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Faculty of Business Administration and Management

Transforming fertility services into remote health care

Master's Thesis

Master's Degree in Business, Product and Service Management

AUTHOR: Almudéver Galán, Miguel Ángel

Tutor: Miguel Molina, María Blanca de

ACADEMIC YEAR: 2021/2022



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1 Introduction

As a former IT consultant and IVIRMA employee for the last 10 years, both Technology and Health Care (with special focus on the field of fertility) have been my background and knowledge areas.

Within a particular context in the last years with the rising of Technology, remote services and more focus on patient-centric initiatives, providing Health Care at home is becoming a must for organisations. There are many opportunities in the market to make it possible and to make it happen.

As the world evolves and the different scenarios (social, environmental, technological...) approach patients to the acceptance of remote services, the fertility clinics adapt to their patient's demands in three major steps:

1. Evolve their current model, *the fully presential model*, so that patients need to visit their locations less and less
2. Transition to a *hybrid model*, where video-consultations, applications to interact with patients and basic remote services are part of their offering
3. Reach the fully *non-presential model*, where remote services along with at-home and third-party services integrate to improve the patient's time to pregnancy, service level and overall satisfaction

These models are based on we could refer to as the clinic's offering. Depending on the services provided and the patient's willingness to accept these services, the model in which a clinic might sit depends on:

- If patient's attendance to the clinics is required for all type of services or just specific services such as pick-ups, transfers or surgeries that happen in operating theatres
- How automated is the interaction and the human supervision on the results of the needed patient monitoring
- If space and time is aligned or dissociated between patient's monitoring and consultation-doctor's review and clinical decision making
- The degree of artificial intelligence integration in the technology related processes where AI can be used as support for decision making
- The personalization (and automation) of the required reporting for patient's information on their treatment and expectation in results
- And finally, how affordable this might be in the overall context of the cost of a fertility treatment

1.1 Objective

The objective of the TFM is to analyse in depth the convenience of transforming every medical interaction with patients that is required on fertility care as a remote service.

In another words: to redefine the patient journey to evaluate how many of the compulsory visits to the clinics can be replaced by a patient-at-home service. With a look on the current or upcoming state of art of technology.

1.2 Why is this important?

The provision of high-quality services for family-planning, including fertility care services, is one of the core elements of reproductive health. That is why there are so many laws/policies around the world supported by national and global fertility societies.

It is important to recognize the impact of infertility on people's quality of life and well-being, and therefore investing on fertility care by collaborating with partners to conduct global epidemiological and etiological research into infertility.

1.3 Are there new opportunities to transform fertility care today?

Supporting the generation of data on the burden of infertility to inform resource allocation and provision of services is one of the options.

This could be rewritten as something like this: let's make it possible to collect patient's data remotely and provide fertility care from home. It would be a huge step forward for patients to be able to be treated and monitored from home avoiding the need to visit the clinics – except for surgery needs.

Diagnosis and treatment of male and female infertility with global norms and new standards of quality care related to fertility, considering it as a remote service with the patient's comfort to be at home is about to come.

1.4 Methodology

The approach to this TFM will be driven towards the understanding on how a new product/service could be set to provide remote health care on fertility.

As a combination of several paths to reach the final goal, we can count on the following methods throughout the coming pages:

- Bibliographic reviews
- Experience and observation of the infertility market
- Process analysis.

So, as stated above, data used in these methods are obtained from both primary (experience, observation, process analysis) and secondary sources (bibliographic review, market, technologies).

Qualitative research is therefore the main driver of the document along with some quantitative references to the current situation and opportunities on the market.

1.5 Document structure

The structure of this document is as follows.

After this introduction, section 2 includes Maturity to accept remote and at-home services, which analyses companies offering remote services followed by some figures around the fertility market and required digital competences.

After that, we will find in section 3 some business models in the market and technology opportunities followed by the value proposition on section 4.

The most extended description of the document happens in the implementation of the service, split into section 5 and section 6.

In section 5 we will find the journeys for patient and clients, if we want to make that distinction... along with the required core services and organization in the clinic.

On the next section, named as steps forward in the implementation, the covered topics are related to online consultations, patient portal, testing kits and ultrasound images.

This document review will end up with a service cost and service value description, detailing aspects related to services, software and devices to continue with a relevant item to cover at home service which is section 8, about logistics.

2 Matureness to accept remote and at-home services

To be able to cover the matureness of the market and the services, the review will be segmented in three different aspects to cover complementary views: on one side, companies offering remote services; on another side, the digital competences that those companies have had to develop to reach that stage... and finally some figures around the fertility market.

2.1 Companies offering remote services

We will find below some samples on how remote and/or at-home services are changing the way patients interact with healthcare professionals, not only in the infertility world but also in other specialties or health service offerings.

Market data indicates that remote health services, including those related to fertility, have grown in recent years and will continue to do so in the future – see links to Statista data:

- <https://es.statista.com/outlook/dmo/digital-health/ehealth/ehealth-apps/worldwide>
- <https://www.statista.com/outlook/dmo/digital-health/ehealth/spain#revenue>
- <https://www.statista.com/outlook/dmo/digital-health/ehealth/ehealth-apps/contraception-fertility-apps/worldwide?currency=usd#revenue>
- <https://www.statista.com/statistics/1266681/fertility-services-market-value-worldwide/>

Many examples of application of remote services, some of them developed from confinement and some others with a longer run and experience as a company can be found to sustain the statements shared above.

Let's take a look at some examples, close in most of the cases to the fertility market, that help understand the growth of remote services.

1. [E-Procreate]. Virginia, USA. Sample of a clinic

e-Procreate provides remote consultations, fertility testing, and evaluation from the comfort of home, specializing in managing all fertility issues.

Patients can be seen remotely (or in person, of course) and all type of treatments will accommodate to the patients' needs with the remote option.



Figure 1. Workflow on patient treatment provided by e-Procreate

Testing kits and collecting the samples at home are the way to manage analysis... compared to the non-remote option consisting in using nearby labs for blood draw. Pelvic ultrasounds and tubal dye studies can also be arranged to happen at home.

2. [Embryolab]. Greece. Sample of a clinic

As technology and science have evolved dramatically, the vast majority of couples will eventually seek treatment far from their place of residence. Especially during the period of social distancing that showed up after COVID-19, it is extremely important for a couple to be able to proceed seamlessly with their treatment, even from home.

Embryolab welcomes hundreds of couples from all over Europe and around the globe with innovation in the field of online communication and Internet services; new applications like [Embryolab Connect](#), [OnlineIVF](#), [MyEmbryolab App](#) are samples of how to provide remote audiovisual services to everyone.

3. [Equipo Juana Crespo]. Valencia. Sample of a clinic

Telemedicine has been the solution in a pandemic but, in the case of fertility clinics, it has reached another level. Forced by circumstances, the solutions have gone much further than video consultations or the use of mobile applications, involving the patient in medical procedures in the purest "Ikea style": good instructions, appropriate tools and do it yourself.

For example, to avoid travel and reduce visits to the consultation, patients were proposed to have the follicular examination themselves. In the first moments of the pandemic, the clinic started with telemedicine, both to carry out consultations with specialists and for ultrasound follow-ups of their patients where, in October 2020, they offered the option of having an ultrasound self-examination in their own home.

New protocols were created, adapting the available technology: through portable probes, which patients receive at home at no additional cost, woman can perform a vaginal ultrasound guided by her specialist with the same quality as in person. Thanks to this system they can follow the treatment in the stimulation phase comfortably from home reducing the need to move to the oocyte puncture and the embryo transfer in the case of in vitro fertilization treatments.

4. [Instituto Marqués]. Barcelona. Sample of a clinic

In Barcelona, Instituto Marqués offers its male patients the possibility of freezing the semen sample themselves in their own homes to send it to the clinic. Thus, they developed a simple protocol for the self-freezing of semen, called *Sperm Freezekit*, which they offer to their patients thanks to which people without previous training are able to follow it outside the laboratory with the same result as biologists.

Although its emergence took place during the COVID health crisis, they began to study the technique in 2017. In fact, at the last congress of the *Association for the Study of the Biology of Reproduction (Asebir)*, the case of the first live birth from a seminal sample frozen at home by the patient himself and following a study to evaluate the effectiveness of this method was presented. First in the pilot phase and then in the validation phase, they found that, after evaluating the mobility, morphology, vitality and fragmentation of their DNA, the quality of the sample was the same as if it were done in the laboratory.

Until April 2021, 21 patients performed the self-freezing kit and nine of the samples were used in assisted reproduction treatments. No significant differences were found in terms of fertilization rates with respect to the control group, blastocyst, or pregnancy. The fact of having a live birth of a sample frozen by the patient himself demonstrated the safety and clinical utility of this novel freezing protocol as a conclusion of their work.

5. [Arpa Médica]. Madrid. Sample of a laboratory

Since the coronavirus pandemic began, Arpa Médica has developed a team of health workers from the Covid-19 Unit that has not stopped performing PCR tests, antigens, antibody tests or serological tests – serologies are a common test on infertility treatments.

On many occasions, the tests have been carried out with home care due to the recommendations and restrictions that the Ministry of Health has been marking.

In the first place, the elderly have been the most affected population group of all this fact that has marked a before and after in our lives. These people often cannot travel to a center to perform a blood test, a medical exam or any other test.

But after them, the service remained as an offering for the general population and, therefore, as a sample of health at home.

6. [SEF]. Spanish Society of Fertility

Sample collections and embryo transfers could happen at home as stated by Luis Martínez Navarro, president of the society in 2021 and others.

It can be useful in situations of remoteness and this formula allows to defer the process, because there is a profit if you live far away from the place where you need to deliver the sample. Or also in cases such as when the future father is, for example, an international patient for a clinic outside the country.

The sky is the limit. Some doctors belonging to SEF intend to go a step further and proposes to perform the above stated options. It has not yet been done; but it is ready: an embryologist goes to the house with sterile legs and an embryo already loaded. It has all the amenities. So, the only missing aspect is to do it with real patients.

The *Generalitat of Catalonia* has begun to validate this process and the requested move is to create an Ethics and Legal Medicine Committee to make sure that the embryo belongs to the right patients and that the embryo transfers have the same results as in the clinic. Work is ongoing on this within R&D departments.

Letting aside the Spanish Society for Fertility (SEF) we can see on the table below the final briefing of what clinics have been able to do, in some cases due to the COVID19 pandemic and, in some others, just because they believe in remote care for patients.

	Remote consultations?	Testing kits?	Remote images?	Sperm kit?	Fully at home?
[E-Procreate]	YES	YES	YES	NO	NO
[Embryolab]	YES	YES	YES	NO	NO
[Equipo Juana Crespo]	YES	YES	YES	NO	NO
[Instituto Marqués]	NO	NO	NO	YES	NO
[Arpa Médica]	YES	YES	YES	NO	NO

Table 1. Table briefing some of the remote care services on fertility

None of the above samples could be fully completed from home. And let's keep in mind that, in any case, the oocyte retrieval required for some treatments has not been considered... so even in that case there is a need to look beyond.

But it is also important to understand that SEF is promoting and supporting the services provided by these companies and, therefore, it has become a great help for companies to be able to change/adapt regulations in the healthcare sector.

On the table below we can see the extended table including SEF, not because SEF is doing anything (SEF is a Society) but because it supports there associated clinics performing those services:

	Remote consultations?	Testing kits?	Remote images?	Sperm kit?	Fully at home?
[E-Procreate]	YES	YES	YES	NO	NO
[Embryolab]	YES	YES	YES	NO	NO
[Equipo Juana Crespo]	YES	YES	YES	NO	NO
[Instituto Marqués]	NO	NO	NO	YES	NO
[Arpa Médica]	YES	YES	YES	NO	NO
SEF	YES	YES	YES	YES	YES

Table 2. Extended table briefing some of the remote care services on fertility

As stated before, we need to keep in mind that the oocyte retrieval has not been considered in this table.

2.2 Some figures around the fertility market

The Ministry of Health, together with the Spanish Fertility Society (SEF), presents every year the National Activity Registry (SEF Registry).

According to the statistical data of this registry, which come from 319 centers that perform fertility treatments in Spain, in 2018 a total of 149,337 IVF cycles were carried out, which means an increase of 6% compared to 2017 and 28% compared to the first National Registry that was that of 2014. It is the period where a most significant growth has been identified. In this period, only 20% of the appointments were online, and only referred to a first visit.

In the next two-year period, meaning the years 2019 and 2020, the above figures have made increase the number of treatments, but not in such a significant way. Nevertheless, the number of online first visits for new patients has moved from 20% to 80% in the international market – meaning non-Spanish patients coming to Spain for treatment.

The move from physical to digital interaction between patients and clinics has really been accelerated by the COVID-19 pandemic and there is no way back. Just the opposite, patients require more and more digital and remote services from the clinics.

Based on the feedback provided by the clinics, there are four main concerns that drive their digital transformation:

1. [To improve the virtual experience](#)

To create interactive elements, providing value to the patient and additional information to the medical staff

2. [Generate engagement with the first online contact](#)

This is a desire in order for patients to commit to a presential visit to the clinic for advice and becoming a patient

3. [Brand innovation and value proposition](#)

4. [Simplify and digitalize the doctor-patient conversation](#)

It is fundamental to capture of relevant information/data for subsequent diagnosis and treatment and, therefore, both patient and clinics success

2.3 Digital competences

A Key factor to measure matureness is the digital skills level of the population as of today, not only from the patient side, but also from the provider: in this case, the staff of the clinics trying to provide an improved service through digitalisation.

The competences around digital knowledge and assets are usually distributed into five different areas that we could summarize below:

1. Information and data literacy:

It is relevant to identify patient's information needs, to create digital data, information and content. And patients should be illustrated enough to judge the relevance of the source and its content. Also, to have the ability to store, manage, and organise digital data, information and content provided by the clinics.

2. Communication and collaboration:

The clinics and the doctors must take a step forward to interact, communicate and collaborate through digital technologies while being aware of cultural and generational limitations. They have to manage the digital presence, identity and reputation.

3. Digital content creation:

It is critical to improve and integrate information and content into an existing body of knowledge. It is very important for the clinics and their staff to give understandable instructions for their own employees and patients to properly use computer systems.

4. Safety:

To protect devices, content, personal data and privacy in digital environments is a must; and it needs to be extended to physical and psychological health, to be aware that the digital interactions provide well-being and inclusion. There is a need to be aware of the impact of digital technologies and their use.

5. Problem solving:

To use digital tools to innovate processes and products also means to identify needs and problems, and to resolve problem situations in digital assets and environments.

