal of RPM in the context of conception and fertility care treatment is to enhance the management of fertility treatment(s) that increase the rate of conception and pregnancy. Successful outcomes include implantation with reduced in-person visits prior to the required in-person procedures (e.g., egg retrieval and embryo transfer)

Actors and Actor Profiles:

- **Patient ("Leah"):** 34-year-old female trying to conceive through IUI for over a year without success with a female partner. Leah is in good physical health, has not been pregnant previously, and has no reported familial history of infertility. Initial fertility workup does not indicate significant abnormalities. Leah and her partner seek other assisted reproduction procedures, which are covered by their insurance. Leah lives on one of the islands in Hawai'i that do not have a fertility clinic available.

- **HCP:** The primary care team consists of a reproductive endocrinologist, nurses, physician assistants, and medical assistants. Leah's doctor is a reproductive endocrinologist in a fertility clinic on the nearby island. The clinic is equipped with advanced technologies, including direct, digital communications and electronic health records.

Pre-conditions:

- Leah has been evaluated by an IVF specialist and is considered a candidate for IVF treatment.
- Leah voluntarily enrolls in an RPM program.
- The fertility care team provides all necessary RPM devices to be used at home, including at-home hormone kits, instructions to connect to the RPM system through a mobile application, and medications associated with IVF treatment.
- HCP and supporting staff have access to data reported via the RPM system.

Post-conditions:

- Leah receives regular updates and personalized recommendations based on the monitored data.
- HCP and/or staff review collected data and provide any adjustments to treatment.
- Monitoring continues when the trigger shot is administered through successful embryo transfer and implantation, indicating IVF success.

RPM Features:

Because of insurance coverage and the tools that the fertility clinic has established, Leah is able to receive a reasonably comprehensive RPM kit to support her IVF treatment. The kit contains the standard IVF medications required to be administered throughout her cycle.

Figure 35. Potential RPM concept for a fertility treatment use case

- *Virtual Consultations and Continual Monitoring:* The RPM system allows Leah to have regular virtual consultations with her reproductive endocrinologist and the care team. This feature is crucial for Leah, who cannot easily travel to the clinic on another island for frequent visits. Based on information generated through the system, consultations may also include support for the next step of the IVF process, including virtual scheduling of follow-up in-person visits.
- *Comprehensive Hormonal Monitoring:* During the IVF process, hormonal medications are administered to stimulate the ovaries to produce multiple eggs. Monitoring hormone levels (e.g., FSH, LH, estradiol) will help assess the response to the stimulation and adjust dosages if needed. Assessment of hormones also allows for ovulation to be predicted more accurately and when the trigger shot should be administered. The system includes a comprehensive fertility tracking tool that Leah can use to enter relevant fertility data. The HCP team has access to real-time data inputs, enabling timely interventions and adjustments to her treatment plan based on her response to treatments.
- *Medication Management and Reminders:* As Leah undergoes fertility treatments, managing medication schedules becomes critical. The RPM system offers medication reminders, alerts, and notifications for any complications that may arise and require immediate attention.

5.4.3 Fertility Use Case #3: Pregnancy Care

In conception and ongoing pregnancy care scenarios, the system should enable providers to remotely monitor gestational age-specific metrics, adjust medications, and detect early signs of complications such as ectopic pregnancies or miscarriages, thereby facilitating timely interventions. The remote patient monitoring system aims to promote a healthy pregnancy up to delivery, ensuring the safety of both mother and baby throughout the process. The RPM enables early detection and management of potential complications, especially for those with significant needs due to riskier profiles.

Actors and Actor Profiles:

- **Patient ("Daisy"):** 39-year-old pregnant female (16 weeks gestation). Daisy has two previous pregnancies, with the most recent resulting in preterm labor at 30 weeks. Due to Daisy's advanced maternal age and history of preterm delivery, her pregnancy is considered high risk for complications such as high blood pressure, preeclampsia, and gestational diabetes. Daisy works full-time with a standard work schedule of Monday to Friday. Daisy's employer provides medical insurance covering maternity care and delivery.

- **HCP:** The HCP working with Daisy is an OB-GYN at the nearby Women's Health Center of a large hospital. The hospital has a dedicated department specializing in high-risk pregnancies, supported by nursing staff, medical assistants, nutritionists, and maternal-fetal specialists.

Pre-conditions:

- Daisy's pregnancy is considered high-risk by their healthcare provider, and she agrees to engage in an RPM program.
- Daisy receives training on how to use RPM devices and the associated mobile application effectively.
- A secure, compliant system is set up for collecting, transmitting, and storing sensitive health data.

Post-conditions:

- Continuous real-time health data is available to the healthcare team.
- The patient receives regular, personalized feedback and instructions based on her health data.
- The RPM program ends with the delivery of the baby.

