SPECIAL CONTRIBUTION

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Infertility services integrated within the maternal health department of a public hospital in a low-income country, Rwanda

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Objective: To describe the initiation, integration, and costs of reduced-cost infertility services within the maternal health department of a public hospital in a low-income country.
Design: Retrospective review of the clinical and laboratory components of patients undergoing in vitro fertilization (IVF) treatment in Rwanda from 2018 to 2020.
Setting: Academic tertiary referral hospital in Rwanda.
Patients: Patients seeking infertility services beyond the primary gynecological options.
Interventions: The national government furnished facilities and personnel, and the Rwanda Infertility Initiative, an international nongovernmental organization, provided training, equipment, and materials. The incidence of retrieval, fertilization, embryo cleavage, transfer, and conception (observed until ultrasound verification of intrauterine pregnancy with fetal heartbeat) were analyzed. Cost calculations used the government-issued tariff specifying insurers' payments and patients' copayments with projected delivery rates using early literature.
Main Outcome Measures: Assessment of functional clinical and laboratory infertility services and costs.
Results: A total of 207 IVF cycles were initiated, 60 of which led to transfer of ≥ 1 high-grade embryo and 5 to ongoing pregnancies. The projected average cost per cycle was 1,521 USD. Using optimistic and conservative assumptions, the estimated costs per delivery for women <35 years were 4,540 and 5,156 USD, respectively.
Conclusions: Reduced-cost infertility services were initiated and integrated within a maternal health department of a public hospital in a low-income country. This integration required commitment, collaboration, leadership, and a universal health financing system. Low-income countries, such as Rwanda, might consider infertility treatment and IVF for younger patients as part of an equitable and affordable health care benefit. (Fertil Steril Rep® 2023;4:130–42. ©2023 by American Society for Reproductive Medicine.)
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The World Health Organization (WHO) defines infertility as inability to achieve pregnancy after 12 months of regular, unprotected sexual intercourse (1). Infertility is a significant, but neglected, problem worldwide. In 2012, WHO researchers estimated that overall trends in infertility rates had remained largely unchanged from 1990 to 2010, with Asia and subSaharan Africa leading the global burden (2). Using studies

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through 2021, WHO estimated the lifetime and period prevalence of infertility in low-income countries at 16.5% and 12.6%, respectively. High-income countries had an even greater lifetime prevalence (17.8%), which may be due to women in those countries delaying pregnancy (3). Infertility causes psychological distress, stigma, and social challenges, including marital discord (4), intimate partner violence (5, 6), and economic hardship (1). The WHO concluded that addressing infertility is an important component of sexual and reproductive health and rights, but in most countries, infertility policies and services are inadequate (1).

In Rwanda, the female is traditionally believed to be the source of infertility. One million Rwandans perished in the 1994 genocide, with some family lineages eliminated. For all Rwandans who feel pressure to rebuild or build their families, problems with attempting pregnancy or bringing a pregnancy to a live birth can be devastating. However, access to public-sector infertility treatment was not being addressed systematically before our initiative. Indeed, some couples would endure catastrophic health expenditures, especially for treatment abroad.

The Rwanda Military Medical Insurance (MMI), which covers military, police, and other security services, had attempted to provide infertility coverage through treatment in India, but the costs were unsustainable. To receive in vitro fertilization (IVF) treatment in India, including all procedures, accommodations, and travel, MMI insurance had allotted 15,000 USD per cycle for selected couples. A private clinic had opened in Rwanda, coowned by visiting Indian physicians, charging approximately 5,000 USD per fresh cycle. However, these prices were expensive for a country with a 2020 per capita GDP of 798 USD (7) and an estimated 38% (8) to 57% (9) poverty rate.

Establishing more affordable, high-quality in-country infertility services would substantially help address this critical public health concern. Therefore, the nonprofit nongovernmental organization, the Rwanda Infertility Initiative (RII), was launched to help address this need. The initiative, which was based in Los Angeles, CA, was launched in 2015 when a 5-year memorandum of understanding (MOU) was signed with the Rwanda Military Hospital (RMH). This initiative's goal, to plan and establish an infertility clinic, was presented at the International Federation of Gynecology and Obstetrics World Congress in 2021 (10). The present write-up was also encouraged and requested by WHO/Sexual and Reproductive Health/Human Reproduction Programme and describes the strategy, achievements, challenges, and lessons learned when establishing public infertility services in a low-income country. We hope that our report will be of help to other countries and policymakers that decide to initiate reduced-cost infertility services and that are faced with similar resource limitations.