Going into details on the above competences, the digital content creation and the safety will be the items that will be more important in daily interactions. Therefore, we need to take a deeper look at them to list the important items to be taken into account:

a. Developing digital content

To create and edit digital content in different formats will be a requirement to reach different types of patients, origins, nationalities and, even, cultures.

b. Integrating and re-elaborating digital content

As a next step to development, it will be requested to count on a responsive team in charge of the needs to modify, refine, improve and integrate information and content into an existing body of knowledge.

c. Copyright and licenses

To avoid the competition to reuse what has been created for private use and not to be shared publicly, it is a need to understand how copyright and licences apply to data, information and digital content.

d. Programming

Applications are a key success factor and to plan and develop those new features to make them available to patients and staff in the clinics to solve a given problem or perform a specific task is a must.

e. Protecting devices

The software that has been programmed runs on devices that will need to be protected, along with the digital content; the IT teams must understand risks and threats in digital environments and provide safety and security measures to have due regard to reliability and privacy.

f. Protecting personal data and privacy

In remote interactions with patients in the context of telehealth, to protect personal data and privacy becomes more important. Critical to understand how to use and share personal information while being able to protect both the patient and the clinic from damages. To inform how personal data is used is not negotiable.

g. Protecting health

There must be a focus on being able to avoid health-risks and threats to physical and psychological well-being (for example, frustration and will to abandon) while using digital technologies (devices that are new to patients under treatment and that they might feel uncomfortable with).

As the above items are better managed, the access to remote health services and fertility treatments at home will be easier for patients and clinics.

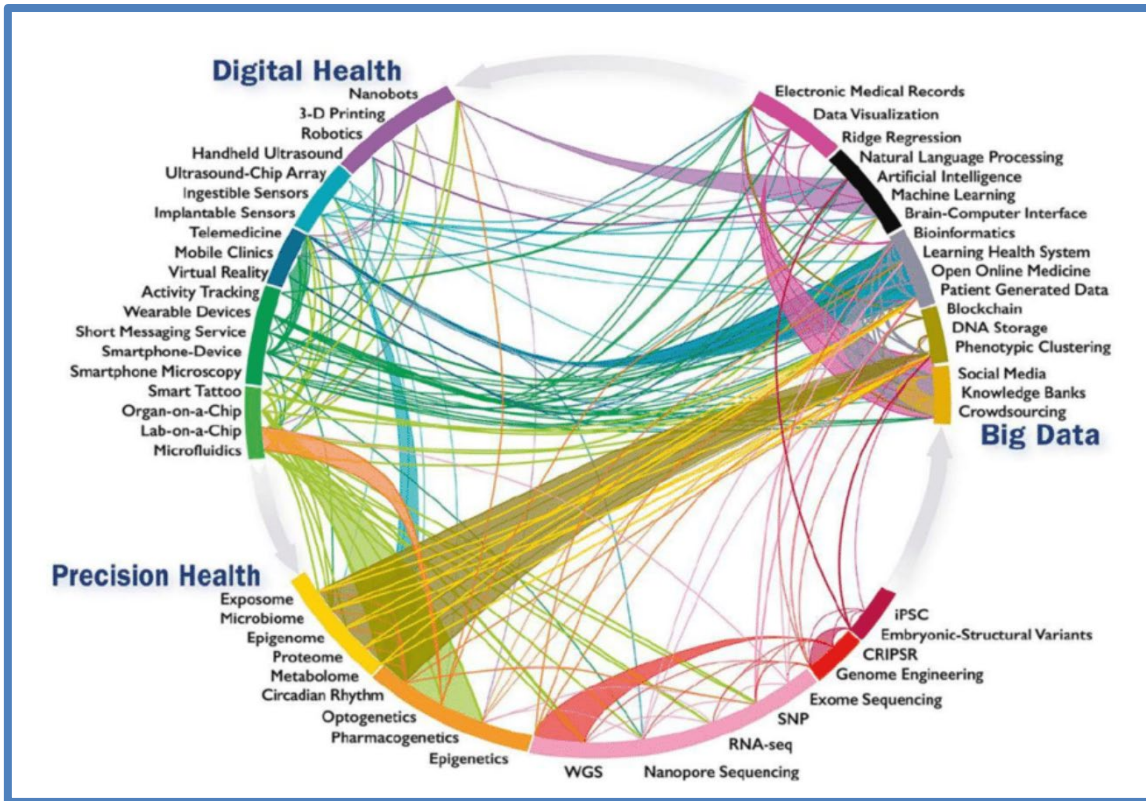


Figure 2. Digital Health and competences. Bhavani et al. JACC 2017

The image above is an infographic aiming to be a view at a glance of digital health and its associated competences.

For people who need to have a scope for digital health and about the digital skills applied to the health environment, it is a way to provide a simple and concrete vision of what digital skills mean in health, their current importance and which are those most necessary for the professional development of health workers.

3 Business models in the market and technology opportunities

The document will now refer and analyze existing ideas in the market, meaning business models that the main competitors in fertility (and others not strictly on fertility) currently have.

Some of these opportunities are really offered by technology and therefore not limited to their use by companies focused on fertility. Let's take a step forward to have a view at a glance of what some examples of these companies do and let's see afterwards what they do in detail.

	Value proposition	Resources	Activities	Clients
Apricity	Educate patients in fertility treatments and refer them to the best clinic after diagnose and treatment proposal	Doctors to diagnose and small sites for consultation	To diagnose patients, propose the best treatment and follow up the patient's success with the suggested clinic they have been referred to	Patients
Ovobank	To provide oocyte (eggs) to patients and clinics who need to go an egg donation treatment	Donors and oocyte banks to store the oocytes	Provide oocytes to patients or clinics; in the case of patients, refer them to a partner clinic for treatment	Patients & Clinics
RI Witness	To improve IVF lab safety and efficiency around witnessing	Monitoring devices and software to manage lab processes	To set up procedures in the lab for an improved control (safety, performance and overall management of devices and media)	Clinics
AIVF	To improve lab results (patient pregnancy rates) with the use of Artificial Intelligence	Algorithms and data	To collect data from as many sources as possible to improve AI algorithms to select embryos that will end up in pregnancy	Clinics
Overture	Automate as much as possible of the current manual work in an IVF laboratory to standardize processes	Robots and software to automate processes	Robotize and monitor processes in the IVF labs	Clinics

Table 3. Examples of companies offering digital services around the fertility care.

1. [Apricity.Life].

<https://www.apricity.life/>

Apricity is a company half-way through a clinic and a referral.

Their target is to help patients because in fertility treatments, just like in any other type of service, clinical or not, a certain price is shown first, and unexpected costs come up along the way. They offer transparency and therefore show entire treatment cost upfront, inclusive of all medication, tests and even blastocyst. That way patients can undergo treatments with no surprises – or at least, few of them.

Some consultations are completed by their own doctors, while treatments are referred to clinics they collaborate with. This is how they work:

- I. An Apricity advisor discusses the patient's fertility history, background and location and walks them through the treatments and benefits they offer
- II. Based on the patient's needs and preferences, the advisor will arrange a consultation within one of their selected/partner clinics
- III. The advisor is the one in charge of creating a treatment plan for to review and tailor the patient's wishes
- IV. Payment is made to Apricity and not to the clinic where the treatment happens; in exchange of which there are complementary benefits and continuous support during and after the treatment

Apricity's offering is to pair patients with the most suitable clinic.

Although they only work with regularly audited fertility clinics, they do not have access to all the clinics in the market.

Nevertheless, it is true that their partner clinics are licensed by the HFEA, which is the organization in the UK that aims to ensure that everyone who steps into a fertility clinic, and everyone born as a result of treatment, receives high quality care.

2. [Ovobank].

<https://ovobank.com/>

Ovobank, as in their own name is defined, can be considered an oocyte bank. But their service offering goes beyond oocytes.

It was created with the aim to give solution to assisted reproduction centers in the search and selection of a suitable donor for their patients, knowing how hard it is for fertility clinics to find and select oocyte donors for egg donation treatments.

As there is a higher need to satisfy the increasing demand of oocytes, Ovobank helps to optimize fertility treatments easing the way for future parents as well... because they also own facilities where they can provide fertility services within the Assisted Reproduction Clinic at Ovoclinic.

Their offering can be briefed as:

- I. They offer vitrified oocytes for clinics and patients who need them
- II. A meticulous donor selection process is their value proposition
- III. Their offering includes systems of transportation, storage and traceability of the samples

Ovobank can be addressed in two different ways:

As a collaboration with a clinic

In this case, it is required to register as a collaborating centre through their systems. Once the collaboration contract is signed, through their *Ovotracker system*, clinics can fill in the request with physical and immunological characteristics of the recipient couples. Ovobank has a Donor Coordination Department that offers a proposal with the most compatible donors for the couple (or patient).

Their offering is completed with a report with the donor data, with the results of the analytical, gynecological, psychological and genetic studies carried out according to the established by the Law 14/2006, Royal Decree 1301/2006 and in the signed collaboration agreement.

As a patient

Ovobank allows patients to request oocytes directly, without intermediaries, and they can send them to the collaborating centre of the patient's choice, where the treatment will be performed.

If patients do not have a fertility centre where they can receive treatment, Ovobank will make an offering so that patients can choose from one of their collaborating centers.

3. [RI Witness].

<https://fertility.coopersurgical.com/equipment/ri-witness/>

RI Witness is a company created to satisfy the need of the UK regulators to witness every interaction happening in a clinic when managing oocytes or sperm, to avoid identification mistakes that could potentially lead to an error on the property of the samples.

RI Witness uses Radio Frequency Identification (RFID) to detect and monitor all activity in the IVF Laboratory. The system helps mitigate the risk of human error every time samples are moved from one dish or tube to another and safeguards every step of the IVF cycle.

Throughout the lab, RI Witness readers are situated wherever work is undertaken, critically where samples are handled. Embryology heated or unheated plates with in-built RFID readers can be integrated into a worktop. They are active all day, every day, so a check cannot be overlooked. Their offering is:

- I. RI Witness locks patient identity to every gamete, oocyte, embryo, biopsy and cryo sample for continuous monitoring
- II. Acceleration of ID witnessing throughout the patient cycle
- III. RI Witness is active all day, every day: no process goes unchecked

RI Witness, from its beginnings as a witness tool, has been gaining control over the process in the IVF laboratories and it is growing slowly and steadily in the software market, by providing tools to completely monitor the lab. So, they have been transitioning from a witness company to an IVF lab management company through the software with the following principles:

- Reduced non-clinical work
 - i. Supports audit activity and changes to documentation
 - ii. Records and organizes consumables cross-referencing patient cycles and material batches for traceability
- Data collection and time saving per treatment/procedure
 - iii. Potentially reduces each embryo's time outside the incubator
 - iv. Supports and guides staff through clinic SOPs
 - v. Paperless data capture via a tablet touchscreen
 - vi. Direct data input minimizes transcription errors by connecting to your patient database
- Information is easily accessible
 - vii. Data is centralized and displayed in the lab
 - viii. Uninterrupted workflow and communication for the team
- Manage and analyze your workflow
 - ix. Oversees lab activity in real time
 - x. Allows comparison of lab efficiencies/performance from multiple labs
 - xi. Assigns accountability and identifies training requirements
 - xii. Standardizes procedures across workstations or multiple labs
 - xiii. Reports workflow bottlenecks

4. [AIVF].

<https://www.aivf.co/>

AIVF joins this paper as a sample on how Artificial Intelligence can change the businesses and, in particular, how it can improve the fertility procedures and/or results.

AIVF is a reproductive technology company that defines itself as a transformer of the fertility journey. The company was founded by fertility experts for fertility experts, and it has a proprietary AI software platform based on scientific research and driven by real-world clinical use.

The expectation is to help fertility clinics optimize IVF processes and outcomes.

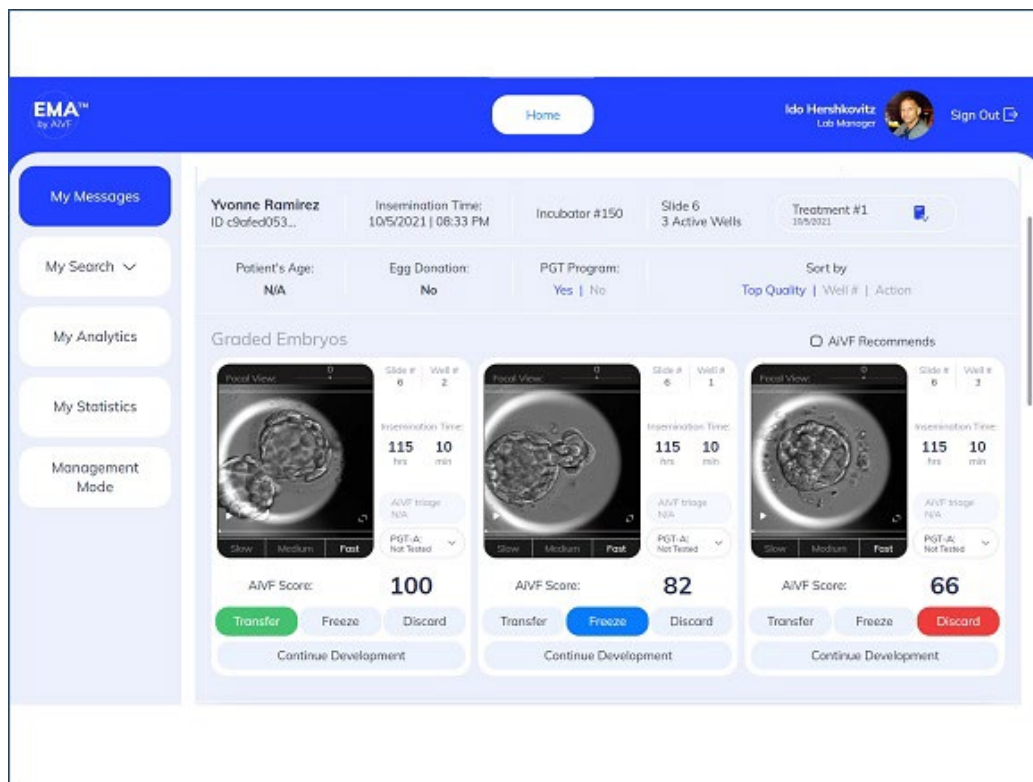


Figure 3. AIVF software image to illustrate AI features provided by AIVF.

EMA™ is a SaaS platform which uses proven artificial intelligence (AI) technology to assist embryo evaluation and support operational efficiencies in IVF clinics. It was developed on a large and diverse database of hundreds of thousands of embryo images and health records in collaboration with leading healthcare institutions across the US, Europe and Asia.

Embryo evaluation is performed by trained scientists, known as clinical embryologists, in the IVF lab. The EMA platform acts as the Fertility Operating System, providing automated and objective insights to augment the embryologist in evaluating embryo quality. This is the so called Fertility Intelligence by AIVF

5. [Overture].