RPM Features:

Daisy's medical risk requires tracking of multiple metrics. The devices assigned include a handheld EKG device, a smart blood pressure cuff, and a non-continuous glucometer.

Figure 36. Potential RPM concept for a high-risk pregnancy use case

- *Periodic Health Monitoring:* Devices integrated with the RPM system monitor Daisy's vital signs, including blood pressure and heart rate, necessary for detecting signs of hypertension or preeclampsia. Blood glucose levels are to be monitored daily for signs of gestational diabetes. A fetal monitoring system is also provided to monitor fetal heart rate.
- *Custom Alerts and Notifications:* The system is configured to alert Daisy and her healthcare team if any monitored parameters deviate from normal ranges. This feature allows for prompt response to potential complications, potentially preventing emergencies. Additionally, the custom notifications allow for reminders of prenatal appointments. Customization of treatments may also be deployed through this portal to push notifications for required medications or dietary recommendations to manage any health-related responses to the pregnancy.
- *Telehealth Consultations:* The RPM system enables Daisy to have regular telehealth consultations with her OB-GYN and other Women's Health Center specialists. These visits can be used for non-urgent consultations and health checks but should be supplemented by in-person visits due to the high-risk nature of the pregnancy.

5.4.4 Fertility Use Case #4: Postpartum Care

The fertility journey definition ends with postpartum care. In post-delivery scenarios, the RPM system should enable continuum care for mothers recovering from childbirth. The goal of the system is to track vital health indicators that would indicate any signs of postpartum complications.

Actors and Actor Profiles:

- **Patient ("Ella"):** 26-year-old new mother of a healthy baby boy. Ella is a first-time mother and was recently discharged from the hospital after a normal delivery. Ella has no prior existing conditions and received standard prenatal care, but experienced some anxiety during pregnancy. Ella lives in the city and relies on public transportation to move around for work and medical appointments.

- **HCP:** The HCP working with Ella is an OB-GYN in the city hospital. The OB-GYN is the same physician who has provided prenatal care to Ella during her pregnancy and delivered the baby. Therefore, the doctor is familiar with Ella's medical history.

Pre-conditions:

- Ella agrees to enroll in an RPM program.
- Ella receives training on how to use RPM devices and the associated mobile application effectively.
- A secure, compliant system is set up for collecting, transmitting, and storing sensitive health data.

Post-conditions:

- Continuous real-time health data is available to the healthcare team.
- The patient receives regular, personalized feedback and instructions based on her health data.
- The RPM program ends after the postpartum period (~6 weeks post-delivery) or clearance from the care team.

RPM Features:

With an overall healthy pregnancy and delivery, Ella's needs are simpler, primarily focusing on any risks of hypertension and symptom tracking for potential complications like infections or hemorrhaging.

Figure 37. Potential RPM concept for a healthy postpartum use case

- *Vital Signs Monitoring:* Postpartum hypertension remains a risk even after an uncomplicated delivery, so consistent monitoring is key for early detection and management. Weight is also tracked to ensure there are no sudden losses or failures to return to pre-pregnancy weight, which can indicate further health issues.

- *Telehealth Consultations:* The RPM system enables Ella to have established communication channels with her OB-GYN to discuss any concerns or questions. Additionally, the care team can regularly check in with Ella on her recovery and be alert for symptoms of excessive bleeding, hypertension, or depression.
- *Custom Alerts and Notifications:* The system is set up to alert Ella and her healthcare team if any monitored parameters fall outside the normal range. This functionality enables timely intervention to potential complications, which can prevent emergencies. Moreover, the system includes customized notifications that remind her of postpartum appointments.
- *Educational resource:* The system provides Ella with access to educational materials prepared by her care team, covering topics such as physical recovery, breastfeeding, and mental health services. These resources are designed to guide her through the postpartum period, providing essential information on health management and expectations, which is especially valuable as she navigates motherhood for the first time.

Table 8. Summary of architectural concepts for example use cases

	Jane (Preconception)	**Leah (Conception)**	**Daisy (Pregnancy)**	**Ella (Postpartum)**
Monitoring frequency	Periodic	Continuous	Periodic (Daily)	Periodic
Kit contents	Device	Device and medications	Device	Device
Device type(s)	Mix (standalone and wearables)	Mix (standalone and wearables)	Mix (standalone and wearables)	Standalone
Data storage	Local	EMR/EHR connected	Cloud server	Cloud server
Interaction platform	Standalone	Mix (mobile app and web portal)	Mix (mobile app and web portal)	Phone / mobile app
Interaction with HCP	Indirect	Direct communication with HCP	Direct communication with HCP	Direct communication with HCP
Notifications	None	Active	Passive	Passive
Training availability	Printed manual from kit	Mix	Mix	Online guidance
Device to DMS connection	None	Mix (Wi-Fi and Bluetooth)	Mix (Wi-Fi and Bluetooth)	Bluetooth
Information entry	Manual data entry	Automatic	Manual data entry	Automatic
Data push frequency	Periodic	Continuous	Periodic	Continuous
Results interpretation	HCP-driven	HCP-driven, AI-aided	HCP-driven	HCP-driven, AI-aided

Chapter 6

Future of Fertility Care

6.1 Conclusion

This study highlights the intricate and diverse nature of the fertility journey and explores how remote patient monitoring systems within this spectrum of care can be tailored to harness the opportunities they present for enhanced connected care across different stages of fertility. A design framework is proposed by analyzing essential fertility metrics and the technologies available to track them. This framework enables healthcare institutions to customize and integrate remote monitoring solutions into their range of fertility services, thereby enhancing the options available to patients.