<https://www.overture.life/>

Overture is a company that defines itself as revolutionizing embryology and who attempts to make In Vitro Fertilization (IVF) more accessible than ever by automating all the processes in the laboratory.

Their founder and Chairman, a well-known entrepreneur called Martin Varsavsky, is a keynote speaker in many conferences around innovation and, in particular to our case, he presents Overture to the world as the democratization of in vitro fertilization.

What is Overture really creating?

A robot capable of doing the same work of an embryologist, without human error and in fewer hours of work



Figure 4. Illustration of ICSI in an In Vitro Fertilization laboratory

Overture Life IVF raised \$15M in Series B Funding to change the rules in the lab.

The current procedure lasts about 20 hours, requires an embryologist, laboratories and instruments. When this project is underway, the expectation is to carry out the same work in five hours and a single technician doing everything with the robot.

6. [Other business models at a glance].

I. HRS: <https://www.healthrecoveryolutions.com/who-we-help>

Health Recovery Solutions (HRS) is a company based in USA ranked #1 by KLAS for Remote Patient Monitoring in 2020, 2021 and 2022.

HRS empowers the USA's largest healthcare providers to deliver telehealth and remote patient management solutions, with different care settings:

- Hospital + Health Systems
- Home Health Agencies
- Hospice + Palliative Care
- Physician + Group Practices

II. Elsevier. Home Health Care

Elsevier is a global information analysis company that assists institutions and professionals in advancing science, advanced health care, and improving their execution for the benefit of humanity. In this sense, they work with public hospitals to provide the benefits of remote and/or home health care by defining the core four items to be able to succeed on primary care:

○ Duration of care

A short duration (about 15 days) allows an intensity of the intervention unthinkable if the duration of attention is long (up to 60 days) or indefinite.

○ Complexity

Complexity is not easy to define, but the need for appliances (a ventilator, food infusion pumps, among others), the significance of decision-making (e.g., deciding on a tracheostomy in a patient with a neuromuscular disease) or the magnitude of the aids needed to perform activities of daily living will determine many aspects of the intervention pattern.

○ Intensity

The number of daily visits required also determines the pattern of intervention. It is unlikely that a primary care team can make daily visits for about 15 days, in a systematic and routine manner.

○ Speed of response

The response must be all the faster the greater the acute situation of the patient or the greater the fragility of the patient.

Respecting these limitations and/or boundary situations, it has been proved the success of home health care in primary care.

How could these companies with the above samples help in the process of moving from traditional fertility care to remote/at home services? Let's take a look at some ideas that we can extract and learnings from each one of these companies...

- **Apricity**
Remote fertility means doing things in different ways... and part of what Apricity does is referring patients. Could we split the current idea of a fertility clinic into several sub-companies specialized in certain processes? This is what they do, since they diagnose and refer; and maybe it is a challenge with remote fertility to specialize in certain aspects of the patient care
- **Ovobank**
As a continuation of the above idea to specialize in certain processes of the fertility care, Ovobank provides a very specific service to patients and clinics
- **RI Witness**
Witnessing in the IVF lab is a must for corporate responsibility reasons. Why not to extend witnessing tools at the patient's home? That way we would be able to safely confirm that the samples provided by patients are theirs and not someone else's.
- **AIVF**
Can we add AI to the entire fertility process? We could probably extend AI services not only to select embryos in the lab, but also to support diagnosis and treatment proposal. A path to be followed.
- **Overture**
Automating tasks in the lab seems much more challenging than automating processes such as managing kits to be delivered at home for patients or validating samples. These steps could be part of the automation.

We should also consider if there is anything else that they do not cover. And of course there is, because remote fertility is not their business. So let's see what are the additional offerings needed when we focus on at home services around fertility:

- Tools to manage patients online
- Kits and devices to diagnose and monitor patients
- Imaging services – specially around ultrasound machines
- ...

The items above, of course, will be covered in detail through the implementation section.

4 Value proposition

On-demand home services seem to be the new demand around the world. So we need to understand why these services are becoming more and more popular.

We can have such services as a beauty service to get pampered within the comfort of our home. Therefore, with more people seeking convenience in everything under the sun, growing urbanization and increasing popularity of internet and smartphones, the demand for on-demand home services is on the rise.

The question then would something like: is this also happening around the healthcare services?

In Europe, home care aims at satisfying people's health and social needs while in their home by providing appropriate and high-quality home-based health care and social services, by formal and informal caregivers.

Life expectancy has risen sharply in the Europe in the last few decades. This will mean increasing rates of care-dependent older people. Therefore, the next decades will also see dramatic changes in the needs of those with noncommunicable diseases; a variety of people with chronic conditions who may stay at home given difficulty in mobility, and dependent children with severe health problems or people with mental disorders that may also require home care.

Although the services, willing to change and political responses are very different across Europe, all countries are similarly facing a demographic, social, technological, epidemiological, and political pressures that influence both the demand and supply of home care demand and provision. Is it then the right moment to offer fertility treatment services at home?

To be able to provide home care fertility we will need to define the assets to be considered the pillars of the new offering. From a patient perspective, meaning that the service needs to be desired by the patient, we could group these pillars in the following way:

1. [Patient experience].

A desirable patient experience, focusing on the comfort of being home and reducing the commuting to clinics plus the waiting times that might happen... along to that, increasing accompaniment during the digital interaction with access to online consultations with the whole staff of the clinic, not only with doctors.

2. [Process].

New processes and the associated protocols will be established and, since they will be online and centralized, the correct development of the video consultations is ensured, with a greater involvement of patient care service and online specialized teams, in order to increase patient loyalty and satisfaction. Patients will all feel the same standards of care, no matter their location.

3. [Design | Content].

Patients, doctors and the whole experience will be redesigned to reinforce the patient brand experience: digital personalized contents along with tools providing a better monitoring and feedback on the process to excel the overall experience should reinforce the patient's comfort.

4. [Technology].

Video call technology solutions, contents streamed to patients, interaction with the staff through new channels like APPs and fast response to deprecate phone calls or emails would be the pillar to reach simplicity and comfort for both doctors and patients.

As life and technology move forward, the world is changing and traditional services such as an electrician or a plumber are managed by many home service companies that try to eliminate the pain of finding a reliable person/professional.

In healthcare and, in particular, in the context of human reproduction, we can find more and more papers and literature around the need to start offering remote services, not only to simplify patient's logistics, but also to be less invasive in the way patients are monitored through the treatments. Let's see some examples below:

- Self-Monitoring of Urinary Hormones in Combination with Telemedicine — a Timely Review and Opinion Piece in Medically Assisted Reproduction

(Roger J. Hart, Thomas D'Hooghe, Eline A. F. Dancet, Ramón Aurell, Bruno Lunenfeld, Raoul Orvieto, Antonio Pellicer, Nikolaos P. Polyzos, Wenjing Zheng, 2021)

[...] Cycle monitoring via ultrasound and serum-based hormonal assays during medically assisted reproduction (MAR) can provide information on ovarian response and assist in optimizing treatment strategies in addition to reducing complications such as ovarian hyperstimulation syndrome (OHSS). [...] However, blood tests may cause inconvenience to patients. The reported drawbacks of blood tests identified by the survey included the validity of results from different service providers, long waiting times and discomfort to patients due to travelling to clinics for tests and repeated venepunctures. [...] Historically, urine-based assays were used by fertility specialists in clinics but were subsequently replaced by more practical and automated serum-based assays. A remote urine-based hormonal assay could be an alternative to current serum-based testing at clinics, reducing the inconvenience of blood tests and the frequency of appointments, waiting times and patient burden. [...] In addition, in this review, we discuss the evidence supporting the introduction of remote urine-based hormonal monitoring as part of a novel digital health solution that includes remote ultrasound and tele-counselling to link clinics and patients at home [...]

- Self-operated endovaginal telemonitoring (SOET): a step towards more patient-centred ART (Assisted Reproduction Techniques)

(Jan Gerris and Petra De Sutter, 2009)

[...] The need for serial vaginal sonographies to monitor ovarian stimulation for artificial reproductive technology (ART) treatments remains a major practical and organizational drawback both for patients and health-care providers. We explore the possibility of patients and/or their partners performing their own vaginal sonographies at home. To make this a reality, a portable, easy-to-use, home-applied vaginal probe for recording relevant images would have to be developed, as well as appropriate software to transfer images using modern communication technology to the centre, to analyse the recordings and to send a swift structured response, comprising dosing advice and next-step instructions. A simplification of the uncontested need to perform these sonographies, even if applicable to just a selected proportion of IVF patients, could fit in the general tendency to make IVF more patient centred and friendly, to implement telemedicine and to increase patient empowerment by supervised active participation to their treatment. The advantages of such a technology are explored in this paper, aiming at opening up a debate on whether patients themselves would, could and should achieve a further substantial simplification of ART without loss of quality while strongly curbing costs [...]

Therefore, the value proposition of this document is to analyze how to make an offering that covers statements such as the ones above, supported by literature, that help patients, doctors and clinics to follow the path from the current fertility care to remote services where patients can remain at home during most of the treatment.

5 Implementation. Overview

Let's start introducing the core feature that a remote fertility service needs to integrate into its implementation: the patient journey.

Keeping in mind that the service blueprint would serve to be taken as an example on how to integrate using the levels, but it does not include the before and after of the customer journey.

In this case, the integration would be better because we could build different levels:

1. the first level would be the one related to the patient
2. the second level would include doctors and direct patient care
3. the third level would be services affecting IT infrastructure and architecture
4. we could consider the data as a fourth level

To be able to properly analyse how feasible the implementation of remote fertility care is, we can list what's included in each one of the levels. And to simplify so, we will consider IT and data as a single level (we will call it technical).

It is important to review the process in depth to figure out how many patient interactions with the clinics can happen remotely and how this is going to happen. That's why the following items will split the process in ideas and procedures to move forward step by step.

❖ From a patient perspective

We will need to review the patient journey and the patient interactions

1. Description of the current patient journeys in fertility care
2. Is it possible to attract and diagnose patients who have not visited a clinic?

❖ From a doctor/clinic perspective

We will need to review diagnosis, stimulation and embryo development

3. Scheduling and organizational changes
4. Understanding of the problem (diagnosis) and treatment evaluation
5. Fertility treatments and embryo development in laboratories

❖ From a technical perspective

We will need to review tools to support the remote process

6. Online consultations
7. Testing kits
8. Ultrasounds and imaging

Let's move forwarding by reviewing each one of them separately.

5.1 Description of the current patient journeys in fertility care

There are many ways to describe a patient journey in fertility care. Although it is common to use images to graphically help in the process of understanding, it is also true that, depending on the source (medical, operational, business, IT...) the views are slightly different.

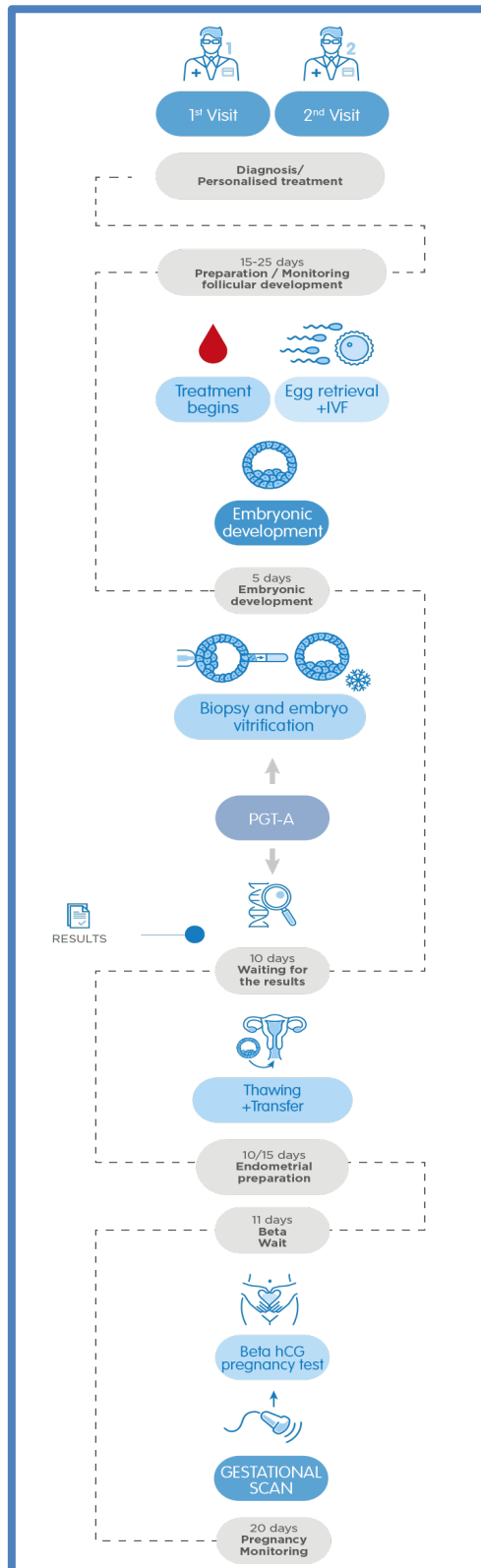


Figure 5. Patient Journey provided by IVI clinics

The one aside shows how a clinic offers this view of the patient process to patients where there is a clear difference between the steps to be taken; assuming that there is a need to be sure that a treatment is required, we would find:

- a first visit (and a second one, for additional medical results) that provides a diagnosis to personalize the treatment
- a cycle/treatment, that starts with the preparation and goes up to the embryo development. Embryos might be frozen and/or genetically analysed
- the genetic analysis for those clinics that provide this service to improve pregnancy rates and time to pregnancy
- embryo transfer or endometrial preparation prior to transfer in case of frozen embryos
- beta result waiting (positive or negative pregnancy test) plus a gestational scan and pregnancy monitoring if positive pregnancy.

The above steps combine emotional and operational acts, along with a combination of remote and presentational interactions.

Through the next descriptions of the process, we will extend the content of the image and its details to explain in detail de journey that a patient or a couple can undergo.

1. IVF Step 1: Need for treatment and first visit to the clinic

Before a patient's or couple's IVF treatment is even considered, there are some conditions to be taken into account: age, time looking for pregnancy, etc.

Assuming that visiting a doctor/clinic is a real need and that a treatment is required, it will all start with a first appointment to understand the clinical situation of the patient and the image below shows how this process could be briefed:

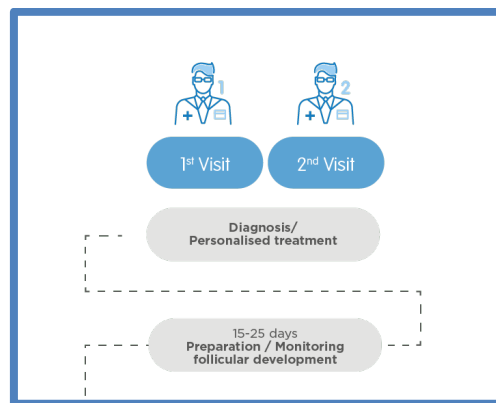


Figure 6. Zoom on a subset the Patient Journey (1)

With one visit to understand the patient's situations and a second visit to review the situation after the medical results of the required analytics, a diagnose and a proposal for treatment can be personalized for the patient. And from there on, as the patient/couple start the treatment, the new phases of preparation and monitoring will start.

For preparation patients might be put on birth control pills. Although it sounds like contradictory, using birth control pills before a treatment cycle may improve success rates. Also, it may decrease the risk of problems such as ovarian hyperstimulation syndrome or cysts.

Not every healthcare provider uses birth control pills the cycle before. But all of them will request patients to prevent them as soon as women patients detect ovulation. Sometime after ovulation, the fertility clinic may then have patients start taking medication: usually, injectable drugs.

These medications allow doctors to have complete control over ovulation once the treatment cycle begins. But some patients don't get cycles on their own and they need donor gamets (oocytes or sperm); in this case, doctor may prescribe differently but they will need to synchronize the donor and the patient... so that the patient is ready to receive the embryos after the donation and the embryo development in the lab.

This step/process can be fully completed at home as a remote service.

2. IVF Step 2: A treatment cycle is to be started

As a general agreement, a treatment cycle starts with the patient's period. Around that day, doctors/clinics will be likely ordering bloodwork and transvaginal ultrasounds. This is what it looks like if we extend the initial image that we had on the previous step:

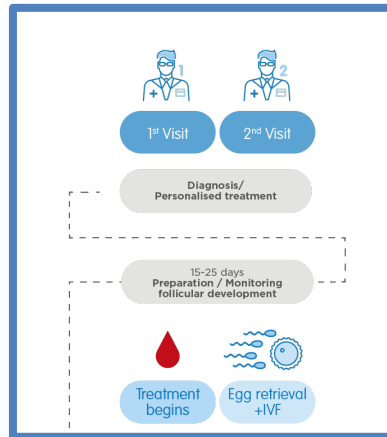


Figure 7. Zoom on a subset of the Patient Journey (2)

Initial tests are considered baseline results and baseline ultrasound. Strogen levels and the anti-mullerian hormone test are part of this baseline to make sure that ovaries are waiting to be activated.

The ultrasound is a physical interaction where doctors check the patient ovaries: if any pathology is found that might require surgery, the treatment cycle might need to wait until the surgery is completed to remove any cyst or problem the patient might need to solve. As soon as the initial pathology is addressed, the treatment will move on.

This step/process can be fully completed at home as a remote service.

3. IVF Step 3: Patient stimulation and monitoring

A treatment requires ovarian stimulation; to do so, fertility drugs are the next step. There should always be a treatment protocol and, therefore, different medication dosage meaning that within the period of about a week to 10-12 days patients will be using injections to stimulate the ovary to retrieve the desired number of oocytes.

The ovarian stimulation is a process where doctors/clinics will monitor the growth and development of the follicles. Follicles are what at a later stage become oocytes. Most commonly this control happens over bloodwork and ultrasounds every few days and happen in a presential way in the clinic. Oestradiol, progesterone and other hormone levels are monitored through bloodwork while the ultrasounds will help monitor the oocyte growth.

Monitoring will help doctors to decide how to adjust medications. It might be needed to increase or decrease dosages based on the patient's response at, as the final days of medication are reached, visits to the clinic for monitoring may be more often.

This step/process can be fully completed at home as a remote service.

4. IVF Step 4: Oocyte maturation

The oocytes must complete their growth and development before the surgery to retrieve them happens (puncture or oocyte retrieval are the common names for this process which happens in an operating theatre).

There is a last medication, usually referred as a trigger, where timing is critical: if it happens too early, the oocytes will not be mature enough; if too late, oocytes might not fertilize properly, so this is why ultrasounds help time this trigger shot just right. This is typically a one-time injection. Some patients end up going to the clinic for help on this injection to be sure that they do it right, since it is so important.

As different patients suffer different pathologies, it is important to understand that patient stimulation and oocyte maturation does not always happen as desired. Some of the common problems are:

- Follicles do not grow

The treatment/cycle will likely be cancelled... meaning that different medications are needed, or, in the worst scenario, a donor is required.

- Risk for ovarian hyper-stimulation

This is situation due to ovaries not responding as expected. The trigger injection (and the cycle) might be cancelled at this point... but it is also possible to retrieve the eggs, fertilize them and delay the embryo transfer.

- Premature ovulation

Another one of the most common scenarios in case of trouble is when ovulation occurs before retrieval can take place. It is important to show that cancellation happens in 10% to 20% of IVF treatment cycles and the cancellation risk rises with age, especially after the age of 35

This step/process can be fully completed at home as a remote service.

5. IVF Step 5: Egg (oocyte) retrieval and fertilization

Assuming that everything goes right on the stimulation process and the oocyte maturation, the egg retrieval will take place. Most people go through it without much trouble or pain, but it does need an anesthesiologist who will give you some medication. It is most commonly local and not general anesthesia and patients can go home after a short period of time – typically between one and two hours.

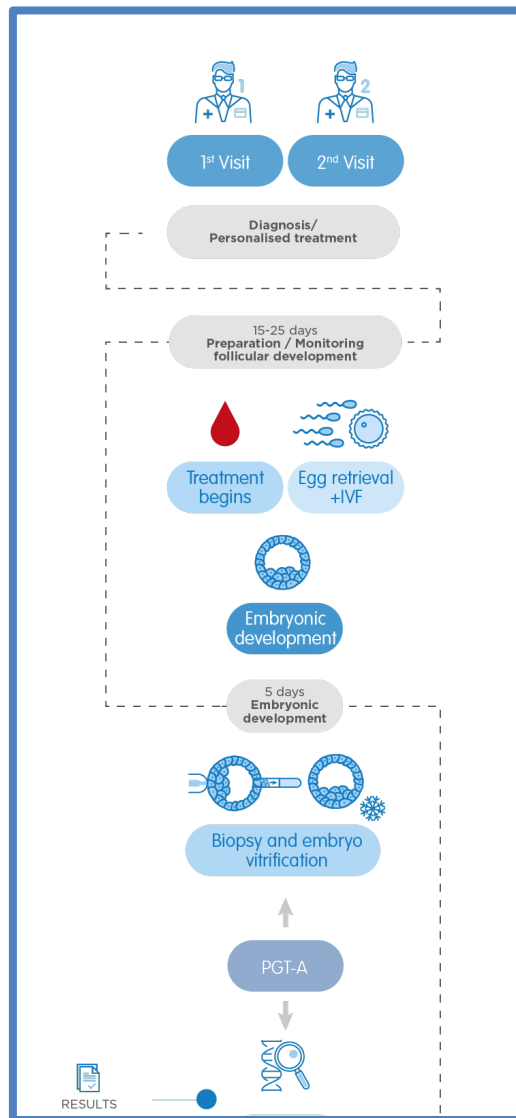


Figure 8. Zoom on a subset of the Patient Journey (3)

This process cannot happen at home.

Doctors will use a transvaginal ultrasound to guide a needle through the back wall of the vagina, up to the ovaries. This is how they will aspirate each follicle – in another words, they will suck the fluid and oocyte from the follicle into the needle. There is one oocyte per follicle. These are the oocytes that will be transferred to the embryology lab for fertilization.

The number of oocytes can usually be estimated before retrieval via ultrasound, being the average number between 8 and 15. After the retrieval, while patients are recovering, the follicles that were aspirated will be searched for oocytes, or eggs. Not every follicle will contain an oocyte, but most will. And this is where the in-vitro process starts:

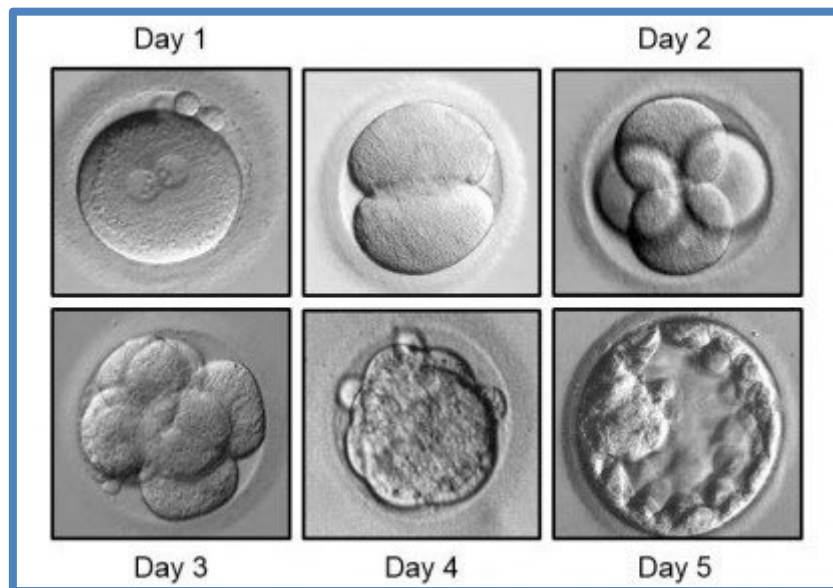


Figure 9. Images to illustrate the evolution of embryos in a laboratory

❖ Day 0

Once an egg is collected, it is washed and prepared for either insemination (IVF) or ICSI. Sperm is similarly washed and primed for the chosen procedure.

❖ Day 1. Zygote

The egg is checked for evidence of fertilisation. A zygote is the union of an oocyte (egg) and the sperm. And this will be a new embryo that needs to develop.

❖ Day 2

The embryo's single cell should have replicated into two by now, and those two cells may also have further split, giving a four-cell embryo.

❖ Day 3

The cells will keep splitting into two in a healthy embryo, gradually increasing the cell number. At this point, it may be decided to transfer the embryo back into the uterus.

❖ Day 4. Morula

The embryo's cells will begin to compact on this day, preparing to form a blastocyst.

❖ Day 5. Blastocyst

A healthy embryo will form a blastocyst by now, dividing its cells into sections that will form the foetal matter and placenta.

This is the only step/process that cannot be fully completed at home as a remote service, since it might require oocyte puncture in some cases.

6. IVF Step 6: Embryo transfer and cryopreservation

Selecting the best embryo to be transferred and preparing the process is part of what an embryologist will do in the lab. This is typically done by observation with a microscope, but in some cases, genetic screening is performed. Furthermore, Artificial Intelligence is helping nowadays to select the best embryo to be transferred.

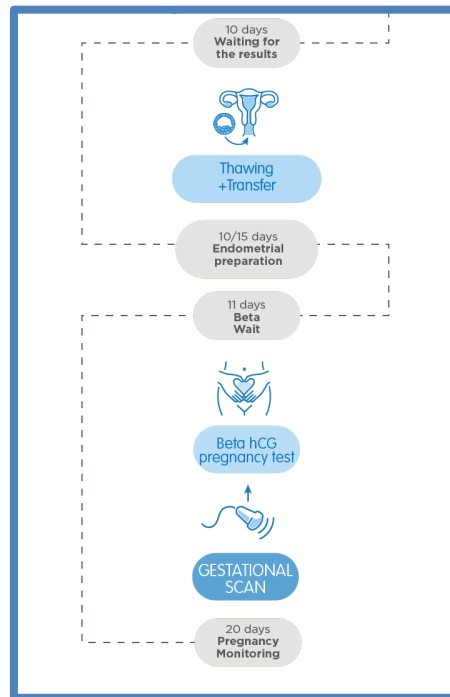


Figure 10. Zoom on a subset of the Patient Journey (4)

PGD or PGS (preimplantation genetic diagnosis or preimplantation genetic screening) helps understand if there is any anomaly in the embryo that will prevent the embryo from implanting properly. This would end up in an abortion, so embryos with genetic anomalies are discarded. But time is needed for the results... so embryos genetically analyzed need to be frozen (cryopreserved) and transfer is postponed to another (stimulation) cycle.

Embryo transfers do not need anaesthesia.

The number of embryos transferred will depend on the quality of the embryos... but most of the clinics and even governments with their regulations request to have single embryo transfers (SET) to avoid multiple pregnancies (twins). After the transfer, patients will rest lying down for around 1-2 before they can leave the clinic. Embryos left (not transferred) will be cryopreserved in case they are needed later on or for future pregnancies if the current pregnancy ends up in a living baby.

This step/process can be fully completed at home as a remote service.

7. IVF Step 7: Waiting time, test and follow-up

Right after the embryo transfer, patients will continue with medication – in this case, they will start taking progesterone supplements and, as before, these are self-injections. Patients do this on their own and visits to the clinic are not required.

And then... waiting time is needed for around the next two weeks. It is a difficult moment, emotionally speaking, so patients might need contact with the clinics but, as said before, there are not visits scheduled at this point.

And then, around 9 to 12 days after the embryo transfer, the pregnancy test will happen – in some cases in the clinic; in some others, wherever the patient prefers to do it, even considering home. It is most commonly a blood test that also measures the level of progesterone... and if the result is not clear, it can happen again after a few days.

When the pregnancy is positive... everyone is excited, and patients need to keep taking their drugs/medication for another several weeks. It is not common to go through bloodwork and ultrasounds, but they might happen. Some clinics monitor pregnancy around 3 weeks after the positive pregnancy and then patients are not requested to interact with the clinic anymore. This does not mean that they will not be in touch with the clinic... but it means they will not need to have consultation with their doctors.

If the case that the pregnancy test is negative... patients will stop taking the medication and they will have to wait for their period to start for a new treatment. In the case of abortion, the follow-up requires more emotional care because it is much harder for a patient to start a new treatment after pregnancy than after a negative test. In both cases, these pre-scheduled appointments are preferred to happen in the clinics and not online.

This step/process can be fully completed at home as a remote service.

On the table below, there is a final description of the steps that a patient needs to go through when thinking about a fertility treatment.

	Need to visit the clinic?
IVF Step 1: Need for treatment and first visit to the clinic	NO
IVF Step 2: A treatment cycle is to be started	NO
IVF Step 3: Patient stimulation and monitoring	NO
IVF Step 4: Oocyte maturation	NO
IVF Step 5: Egg (oocyte) retrieval and fertilization	Depends on the treatment*
IVF Step 6: Embryo transfer and cryopreservation	NO
IVF Step 7: Waiting time, test and follow-up	NO

Table 4. Steps on a fertility treatment

The column on the right shows the treatment that the only process that could not be completed from home would be oocyte retrieval.