Integrating remote patient monitoring systems in fertility care marks a pivotal shift towards a more patient-centric, accessible, and data-informed approach in reproductive healthcare. This transition, propelled by digital solutions such as advanced medical devices, mobile health apps, and telehealth platforms, promises to revolutionize how individuals and couples manage their fertility journeys from preconception to postpartum. These technologies provide opportunities for improved decision-making and enable healthcare providers to deliver tailored and timely interventions essential at various stages of fertility.

Designing effective, customizable, and cost-efficient RPM systems demands a nuanced understanding of the unique needs at each phase of the fertility process. The systems must be highly accurate to meet performance metrics critical for monitoring physiological parameters like hormone levels, basal body temperature, and heart rate variability. This precision is crucial in providing patients with reliable data, enhancing their ability to make informed fertility decisions.

Customization is fundamental to RPM design in fertility care. Given the complex and highly personal nature of fertility issues, RPM solutions must be adaptable to meet diverse patient needs across various stages, including conception, ongoing fertility treatments,

pregnancy, and the postpartum period. This concept acknowledges that fertility issues can vary widely among individuals and that a one-size-fits-all approach may not be effective in addressing the diverse range of fertility challenges. The design of an RPM system involves evaluating architectural decisions and requires modularization of different components. Such adaptability ensures that interventions are timely and precisely aligned with individual patient profiles and treatment plans.

Additionally, cost-effectiveness is vital in RPM system design. By reducing the frequency of in-person consultations and optimizing resource allocation, RPM can decrease the overall costs associated with fertility treatments. Improved timing of interventions through continuous monitoring can also enhance treatment efficacy, potentially reducing the duration and intensity of fertility treatments required.

To fully harness the benefits of RPM in fertility care, a robust technological infrastructure is essential, which includes interoperable electronic health records, secure telehealth services, and advanced data analytics capable of processing extensive datasets to extract meaningful insights.

In conclusion, the future of RPM in fertility care looks promising, offering significant improvements in the quality, accessibility, and personalization of reproductive health services. Fully realizing this potential requires addressing both technological and interoperability challenges. It necessitates a collaborative approach involving patients, healthcare providers, technologists, and policymakers.

6.2 Suggestions for Future Work

The path ahead for RPM in fertility care is about bridging the gap between technological potential and patient-centric care, ensuring that the solutions developed integrate seamlessly into patients' lives and contribute positively to the journey toward parenthood.

Firstly, it is crucial to undertake effectiveness and receptiveness studies that quantitatively analyze the success of RPM systems. These studies should measure clinical outcomes such as pregnancy rates, patient adherence to treatment plans, and overall treatment duration. In addition to empirical data, understanding patient and provider acceptance of RPM technologies is essential. This data can be collected from pilot studies and clinical trials aimed to validate the practicality, patient satisfaction, and clinical impact of these systems in real-world settings.

Technological advancements also play a pivotal role in the evolution of RPM in fertility care. There is a pressing need for more sophisticated monitoring devices that offer enhanced imaging and hormone-monitoring capabilities. Such innovations would allow for precise, non-intrusive tracking of fertility-related parameters. Furthermore, addressing interoperability issues between different RPM devices and existing medical records systems is critical. Ensuring robust data privacy and security protocols is equally important, given the sensitive nature of health data involved.

Economic considerations are another crucial aspect. Conducting cost-effectiveness analyses to evaluate whether RPM systems can reduce the high costs associated with fertility treatments is essential. These studies should consider direct and indirect costs to determine the overall economic benefits. Moreover, engaging insurance providers to integrate RPM into reimbursement codes will be vital for its broader adoption and sustainability.

Finally, RPM's ethical, legal, and social implications in fertility care cannot be overlooked. The sensitive nature of reproductive health data necessitates strict adherence to ethical and legal standards to protect patient privacy and ensure data security. Comprehensive regulatory frameworks need to be established to guide the use of RPM technologies specifically tailored to the nuances of reproductive health. Additionally, the integration of RPM in fertility treatments might provoke broader social and political discussions, especially in regions where reproductive rights are a contentious issue, highlighting the need for thoughtful policy-making that considers the unique vulnerabilities associated with fertility data.

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