And even in this case, if we are talking about specific treatments such as embryo donation or egg donation, patients could be fully supported from home.

It is also important to understand that a patient could need surgery as a previous step to the fertility treatment. In this case, it is easy to understand that surgery needs to happen in a clinic or hospital, depending on the type of surgery.

On the table below we can see the extended table including surgeries, that can be handled at any point in the process/steps of the treatment:

	Need to visit the clinic?
IVF Step 1: Need for treatment and first visit to the clinic	NO
IVF Step 2: A treatment cycle is to be started	NO
IVF Step 3: Patient stimulation and monitoring	NO
IVF Step 4: Oocyte maturation	NO
IVF Step 5: Egg (oocyte) retrieval and fertilization	Depends on the treatment*
IVF Step 6: Embryo transfer and cryopreservation	NO
IVF Step 7: Waiting time, test and follow-up	NO
Surgery	YES

Table 5. Steps on a fertility treatment, including surgery

5.2 From patient journey to customer journey

After knowing a little bit more on the patient journey we might have a better understanding of how interactions happen in the clinic with patients to be able to refer to the question above. From now on, we will review those interactions to figure out which ones might happen remotely and how many points of touch with patients are required in the clinics. If we switch from a patient perspective to a process view, we could group them in three different blocks:

1. Prior to a first visit
2. During the first visit
3. Post-first visit

[1]. Let's start with the needs prior to the first visit:

- **Appointments. How to schedule the first visit**

This can be done through services such as Contact Center that are usually centralized... .. and patients can also manage the first visit themselves, in some cases, through the web sites or patient's apps where they can choose a clinic, doctor and a date available for the first visit.

- **Patient portals**

Keeping in touch with patients after the appointment is essential to feed them about how the visit will happen and the required documentation to be shared. Patient portals play a significant role in this sense.

Assuming that there is access to a patient portal, right after the appointment patients could carry out different procedures integrated with the clinical management of the fertility clinic. Usually, these interactions are general and not related to the type of treatment, which requires a previous diagnostic.

- **Functions that can be created on a patient portal**

- **Appointment information should be available**

Practical pre-appointment information; location of the clinic with services such as Google maps; options to cancel the appointment if patients cannot attend. Or even the possibility of contacting the clinic directly by calling from the patient portal itself

- **Frequently asked questions**

Patients have questions and need answers... so there is a need to classify this information, typically into groups of clinical questions and administrative questions. Therefore, patients will be able to see the FAQ or frequently asked questions that usually occur before the first visit... or even after the same and once a treatment has begun

- **Patient's background and clinical information**

Uploading information regarding the patient's most relevant clinical history (such as allergies, known diseases, etc.) and/or previous treatments carried out in other centers is core for understanding the patient's context.

- **Surveys**
Crucial to understand the patient's satisfaction, there is a need to obtain information and feedback from the patient for all the ongoing or past steps of the process as the basis for the quality control of the process

- **General settings to interact, provide privacy and compliance**
There is a list of general settings that patients should be able to manage:
 - Change their photo/image on the patient portal
 - Manage their password
 - Post a complaint/suggestion
 - Enable/Disable notifications – email, SMS, etc.
 - Change some personal data such as address or phone number
 - Invite their partner to join the patient portal
 - Sign the GDPR consents and others that might be required

- **Tasks prior to the first visit: a patient checklist**
Since patients need to know what to do, providing them with a checklist to upload personal documentation that is requested for their filiation and their partner's is usually a way to simplify things.

Apart from the above, it is important to understand that regulations depend on the country and that they are live: this means, they change very often to warranty patient safety and control. That is why some onboarding processes can be extended.

As of today, integrating a digital identity verification (KYC – Know Your Client) process is a given value that might become necessary in the upcoming future. In this sense, developing processes that allow clinics to have scanned identity documents, personal data, biometric images along with a proof of life of the patient is more and more common in health care.

[2]. What happens during the first visit?

After validating that the prior to first visit needs can be covered remotely, let's focus on the first visit itself. And given the scope of this work to promote remote services, we need to be strictly limited to the first online visit and the interaction with the patient in it.

We need to define interactions with patients, so that the service can be properly offered. What is then needed to succeed? Let's go into details:

- **How is the first online visit completed?**

The ideal model would try to replicate on-site models, where patients are guided on the steps to be taken by different teams:

- Patient Care team to contact the patient, verify that patients can correctly access the online meeting and inform them of any possible delay in the consultation... in addition to answering last-minute questions
- Doctors/Nurses for the clinical consultation

Virtual waiting rooms would be an additional extent of the service, so that patients will have content related to the clinic and the first visit before it really happens. In this way, if a waiting time is necessary due to doctor's delays (although the premise would be to avoid it) at least the patients can be reviewing contents.

- **Tools to support the interaction with a patient**

In a non-physical interaction, it is difficult to provide elements different to extend the doctor's message. But sharing clinical content with patients needs to be developed, so that they can visually/graphically understand the clinician's approach.

After the initial examination (based on the documentation provided by the patient) and the anamnesis, there might be a possible orientation of the diagnosis in the online visit and then it would be recommended to make patients feel as if they were in-site:

- Displaying 3D images of the most common diagnostics
- Sharing images of the clinic and laboratories – mainly in vitro fertilization and andrology, as well as the operating room
- Explaining treatments offered by the clinic through corporate presentations and/or videos
- Sharing success rates based on treatment that have also been audited
- Making ad-hoc drawings/designs with feedback for patients

But what about the unknown diagnosis? What about the ultrasound echography? What about the additional tests that patients might need to provide a proper diagnose?

Welcome to the *non-presential model* clinics, where the aim is to simplify processes for patients. In this case, the solution would be to visit the patient at home to perform the ultrasound echography and collect the required samples for the process.

This would be the first point of touch for a remote and at home service for patients.

[3]. Post first visit

After the first visit online, it is important to keep in touch with the patients, because a first visit does not mean the start of a treatment. Several steps are required and, therefore, several interactions to make remote services attiring to patients.

- **What happens after the first online visit?**

Patient's feedback is a must. Patient Care must contact the patient again and, if there is a clear diagnosis and a treatment that can be started, they will have to review them in detail with patients from the perspective of the budget.

In some cases, there is more personalized follow-up depending on the situation of the patient – ongoing treatments elsewhere, just considering the services for the future, etc.

- **What information should patients have?**

The patient portal shows back as a reference for remote interaction with patients and core to information sharing... so there is a set of minimum items to be covered in terms of documentation:

- **A first visit report**

The first visit report should upload to the patient portal in readable formats, and it also should include the images and/or videos of the proposed treatments... so that patients can better understand what their treatment consists of

- **Visualization of the proposed treatments... through a patient timeline**

How long the treatment will take must be shared with a patient in a timeline format to make it understandable. This timeline should be a detailed summary of the previous report, of the proposed treatments and should become the patient's medical area once treatments are started

- **Budgets and electronic signatures**

In the event that budgets have been delivered to patients, they can also consult and sign them electronically. And this is a new must for remote services: electronic signature of any document must be included in the scope of services

- **Informed consents**

In the event that patients are determined to start a treatment, they should also consult and sign them electronically from the documentation of the patient portal

- **Who takes care of the patients?**

The information of the clinic staff (doctor, auxiliaries, patient care) who have attended them is also a must in terms of availability. How in depth the staff information is to be presented depends on the clinic, but patients need to know who they are dealing with.

5.3 Scheduling and organizational changes

Scheduling becomes a headache when not only you need to take into account people's availability, but also visits at home when needed. Let's review how appointments should be managed to keep track and control over the changes that would mean a remote service.

- **Managing appointments from the clinic**

Confirmation of attendance should happen... in fact, confirmation of being at home at the time of the visit when needed. So scheduling should make a clear differentiation between remote (online) services and remote (at patient's home) services.

It becomes very important to review if the patient has shared/uploaded any type of administrative or clinical documentation, no matter how. And clinics should have tracking and deadlines on the requested documentation to count on everything prior to the appointments.

Online consultations will require to have an active digital communication, and therefore to find ways to request and fill in GDPR and/or any other additional and necessary document, such as ID or passport, for example.

Patients who are new to digital appointments with the clinic or the doctor will have to be contacted and explained how to make the video consultation and that only some interactions will happen in the clinic. For this interactions that happen in the clinic, the reception team will need to verify that it is a first time in the clinic for the patient and keep the traditional workflows to notify arrivals, departures or any other situation.

- **Managing a new patient request for online appointments**

The initial appointment has to be managed by a Contact Center team. This is the best possible approach to warranty that the way of assigning appointments is consistent and compliant with the policies of the company, no matter how big the company is.

Either through telephone, email, web request or any other mean, the following information will be gathered to start tracking the (future) patient:

- Name of the patient.
- Date of Birth
- Contact telephone number and email
- Identification of the contact center person
- Date and time desired for the appointment

The above information will allow a Contact Center staff to follow up by telephone those patients who have requested information and have not made an appointment, for example. No matter if it is due to the clinic or the patient.

Hopefully a patient is requesting an appointment and the Contact Center staff consults the availability in the agenda of the requested doctor and proceeds to register the appointment, with the guidelines established for the appointment, with the date of the appointment, the start time and the duration of it.

Since it is a new patient appointment, so far it is not needed to synchronize this appointment with mobility in case of a remote (at patients' home) visit.

Therefore, the important task will remain to confirm patient attendance by any mean (telephone, text message, etc.) verifying the patient's identity. In case it is requested to modify or cancel the appointment, this will imply the updating of the agenda. The Contact Center may assign the canceled appointment to a new patient or advance the visit of other patients who already have an appointment arranged, but just like in presential appointments. No additional concerns will be involved.

- **Managing remote services in a group**

If the clinic where the consultation is located does not have an agenda for the specialty (remote service) it needs to be specified in case of a large group of clinics. Also how far in distance these services will be covered, to avoid false expectations.

In this case, it might be useful to address a patient to another clinic in the group if the required service can be offered... and this means access to the scheduling information in the different clinics of the group.

In case of online appointments, information on the duration and cost of the visit should also be clarified and the payment option should be offered through bank transfer or credit card payment in advance to the consultation. It is important to notice the difference between the consultation in a clinic where the patient is guided through a path in the clinic versus the digital path which makes that, after the online consultation, patient tracking might be lost.

To optimize doctor's time and to be able to avoid delays in the consultation due to technical reasons, patients should be advised to join as much in advance as possible to the appointment. In case of delay, the appointment could be canceled to avoid not being on time for latter visits.

5.4 Diagnosis and treatment evaluation

Patients need to be diagnosed and to evaluate the best treatment option on their case. It is not a need but a must in today's world to personalize a treatment so that the patient is fully aware of the best options to succeed from all points of view.

Usually, treatments are reduced to acting on the woman and succeeding in having her pregnant; but there are other points of view that might help with the diagnose and, consequently, to reach a pregnancy sooner in time and safer in health. These are some factors to succeed:

- **Sperm analysis**

On the anamnesis, the reproductive history of a male should collect information on coital frequency, coital disorders (erectile dysfunction, alterations of libido), existence or not of previous fertility, childhood diseases (viral orchitis, cryptorchidism), systemic medical diseases, surgical history (inguinal, scrotal, pelvic)...

Along with the above description there will be other factors such as medication intake, toxic habits (alcohol, tobacco, drugs...), family history of congenital, mental, reproductive or cystic fibrosis, etc.

And to be able to find out if the sperm itself is part of the treatment, a spermiogram will be carried out with samples that should be collected by masturbation after 2-5 days of sexual abstinence and deposited in the Andrology Laboratory in a period of time less than one hour. The criteria to define the health of the sperm is defined by the World Health Organization (WHO, 2010)

Microscopic analysis will include the evaluation of variables such as concentration, mobility, vitality, agglutination, aggregation and morphology. Normality and nomenclature criteria have also been defined, depending on the seminal characteristics: it will differ the criteria for Artificial Insemination and the criteria for IVF/ICSI.

The number of spermiograms required is established by WHO and it is defined as two seminograms separated from each other by an interval of 15 days. If it is due to collection failure, the second sample can be collected at any time.

Freezing of the sample will happen and referring patients to the urologist's is not uncommon. In any case, it is important to notice that these collections could happen as a remote service... but only if there is the required set of devices (freezers, etc.) to warranty conservation of the sample until it reached the clinic.

- **Genetics**

Genetics are becoming more and more important in reproductive medicine.

Each cell of our body contains all our genetic information. This information is divided into small units called genes, which are the responsible of all our physical characteristics (for example our eyes and hair colour) and the correct function of the organism (for example our heart beating or food digestion).

Our genes are always duplicated, inheriting copies from each of the parents. When a gene has a small condition (known as a mutation), it may not work properly and lead to genetic disease. In 80% of genetic diseases, there is no previous family history.

There are different genetic diseases depending on the inherited pattern. One of them are the genetic recessive disorders, with the particularity that we all can be carriers but without showing any symptoms. In fact, most people are carriers with an average of 2.3 mutations causing disease. To be a carrier means that, out of the two copies of a particular gene, only one of them shows a genetic condition or mutation. By still having an unaltered copy, the gene works correctly and has no implication for the carrier.

The problem occurs when two people carrying the same mutation have children together, because there is the possibility of having an affected offspring. When both parents are carriers, the probability in each pregnancy of having children with the disease is 25% (effectively, 1 out of 4).

Genetic screening tests are performed in blood to analyze the presence of multiple recessive genetic variants, as well as variants linked to the X chromosome. This screening allows patients/doctors to know which of these variants are carriers and, thus, reduce the probability of having children affected by genetic disease.

If both parents are carriers of different genetic diseases, there is no risk of transmitting the said disease to the offspring. In the case that both parents were carriers of the same disease, there would be a 25% probability of transmitting it to their offspring. In these cases, there is the possibility of performing a genetic study in embryos (Preimplantation Genetic Testing or PGT). Once the embryos are analyzed, they can be healthy, carriers or affected, so that we will only transfer those that do not pose a risk of disease for the offspring (healthy or carriers).

The screening tests are very reliable, being more than 99% accurate for the mutations tested, but there are some limitations of the technique and the peculiarities of the genetic assignment.

If genetic testing is required for parents, a blood sample is enough and, therefore, it can be managed remotely by collection of the sample. If the genetic test needs to happen on the embryo, no further action with the patients is needed, since the embryos will be standing in the IVF lab for embryo development.

- **Inmunology**

The association between the immune system and reproductive function has long been an attractive target in research. Unfortunately, much of the early work has been misguided leading to premature implementation of therapeutic measures. Thus, a return to the drawing board approach is necessary.

There is renewed interest in foundational research to further our understanding of the immune interaction between the embryo and the endometrium. These studies will likely give new life to research in reproductive immunology. Building upon this foundational work will allow for more artful manipulation of the immune system to improve reproductive outcomes.

In this case, immunology requires general lab analysis (blood, urine...) and there are not great concerns in remote services around the samples and its validity.

- **Counselling**

When a couple decides to have a child they usually think that in a short time they will get pregnant; however, it often happens that the months pass and the pregnancy does not arrive. This delay in reaching the desired goal can generate some discomfort. It is likely that lately patients are noticing some changes in their life (in their mood, in their relationship, at work, with friends and family ...).

The first time in a Reproduction clinic they will probably have the suspicion that there is some difficulty. The situation might differ depending on the person, but it is possible that they have already done some treatment in another center and want to know someone else's opinion. In any case, the fear and anxiety generated by a situation of uncertainty like this is shared by most of the people who are in that situation. It's common to feel that way.

Once treatments are started, feelings may range from the illusion of starting the process to the fear of not getting pregnant. These emotional changes are going to be frequent throughout the treatment: some these days patients are more restless than usual, and they should not panic if they feel like crying or are more irritable. Some people even blame themselves for it.

Although these changes are part of the emotional process of the people who perform these treatments, counselling is there for help when needed. As it has been evidenced in related scientific research, emotional support throughout assisted reproduction treatments has significant benefits for patients.

5.5 Fertility treatments

After the patients are diagnosed and the best treatment option has been chosen, it is time to start the treatment. Below, the most important treatments in fertility care:

- **Artificial Insemination (AI)**

Artificial insemination is a method of assisted reproduction that consists of the deposit of sperm in the woman's uterus in order to achieve pregnancy.

To carry out an insemination, the patient's ovaries must first be hormonally stimulated in order to obtain an adequate number of eggs, usually one or two. When the follicles containing the eggs are the right size, ovulation induction is done, and insemination is scheduled. On that day, the male's sample is removed and prepared (or thawed, if a donor sample is used). The preparation of the seminal sample from fresh frozen semen consists of analyzing the starting parameters and enabling it to obtain the fraction with the spermatozoa with the best characteristics in terms of mobility, concentration and morphology.

The processed sample is introduced into the woman's uterus using a cannula, so that sperm inseminated in the uterus swim in search of the mature egg. It is an outpatient and painless process, and from that moment the medication (called support of the luteal phase) is started. It is usually in the form of vaginal eggs and should not be interrupted until indicated by the gynecologist.

If fertilization occurs, the fertilized egg develops as an embryo as it continues its journey into the cavity of the uterus, where it arrives about 5 days later. At this point the embryo is in the blastocyst phase, which must be able to implant in the endometrial tissue inside the uterus in order to continue the pregnancy.

It is 17 days after insemination when the blood pregnancy test is performed.

Artificial insemination is the fertility treatment that can be managed from home, since it does not require any type of anesthesia; as long as the sperm is properly managed, the procedure could be completed at the patient's home.

- **In Vitro Fertilization (IVF)...**

Ovarian stimulation consists of the administration of hormonal drugs, injected subcutaneously, to stimulate the ovary to achieve multiple follicular growth. During their natural cycle, women only produce one follicle each month with a single egg.

Ovarian stimulation requires vaginal ultrasound scans to measure the diameter of the follicles until they reach an approximate size of between sixteen and twenty millimetres. When the follicles are of a suitable size, follicular puncture or oocyte retrieval through the vagina will be scheduled.

The liquid drained from each follicle is what contains the eggs or oocytes, which, if they are at their optimum point of maturation, can be fertilized. To perform the fertilization process, we have two alternatives, according to the medical indications.

- The first, in which the oocytes are placed in a medium with the sperm, so that the fertilization can then occur naturally.
- The second option consists of micro-injecting the oocytes to insert a single sperm, a method also known as ICSI.

Each correctly fertilized egg produces one embryo, which continues its development with successive divisions until it reaches the blastocyst stage between days five and six after the ovarian puncture. The transfer to the mother's uterus is performed simply, through the cervix, waiting between ten and eleven days to do the pregnancy test.

In this case, the treatment that cannot be completely managed from home, since it does require anesthesia and puncture.

- **... including genetics**

An IVF treatment can happen with genetic testing of the embryos. At this point, everything will be just like above, until embryos reach day five.

In the blastocyst stage, a biopsy of its cells will be performed, which will be analysed to evaluate the embryo's chromosomes.

Once the biopsy is complete, the embryo is frozen (cryopreserved) until the result of the chromosomal analysis.

Once the report on the embryo or embryos analysed has been received, and, in the case of obtaining an embryo or chromosomally normal embryos, its thawing and transfer will be scheduled.

- **Egg donation (OVODON)**

Egg donation consists of the voluntary delivery of eggs from one woman (donor) to another (patient) who cannot use her own, thus offering her the opportunity to become pregnant.

To this end, a strict selection of donors needs to be made, who must pass exhaustive medical and psychological examinations. Only when donors are admitted to the donation program does the process begin.

Once the clinics have the right donor for the patient who needs it, we must coordinate the process of obtaining the eggs with the preparation of the patient's uterus to receive the future embryo. The donor must be hormonally stimulated the ovaries so that the follicular growth is multiple, and thus obtain a good number of eggs. Once they have the right number and size, the ovarian puncture is carried out. It is a process that is performed in the operating room under sedation, and it is the fluid aspirated from each follicle that contains the eggs that can later be fertilized in the in vitro fertilization laboratory.

After the natural fertilization or after ICSI, just like on the IVF cycle each properly fertilized egg gives rise to an embryo, which continues its development with successive divisions until it reaches the blastocyst stage between days five and six after ovarian puncture.

Of these, one will be transferred to the patient's uterus and the rest of the good quality embryos can be cryopreserved for further treatments.

To make the embryo transfer, the patient's uterus must be prepared properly. To do this, the patient has to administer as many doses of progesterone as days of embryo development, thus ensuring that the endometrium (the inner layer of the uterus) has the appropriate thickness.

The transfer in the mother's uterus is done in a simple way through the cervix, it is a painless and outpatient process, and between ten and eleven days later the pregnancy test is done.

In this case, since the treatment does not require a puncture for the patient, the treatment can be fully managed from home, since it does not require any type of anesthesia; as long as the embryo, in this case, is properly managed, the procedure could be completed at the patient's home.

- **Fertility preservation (FP)**

Fertility preservation treatment consists of obtaining and freezing eggs for future use, at the time when the woman wishes to be a mother.

A woman is born with around a million eggs and, although it seems a high number, it decreases throughout her life in quantity and quality. In each of the menstrual cycles that start month by month, several of them are launched, but only one ovulates on each occasion, the rest degenerate and are lost. In addition, from the age of thirty-five, this decline occurs more quickly.

On the other hand, the quality of eggs decreases with age, since their internal processes and error repair mechanisms are less effective over time. That means that as the woman's age increases there is a higher rate of chromosomal defects and abortions.

The reality of many women today is to have to make decisions regarding their personal project that lead them to postpone motherhood. It is in those cases when egg freezing is considered as the way to save the eggs at their optimum moment of quality and quantity and thus achieve a pregnancy when the right time comes.

The complete treatment comprises different stages. The first is the hormonal stimulation of the ovaries so that the follicular growth is multiple, and thus obtain a good number of eggs. Once they have the right number and size, the ovarian puncture is carried out to extract those eggs and take them to the in vitro fertilization laboratory, where they will be frozen. The most advanced Assisted Reproduction technique that offers the best results in egg freezing is vitrification. It is based on subjecting the eggs to very low temperatures maintaining their properties and with very high survival rates to freezing. Once vitrified they will be stored in nitrogen steam tanks at -196 degrees... and thaw the day they want to be used again.

Just like in an IVF cycle, the treatment that cannot be completely managed from home, since it does require anesthesia and puncture.

- **Embryo donation (ED)**

Embryo Donation is designed for patients that come to infertility consultation and do not want or cannot undergo a fertility treatment.

The embryo donation required medical criteria to be carried out on patients who, at the same time, need to accept by signing informed consents for Embryo Donation.

The In Vitro Laboratory of a clinic is usually in charge of managing the frozen embryos that have been donated by couples who will no longer use their frozen embryos. It is required to perform a search for compatible donated embryos, based on the indication of the Gynecologist.

Once the lab and the gynecologist verify the existence of donated embryos compatible with the couple, there is a procedure to accept/validate the donation that has to include the IVF lab, a psychologist and the doctor responsible for donation.

As in any other donation, patients will have to proceed to perform serologies when necessary. Just like in a donation cycle, once the clinics have the right donated embryo for the patient who needs it, there is a need to prepare the patient's uterus to receive the future embryo.

The couple donating the embryo will not take part in the process, since the the ovarian puncture, fertilization and embryo development happened long ago and before the embryo was frozen.

One more time, since the treatment does not require a puncture for the patient, the treatment can be fully managed from home, since it does not require any type or anesthesia; as long as the embryo, in this case, is properly managed, the procedure could be completed at the patient's home.

On the table below, there is a final description of the treatments that could be fully completed from home:

	Patient puncture?	Insemination?	Embryo transfer?	Fully at home?
Artificial insemination	NO	YES	NO	YES
In Vitro Fertilization	YES	NO	YES	NO
Egg donation	NO	NO	YES	YES
Fertility preservation	YES	NO	YES	NO
Embryo donation	NO	NO	YES	YES

Table 6. Treatments and availability of at home services

The right column on the right shows the treatment that, with the adequate level of safety around the embryos and the sperm could be fully completed from home.

It is also important to understand that a patient can undergo a treatment and finalize it with several frozen embryos. In case of non-pregnancy, another cycle can be started that will be named as a Frozen Embryo Transfer (FET)

On the table below we can see the extended table including Frozen Embryo Transfers if we want to consider them as a treatment.

	Patient puncture?	Insemination?	Embryo transfer?	Fully at home?
Artificial insemination	NO	YES	NO	YES
In Vitro Fertilization	YES	NO	YES	NO
Egg donation	NO	NO	YES	YES
Fertility preservation	YES	NO	YES	NO
Embryo donation	NO	NO	YES	YES
Frozen embryo transfer	NO	NO	YES	YES

Table 7. Treatments and availability of at home services, including Frozen Embryo Transfers

5.6 Embryo development and maintenance

Patient embryos are left in incubators for growth.

The embryo begins its existence as a relatively large cell with a low ratio of nuclear to cytoplasmic volume. Within a few days, cleavage has increased the ratio to near normal and blastocyst formation begins. The formation of the blastocyst is an important event and is the first morphological sign of differentiation. It is also at this time that a variety of metabolic indices markedly increase, including oxygen consumption, incorporation of precursors into nucleic acids and protein synthesis. Let's remember the embryo development days:

- **Day 0**
Once an egg is collected, it is washed and prepared for either insemination (IVF) or ICSI. Sperm is similarly washed and primed for the chosen procedure.
- **Day 1. Zygote**
The egg is checked for evidence of fertilisation. A zygote is the union of an oocyte (egg) and the sperm. And this will be a new embryo that needs to develop.
- **Day 2**
The embryo's single cell should have replicated into two by now, and those two cells may also have further split, giving a four-cell embryo.
- **Day 3**
The cells will keep splitting into two in a healthy embryo, gradually increasing the cell number. At this point, it may be decided to transfer the embryo back into the uterus.
- **Day 4. Morula**
The embryo's cells will begin to compact on this day, preparing to form a blastocyst.
- **Day 5. Blastocyst**
A healthy embryo will form a blastocyst by now, dividing its cells into sections that will form the foetal matter and placenta.

Assisted reproduction techniques (ART) have a long history. We could make a list of the most significant stages of ART innovations ending up on embryo developments:

- **1785.** Conception by artificial insemination in dogs by Lazzaro Spallanzani (University of Pavia, Italy) (Spallanzani, 1785).
- **1900s.** Artificial insemination techniques for use in horses, cattle and sheep developed by Ilya Ivanov (State Veterinary Institute, Russia).
- **1940s.** Techniques to freeze and store animal spermatozoa developed by Chris Polge (University of Cambridge, UK).
- **1934.** IVF of rabbit oocytes followed by transfer into the fallopian tubes by George Pincus and Ernst Enzmann (Harvard University, USA).
- **1954.** First characterization of human pre-implantation embryos (at the 2-cell and later stages) by Arthur Hertig and John Rock (Free Hospital for Women in Brookline, USA).
- **1957.** Development of superovulation in mice using gonadotrophins by Robert Edwards and Ruth Fowler (University of Cambridge, UK).
- **1959.** In vitro fertilized rabbit oocytes capable of proceeding to live birth were demonstrated by Min Chueh Chang (Worcester Foundation, USA).
- **1969.** Early stages of IVF of human eggs by Robert Edwards and colleagues (University of Cambridge, UK).
- **1970.** Successful culture of human cleavage stage embryos by Robert Edwards and colleagues (University of Cambridge, UK).
- **1972.** Cryopreservation techniques for the long-term storage of pre-implantation mammalian embryos by David Whittingham (Oak Ridge National Laboratory, USA).
- **1978.** Birth of the first child conceived via IVF reported by Robert Edwards and Patrick Steptoe (Oldham General Hospital and Bourn Hall Clinic).
- **1992.** Development and successful use of intracytoplasmic sperm injection (ICSI) to assist with infertility by Gianpiero Palermo, Paul Devroey and Andre Van Steirteghem (Vrije Universiteit Brussel, Belgium).

There are techniques to be able to freeze embryos, so that they can be kept from evolving until the patient is ready to receive the embryo into the uterus. Let's take a look to historical steps taking to improve this method for preserving embryos:

- **Cryopreservation**

Traditional cryopreservation methods allow ice to form and solute concentrations to rise during the preservation process: both ice and high solute concentrations can cause damage.

Cryoprotectants are highly soluble, permeating compounds of low toxicity; they reduce the amount of ice that crystallize at any given temperature and thereby limit the solute concentration factor. Vitrification methods use cryoprotectant concentrations that are sufficient to prevent the crystallization of ice altogether the material solidifies as an amorphous glass and both ice and solute concentration are avoided. However, the concentrations of cryoprotectant required are very high indeed and therefore are potentially, and often actually, harmful to cells.

Cryopreservation of human oocytes and embryos or blastocysts is an important choice in assisted reproduction treatment that leads to an increased cumulative outcome while decreasing other attempts' costs. It provides an opportunity for patients to have more than one attempt following an ovarian stimulation cycle, thereby decreasing the exposure of patients to exogenous gonadotrophins.



Figure 11. Image to illustrate cryopreservation in a laboratory

- **Vitrification method**

Vitrification is a method in which not only cells but also the whole solution is solidified without the crystallization of ice.

The vitrification method has advantages over the slow freezing method. Injuries related to ice is less likely to occur, embryo survival is more likely if the embryo treatment is optimized, and embryos can be cryopreserved by a simple method in a short time and cost effective without a programed freezer. Successful cryopreservation of human embryos was first reported in 1983 by Trounson and Mohr using days two and three embryos that had been slow-cooled using dimethyl sulphoxide (DMSO).

Subsequent modifications of the technique had taken place such as introducing 1,2-propanediol and sucrose as cryoprotectants (3) and slow-cooling to $-30\text{ }^{\circ}\text{C}$ prior to plunging into liquid nitrogen. All these resulted in the introduction of cryopreservation as a standard method offered by virtually every IVF program world-wide (4). Recently, lots of reproductive clinics, using embryos and blastocysts cryopreservation depend on vitrification. Vitrification is an ultra-rapid method of cryopreservation whereby the embryo is transitioned from 37 to $-196\text{ }^{\circ}\text{C}$ in $<1\text{ s}$, resulting in extremely fast rates of cooling. High concentrations of cryoprotectants together with rapid cooling rates are essential to cryopreserve embryos in a vitrified, glass-like state.

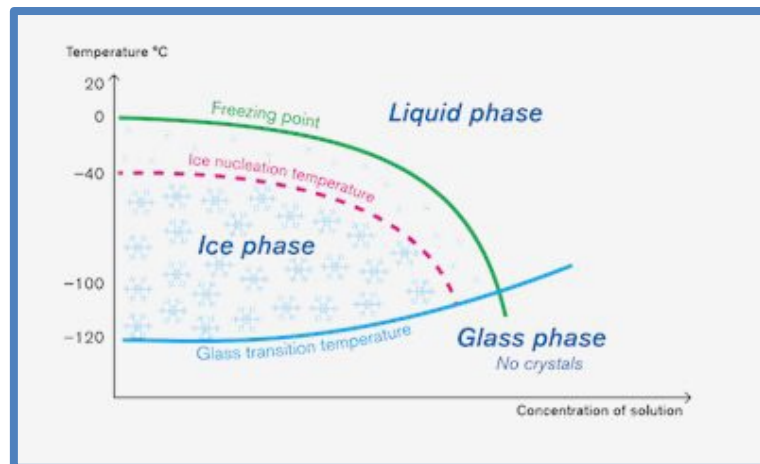


Figure 12. Image to illustrate relevant cryopreservation temperatures

- **Oocyte cryopreservation**

The first human pregnancy from cryopreserved (by slow freezing) oocyte was reported in 1986. This followed many success experiments in other laboratory species that came a few years earlier, such as in mouse and rat.

Vitrification gained a foothold only after 2005, prior to which only ten human pregnancies resulting from vitrified oocytes were reported. Although, high oocyte survival rate is achieved with both methods, fertilization and embryo transfer rates are still considerably lower than when fresh oocytes are used. When comparing slow freezing to vitrification, higher oocyte survival rates are achieved by the latter (95%, 899/948) compared with (75%, 1275/1683) by the former but pregnancy rate per thawed/warmed oocyte is still low – in the range of 1.9–8.6% for slow freezing and 3.9–18.8% for vitrification.

Moreover, oocyte cryopreservation has emerged as a solution that could preserve the fertility without the need of sperms and many women consider fertility preservation as a necessary part of their plan of treatment (34). Many gynecological and non-gynecological cancers as well as their therapeutic treatment may affect the ovarian tissue and its follicles and cause gonadal toxicity. Therefore, oocyte cryopreservation at younger ages or prior to chemotherapy using vitrification had been proposed as a solution to enabling women to yield a normal pregnancy and maintain their fertility (35).

- **Embryo cryopreservation**

Until now, vitrification has been widely used for the cryopreservation of human oocytes, in vitro matured oocytes, pronuclear stage, cleavage stage or blastocyst-stage.

However, there are few publications that show clinical data on the basis of vitrification versus slow freezing, especially for the cleavage stage. A modification to cooling rate that came a few years later resulted in a basic protocol that is still in vast use today.

When considered from conservation standpoint, embryo freezing has the advantage of preserving the entire genetic complement of both parents. Vitrification is a method in which not only cells but also the whole solution is solidified without the crystallization of ice. For blastocysts cryopreservation, the vitrification method has advantages over the slow freezing method also. However, solutions for vitrification must include a high concentration of permeating cryoprotectants, which may cause injury through the toxicity of the agents.

Embryos of various species, including humans, can be cryopreserved by conventional vitrification using insemination straws or by ultrarapid vitrification using minute tools such as electron microscopic grids, thin capillaries, minute loops, or minute sticks, or as microdrops. In the ultrarapid method, solutions with a lower concentration of permeating cryoprotectants, thus having a lower toxicity, can be used, because ultrarapid cooling/warming helps to prevent ice formation.

6 Implementation. Steps forward

To become operational in a digital world, it is a must to offer services to accommodate the needs of patients, doctors, staff in the clinics and automation around the provided services. Let's see some examples on the literature on how these things might happen or have been foreseen:

- How the capabilities related to connectivity have created a technology-led ecosystem to address patients and transform the healthcare system in China.
(Terence C. Cheng, 2022)

[...] The use of digital technologies in the delivery of health care services in China is accelerating, driven by government policy and the growth of Internet enterprises. From 2013 to 2019, the total value of new investments in China's Internet health care market grew from 4.5 billion (US\$675million; 1 = US\$0.15) to 37.9 billion (US\$5.7 billion) [...]

- The evolution of Point-of-Care Ultrasonography (POCUS), which has to do with the fertility process and is a must in technology driven processes
(José L. Díaz-Gómez, 2021)

[...] Point-of-care ultrasonography (POCUS) is defined as the acquisition, interpretation, and immediate clinical integration of ultrasonographic imaging performed by a treating clinician at the patient's bedside rather than by a radiologist or cardiologist. POCUS is an inclusive term; it is not limited to any specialty, protocol, or organ system.¹ With the advent of smaller and more affordable ultrasound machines, combined with evidence that nonradiologists and noncardiologists can become competent in the performance of POCUS, it is now used in many practice settings and in all phases of care — from screening and diagnosis to procedural guidance and monitoring — and has become associated with changes in clinical decision making in medical practice [...]

- Home Care in Europe.
(Rosanna Tarricone & Agis D. Tsouros, 2022)

[...] Demographic, epidemiological, social, and cultural trends in European countries are changing the traditional patterns of care. The next decades will see increasing rates of care-dependent older people and noncommunicable diseases as the leading cause of chronic illness and disability. The break-up of the traditional large family group and urbanization will also lead to gaps in the care of older or disabled family members. These changes in needs and social structure require a different approach to health and social sector policy and services since a disease-oriented approach, alone, is no longer appropriate. An answer to these issues could be home care, a sustainable approach to prevent the need for unnecessary acute or long-term institutionalization and maintain individuals in their home and community as long as possible [...]

- The expected evolution of in vitro fertilizations labs along with andrology laboratories from now until 2030 based on expert visions (Alison Campbell, 2021)

[...] Many aspects of the IVF and andrology laboratory will be automated by 2030. Implementation is likely to be phased, involving several systems that can be linked together, although some comprehensive automated or digitalized solutions may be available. For example:

- *Fully automated, rapid semen analysis with minimal manual input*
- *Increased accuracy and availability of fertility testing and monitoring at home*
- *Assessment and selection of gametes and embryos with artificial intelligence (AI) decision support tools*
- *Automated culture dish preparation with automatic media sampling for quality assurance [...]*

- The New England Journal of Medicine referring frontiers in medicine as far as mobile devices and health are related (Ida Sim, 2019)

[...] Mobile health — the application of sensors, mobile apps, social, media, and location-tracking technology to obtain data pertinent to wellness and disease diagnosis, prevention, and management — makes it theoretically possible to monitor and intervene whenever and wherever acute and chronic medical conditions occur. With 81% of North American adults owning a smartphone,¹ this frontier could be reached in the foreseeable future in the United States and is particularly relevant to the management of chronic diseases [...]

And after this, let's take a look to the most important services that need to be provided: Online consultations, a patient portal to share documents and content and testing kits to remotely manage not only the samples but also the images (ultrasounds) required to offer remote fertility care.

6.1 Online consultations

This is part of the initial steps between patients and doctors/clinics in the patient journey. The process will start with a first visit where, if the patient decides to move forward with a treatment, will be the initial contact of many to come.

Online consultations become the most interactive way in which a patient and a clinic/doctor will exchange their views on the progress of the treatment. It is therefore a need to enhance all the capabilities of the video-conferencing tools to promote the best experience for patients.

As in the real world, there is a need to design a waiting room where patients can interact with the clinics while waiting for the meeting. This requires defining content and experiences so that patients can feel comfortable and learn more about their counterparts.



Figure 13. Image to show a video-conference

Based on Microsoft and Zoom figures, more than 50% of the appointments start at least three minutes late. The waiting time in a physical waiting room and with professionals nearby varies greatly compared to having to wait in front of a screen without anything or anyone telling you that you are in the right place.

As soon as the waiting time is more than 3 minutes, patient begin to doubt the veracity of their appointment, incorporating negative elements in his assessment perception of the service received. That's why action needs to be taken, because the patient feels a sense of loneliness at the time of online waiting.

The first contact that the patient has on an online consultation is with the doctor; there is a need to set up a waiting room similar to a face-to-face room, with messages and personalized information that reduces the feeling of uncertainty. With features such as a chat to avoid feelings of loneliness in the patient.

These virtual waiting rooms should contain features such as the following ones:

- **Doctor's presentations**

Videos where the patient is welcomed by the doctor who is going to treat him is a good way to meet each other virtually. In those videos, doctors should present themselves personally and professionally, explaining the processes and methodology they usually perform, transmitting a message of safety, tranquility and professionalism about the practice and the clinic.

The objectives of this interaction would be to connect with the patient, make a close piece that offers context and information, at the same time empathize with their situation before getting into the context of the treatment.

- **Interactive clinics**

Multimedia elements should present a clinic in an interactive way. There should be videos that physically tour the center explaining all the services and capabilities available.

The interaction should be simple: a patient should visualize virtually the entrance hall of the center where the reception person introduces the clinic and indicates the services they have; patients should be able to select the services/unit they are interested in and each service/unit of the clinic should be presented by the person in charge, explaining its capabilities and benefits.

The objective is that patients, especially the new ones, get to know beforehand the center where they will be treated and transmit, at the same time, a message of safety, professionalism and innovation about the treatments they will follow.

- **Next steps tutorials**

Branded as video-guides, they should describe, in a simple and detailed way, the actions that must be carried out to complete a process/treatment; in this way clinics and doctors focus the knowledge in the patient and generate a content that can be reviewed as many times as necessary.

Those videos can help perform tasks that the patient will face throughout the journey of their online visit: uploading documentation, next steps of the patient, legal procedures, medical guidelines, etc.

Online consultations need to be redesigned. Therefore, a training plan is needed to extend the culture in the organization that moves from the current status to the desired situation. This should involve the following situations:



Figure 14. Organisational areas

Define the areas involved, the staff of the professional team and establish the training models for each of the identified groups.



Figure 15. Check-lists

Identification of new needs to carry out the project: materials, resources and staff



Figure 16. Training sessions

Planning of the training sessions and accompaniment at all times to professionals and transmission of the importance and impacts of the new model for the online consultation.



Figure 17. Validation

Constant checking that each of the steps of the different initiatives are being carried out in the optimal way. Ensure understanding by all users



Figure 18. Team culture

Build a culture where teams are aligned and built towards the same goals. This also means to establish periodic communication plans for project monitoring

From a Quality Assurance perspective and from a Methodology point of view, a culture of process needs to be setup so that performance does not vary depending on the clinician and medical professional. A customized and tailor made definition of the process has to be in place.

This will help, to some extent, improving the quality and consistency in the experience offered. It will also increase satisfaction and loyalty, eliminating barriers to improvement.

Some of the items to be considered to establish a unique way of handling online consultations could be the following ones:

- Homogenize the duration of the online consultations for doctors and clinics
- Structure the development of online consultations by differentiated blocks and thus ensure that all doctors follow the same online methodology
- Standardize the audiovisual material used to give a corporate format where the branding of the company is shown.
- To give the patient the possibility to include their main concerns with the intention that the doctor can better prepare the online consultation according to the specific needs of the patient

The efforts to settle a new methodology and way of doing things needs to be accomplished by the efforts to extend the new culture by all the staff, specially by doctors. This means:

- On the part of doctors, try to be as punctual as possible, transmitting a greater image of professionalism and seriousness
- Training and involvement, taking into account the protocol to be followed, with the required flexibility in its implementation
- Continuous training, monitoring and communication of any technological update
- Involve doctors and motivate them to move to a digital world where they can obtain and share loyalty results and set loyalty goals on behalf of the company.

6.2 Patient portal

The patient portal will cover the whole patient journey of the patient. It might be part of the relation between patients and doctors/clinics even before meeting anyone in person.

A patient portal is required in every health care company. Not only to become a remote or at home care service; but the needs and the service level should be increased in this area as the remote services evolve. Services that should be provided to patients could be listed as seen below:

- **Online registration process**

The registration process is the first step to access services: appointments, documentation, surveys... any type of service needs a prior registration where, even before becoming a patient, the service catalog can be reviewed.

- **User profile and personal data**

The configuration needs to allow users to manage the personal data... and their profile. What is the personal data they want to share, if they are willing to receive notifications through an APP, partner sharing options (to share reports or not with their partner, depending on the will of the patient)... This needs to be based on the current regulations, driven by GDPR in Europe



Figure 19. GDPR representation

- **Active notifications and reminders**

A patient portal needs to have different types of notifications to be close to patients as their process evolves and, in a selfish way, to try to simplify communication with the clinics and, therefore, avoiding phone calls or questions that can be sorted by providing information in advance:

- Appointment reminders
- Medication reminders
- Confirmation on appointment and medication correctly applied
- Messages sent or received
- New documents on the portal

As many as possible to drive operations through automated processes that keep the patient informed on any change in their process.

- **Information and appointment request**

It is ideal that the patient can do it on its own as a self-service process.

Nevertheless, some support will be requested at different stages; that is why these communications need to be centralized in a patient portal that drives the request to the most appropriate team/person in the clinic.

In this sense, a Contact Center will be the most important link between clinics and patients to manage appointments or any other details and additional information to be shared to serve and comfort patients.

- **Surveys**

Surveys are critical to receive patient feedback. Therefore, it must be one of the items to be considered in designing a patient portal and remote services.



Figure 20. Illustration for surveys

- **Clinical background. Medication. Reports. Follow-up**

Medical information will be the core information to be shared.

It will be managed in two different ways: as background information that the patient needs to provide to the doctors/clinics, or as follow-up information that patients need to receive to move on with their treatment and its results. Some samples are:

- Medication to be taken by the patients
- Set up for medication reminders
- Videos to understand how medication needs to be taken
- Confirmation of the taken medication and the lack of issues
- Reports on the evolution of the treatment
- Videos on the different stages a patient is going through during the treatment: stimulation phase, puncture, transfer...
- Reports on the different tests (hormones, blood, urine, etc.)

- **Medical team**

It is important to know the people involved in the treatment with the patient. Getting to know the medical team – images, experiences, background... - helps patients to feel comfortable and, depending on the doctor/clinic, direct access to the doctor might be a service to be provided

- **Document signature, prescriptions, KYC, etc...**

Moving into digital means activating as many integrations as required to validate, from a legal point of view, any interaction with patients. Therefore, daily services that happen on paper or in presence in the clinic, need to be moved to a patient portal:

- Document signature – electronic signature
- Medication prescriptions – electronic prescriptions
- KYC – Know Your Client; digital verification of patient's identity

As an example of companies providing these services we could find NeoCheck.

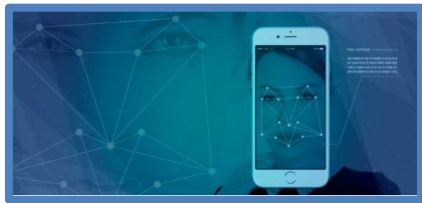


Figure 21. Illustration of biometric scan provided by NeoCheck



Figure 22. Illustration of electronic signature provided by NeoCheck

- **Quick request and response**

FAQs, chats, whatsapp messaging... there is a need to provide access to a quick question-response mechanism that can be used by the patient for urgent needs. Of course, not only through a patient portal but also on the phone... but a patient portal has to be ready to deliver quick responses to patients

- **Payments**

Payment gateways are a must to become digital. They must be integrated in a way that shows confidence to patients... and, of course, need to be properly secured.

6.3 Testing kits

Kits, sample collections and delivery handling is the part of the patient journey that is related to the treatments themselves: Step 2 (meaning prior to stimulation) and step 3 (during stimulation) and the key moments to manage these kits in the right way.

Testing kits are one of the key milestone to be achieved when providing remote and at home services on fertility care. Most of the diagnosis will start with the need to collect blood samples for serologies and different hormone levels to be checked. Let's take a look to the three most important samples to be collected: blood, urine and sperm.

- **Blood samples**

COVID-19 infections have changed many rules in every country on the planet and collecting blood samples is one example of how things can change.

Labs can utilize remote blood collection for serology tests that detect SARS-CoV-2 antibodies and get the world closer to developing effective vaccines and treatments.

Several labs around the world are already running COVID-19 studies that utilize remote blood collection kits to gather blood samples from study participants by mail. These virtual studies are different from those that require study participants... and they enter the new path to be followed since lab or clinics do not need to be visited for blood drawing or plasma drawing using venipuncture.

These labs are now adopting a telehealth approach to COVID-19 studies by sending microsampling devices and blood collection Kits from to study volunteers for at-home blood collection... and this is one of the best options for remote fertility care



Figure 23. Image to show a blood sample collection

- **Urine samples**

Although urine tests are less common, they are following a similar path to the stated above for blood tests. The success from a remote care perspective is achieved sending patients a urine collection kit, which contains the necessary supplies for the collection and transportation of urine.

The urine collection kits are easy to use and contain detailed instructions. Patients will collect their urine and ship it in the kit provided back to the site for screening. Once the kits are received on-site, research staff will first test the urine specimen for adulteration then substance screening. And if tests are positive, meaning there is no adulteration of the sample, the analysis will happen.

- **Sperm samples**

Once again, there is an option to manage collection kits. In fact, the sperm kits are more common in the market because there are commercial products created to undergo a self fertility test on sperm at home.



Figure 24. Image to show a sperm test kit

The challenge in this case is that clinics/doctors cannot trust those tests... and, in any case, they can process samples so that sperm that might not help for the pregnancy is processed in the lab in a way that spermatozoids capable of fertilizing an oocyte can be retrieved and inseminated.

The objective then in sample collection is to provide the patient with the necessary information for the correct collection of the semen sample and to avoid as far as possible, contamination or loss of the ejaculate during the collection process.

The sample together with the document of ownership of the sample – very relevant from a legal stand point - will be received in the andrology laboratory verifying the correct completion of the same:

- Verification of the identity of the sample
- Pick-up time
- Days of abstinence
- ...

The sample preparation will happen by completing liquefaction of the sample by rest for a minimum of ten minutes and, if necessary, the sample shall be incubated at 37 °C until complete liquefaction.

Sperm is homogenized, aliquoted to be able to manage more patient samples, evaluated for spermatozoa counting and evaluation of the sample. In case the patient sample is not good enough to achieve pregnancy, a donor sample will be needed.

In this case, since the property of the sample is so important along with the environmental conditions to keep the sample, this process cannot be managed with a kit. So the remote fertility care service really needs to have somebody visiting the patient at home to validate both legally and clinically the validity of the sample.

6.4 Ultrasounds and imaging

In a similar way to testing kits, the part of the patient journey covered in step 2 (meaning prior to stimulation) and step 3 (during stimulation) is where ultrasounds are needed. Additionally, on step 6 and after the positive or negative pregnancy test will again become relevant.

Ultrasound imaging is part of the required follow-up on a fertility treatment. Through the images provided to doctors by these devices, monitoring of the evolution of the stimulation process is controlled to manage the number, size and proper development of the follicles. In this sense, it is basic to control medication.

There are many types of devices and we can see some of them below.

These devices are the ones that, with different structure but a similar value proposition, allow to monitor patients on the road.

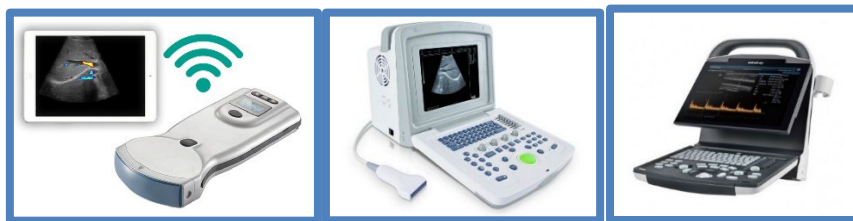


Figure 25. Set of images to show an ultrasound portable device

Taking one step beyond, the future of these devices for remote/at home care service is to provide instructions that allows them to be used by patients on their own.

This brings in new challenges, because images need to be improved to properly capture the relevant information and, further than that, artificial intelligence comes into play to provide automated results for doctors based on the images.



Figure 26. Image to show an ultrasound portable device

If patients can monitor themselves from home... what is the next steps, then?

The system settings need to help to track each patient individually; network configuration issues or image sharing setup must be defined and managed in a simple way so that patients become part of a process where workflows easily integrate monitoring with devices, doctor's review and medication dosage to end up with the best possible results through the treatment.

Digital Imaging and Communications in Medicine (DICOM) is the standard for the communication and management of medical imaging information and related data.

So this is how storing and transmitting medical images enables the integration of medical imaging devices such as scanners, servers, workstations, printers, network hardware, and picture archiving and communication systems (PACS) from multiple manufacturers. It has been widely adopted by hospitals and is making inroads into other healthcare areas.

7 Service needs provide value

Remote services might streamline processes for both patients and clinics, but as a starting point they will provide a better service for the patients at a higher cost, since those remote services do not provide additional benefits for the company – or less cost.

Let's take a look on how these services will behave in terms of resources to be provided by the doctors/clinics to the patients and the value of these services.

7.1 Additional services required to undergo remote fertility care

As referred in the implementation section, depending on the involved section of the patient journey, we have to consider different blocks to add new services:

- Online consultations
This is part of the initial steps between patients and doctors/clinics in the patient journey... but will be used in any step when communication is needed.

The required service will be to redesign the way in which a video-consultation is managed so that it allows content sharing, access to training tools, embedded documentation... all about information sharing with patients.

- Patient portal
As the online consultation, the patient portal will cover the whole patient journey of the patient.

The required services in this case will be to develop software and integrate processes with the electronic medical record or health information system used by doctors and clinics, so that processes can be standardized and patient management and follow-up becomes real step by step workflow.

- Testing kits
Important in step 2 (meaning prior to stimulation) and step 3 (during stimulation) of the patient journey, the most difficult item to cover will be to make sure that they are available at the right time – not only from the patient perspective to collect samples, but also from the perspective of doctors and clinics to make sure they get the results they need at the right moment.

- Ultrasounds and imaging

In a timeline, they are as important as a testing kit and will affect, apart from steps 2 and 3 of the patient journey, step 6 around the pregnancy test.

The new services described above will require an additional effort in logistics. That's why we will consider an additional section of this document to review how to manage logistics.

7.2 Additional software required to manage processes

Software development for tailor-made services requires analysing the processes in depth along with developing the solutions that will respond to the requirements.

The software market does have many tools to respond to many general services, including health and logistics, but the key value to this process is integration among all the parties. Therefore, let's take a look to what's needed to develop to offer the service not only as a remote service but also as a completely digitalised process to ease patients and doctors/clinics' usage and acceptance.

- Health Information System (HIS) and Patient Portal
 - It is a must to count on a HIS or Electronic Medical Record (EMR).
 - It is also a must to count on a Patient Portal.
 - The key factor to success is integrating communications and workflows between both to streamline processes.

- Testing kits and monitoring devices integration
 - Testing kits and monitoring devices can be handled in two ways:
 - As stand-alone kits/devices used by patients... and with information to be manually reported or transferred to the clinics
 - As integrated kits and devices with self-management allowing them to connect to a HIS/EMR to transfer data
 - The second approach will be the desired one... although it would be feasible to start remote fertility care without the device's integration level of service.

- Image integration
 - Images (ultrasound echographies) are not in the same situation as testing kits, because imaging is complex to manage properly.
 - Just like with the patient portal and the HIS/EMR, it is a must to count on a tool that allows integration with the HIS/EMR, so that doctors can count on the patient's monitoring at the right time... and in the right way.

- Logistics integration
 - Logistics is a separate item that can be isolated.
 - Patient appointments should be managed from two different perspectives: the ones that require mobility and the ones that do not. And logistics could be an additional item before offering a slot/appointment to patients.

The table below shows how software should help to create these tailor-made services:

	MUST integrate?	Nice to integrate
HIS or EMR	YES	
Patient Portal	YES	
Testing devices		YES
Monitoring devices		YES
Imaging - ultrasound	YES	
Logistics		YES

Table 8. Software development and integration requirements

7.3 Additional devices needed by a clinic

New devices are required for new services.

The most important device, though, is the portable ultrasound machine... that can collect the images for cycle monitoring.

There are not on the market specific devices to support hormone monitoring or self-captured images from patients... so they have to be built. In the mean time, it is an option to move forward with visits at the patient's home or the usage of testing kits. Let's see how:

- Testing kits and monitoring devices

Many testing kits are already in use for blood and urine.

Self-testing kits are also available for sperm.

The clinical needs go one step beyond... because it is required a laboratory validation to be sure that the sample has been properly managed and, sometimes, the sample is requested to be used in different processes.

Therefore, specific devices to collect blood and sperm will have to be built, although it is not a must to start out.

It is important to point out that blood can be kept (plasma) and that sperm can be also kept (cryopreservation). Nevertheless, urine will be considered as a one time use sample when requested.

- Image integration

Building a device to allow patients self usage is going to be a huge step forward in remote services for fertility.

Nevertheless, there are not any commercial devices that allow that in today's market offer, so it is requested to visit the patient for monitoring when requested. So far, the devices that need to be added to the portfolio are the portable ones, which are not common in clinics.

8 Logistics. Route optimization

There is a need to optimize routes.

How should this be managed? We can imagine that there are different options, each one of them with benefits and disadvantages. Let's take a look at some of them:

[Advantages]

- Economies of scale
- Real time inventory management
- Backoffice management simplification
- ...

[Disadvantages]

- Disconnection with patients/clients
- Quality and pricing control
- Not considering logistics as something strategic

For the purpose of this work and, in order to be able to analyse more items, we will consider that the desired solution is managing logistics as a strategic part of the service and, therefore, to cover the needs internally.

To be able to ensure the most efficient routes, we need to ensure some items that will create the requested environment to provide the service in the best way.

- **Determine skills and capacities available**
The smart appointment scheduling determines if skills are available for each order – in our case, nurses and or other healthcare professionals
- **Create hub for orders - appointments**
A hub or centralized point for orders which makes sure route planning plays its full role. It obviously needs to be integrated with the Health Information System to synchronize appointments
- **Ensure geographical coherence**
The route planning needs to ensure the geographical coherence regarding customer expectations and, therefore, a scope is needed to really be able to offer the service
- **Determine schedules of drivers**
Schedules of drivers and healthcare professionals are determined during the route planning and not before... so this means flexibility on their availability.

Would that be all that is required? No, it is not... we still need to consider many more items to be able to set up a service that really disrupts the market; so the question is: What do we need to review in detail to carry out the service?

- **Factors regarding the order**
Type of order, address, required skills to perform a visit, required material to perform a visit, date and time slot plus duration of the visit
- **All the factors regarding the purpose of deliveries or operations**
Address of delivery, pick-up or visit, date and time slot, type of transport (living, solid, liquid), capacity (weight, volume, material...), maximum transport duration, duration of delivery and pick-up or visit
- **All the factors regarding drivers and field workers**
Working hours, skills and licenses, absences, departure and arrival addresses, duration of breaks
- **All the factors regarding the vehicles**
Type of vehicle, Gross vehicle weight rating, Volume, Equipment of vehicle, Operational costs, Type of contrat (owner / long-term rental), Driving objectives, Availabilities.
- **All the factors regarding the traffic conditions**
Usual congestion areas Constraints of heavy goods vehicle, Topography, Weather

With all the considerations above, the objective should be:

1. Respect driving objectives
2. Cut down costs
3. Create routes with balanced working time
4. Create routes with balanced travel time
5. Maximize the number of orders/appointments per route

Although there is no literature about it, many references on the web help on the usage of Google Maps as a route planner. The limitations below would determine a need to scale and find a new software/tool if all patients were managed at home:

- You can only plan for 1 driver at a time
- You can't optimize routes using constraints like delivery time windows, vehicle load capacities, driver breaks, etc.
- There is a maximum of 10 stops to be managed as of today

The links below help understand its usage:

- <https://blog.routific.com/google-maps-route-planner-for-deliveries>
- <https://www.upperinc.com/blog/how-to-use-google-maps-route-planner/>
- <https://support.route4me.com/faq/plan-routes-guide/how-to-plan-delivery-route-on-google-maps/>

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