MATERIALS AND METHODS

Ethics Approval

Because the infertility clinic was developed and implemented as a clinical service rather than a research study, it was not under the purview of human studies research.

Informed Consent

All patients received extensive verbal counseling and gave written informed consent for all services received. This article is based entirely on existing anonymous data that had been used for clinical purposes.

The Integrated Clinic

The RII worked with international experts, Rwandan officials from a public hospital, the RMH, and the Rwanda Social Security Board to initiate and integrate the infertility service within the maternal health department of RMH, which is affiliated with the University of Rwanda School of Medicine, Kigali.

The infertility clinic was designed to provide both clinical and laboratory services and to be staffed by Rwandan specialists within the RMH's maternal health department. As such, infertility treatment has been positioned as integral to Rwanda's maternal health care services, thereby hopefully ensuring quality services across a continuum of care from pre-pregnancy and antenatal care to maternal and neonatal health. This deep integration with Rwandan physicians and systems was designed to secure sustainability by the Rwandans themselves. The national government furnished the facilities and personnel. The RII provided training, equipment, and materials. Patient diagnostics and treatments were all conducted in Rwanda.

The WHO health system building block framework, which describes requirements for successful integration of quality services, was used for infertility service integration, but with two modifications (Supplemental Fig. 1, available online). First, a key building block for this initiative was to ensure that stakeholders were part of the leadership team to drive the integration of these infertility services. Second, sustainability, which is not included in the above-referenced WHO health system building block framework, was considered to be a critical element to ensure the long-term provision of services at this facility.

The RII's model involved donated new and used clinical and IVF laboratory equipment, as well as initial supplies of laboratory consumables. The hospital provided its operating room with emergency backup generators in the event of a blackout. To accommodate a full-service infertility center, RMH provided the support staff and the building, which was attached to a new maternal health wing (Supplemental Figs. 2–8, available online).

Training Rwandan Personnel

Existing RMH clinical pathology technicians were tutored and trained to become embryologists. The maternal health department's obstetrician-gynecologists (OB-GYNs) were instructed in basic reproductive endocrinology pertinent to hands-on IVF. Certified nurse midwives were trained as advanced IVF physician assistants as well as operating room scrub nurses for IVF procedures. One operating room nurse, with expertise in minimally invasive surgery, was further trained in IVF surgeries. The RII and RMH staff developed clinical and laboratory training protocols and provided

TABLE 1

The teaching of the key fundamentals in theoretical principles and practical techniques to perform embryology for clinical in vitro fertilization.

Theoretical principle	How taught	Practical techniques	How taught
Quality control	Tele-training and in laboratory	Semen analyses and sperm preparation	Tele-training and in laboratory
Contamination mitigation and sterile technique	Tele-training and in laboratory	Culture dish labeling and preparation	In laboratory
Documentation of custody	Tele-training and in laboratory	Dexterity acquisition	In laboratory
Physiology of folliculogenesis	Tele-training	Cumulus-oocyte identification and handling	In laboratory
The culture environment	Tele-training and in laboratory	Insemination procedure	In laboratory
Sperm biology	Tele-training and in laboratory	Fertilization check	Tele-training and in laboratory
Oocyte biology and grading	Tele-training and in laboratory	Embryo evaluation and selection for transfer	Tele-training and in laboratory
Preimplantation embryo development and staging	Tele-training and in laboratory	Loading the embryo transfer catheter	In laboratory

Note: The training components are **7 missions to Rwanda**, an average of 10 working days, i.e., 70 days × 8 hours per day = 560 hours; **Merck Foundation**, 3 months in India; **Women's Specialty and Fertility Center, Clovis, CA**, 3 weeks' hands-on in its in vitro fertilization (IVF) laboratory, 16 working days, 7 hours per day = 112 hours; **minimally invasive gynecologic surgery** (MIGS), 5 missions to Rwanda, average mission being 8 working days in the operating room at 8 hours per day = 320 hours; **tele-training** was provided by Rwanda Infertility Initiative (RII) volunteers, involving didactics and photo images over 3 years; 1 hour per week, 48 weeks per year × 3 years = 144 hours; **American Society for Reproductive Medicine (ASRM) e-Learning** modules involved virtual lectures and taking tests; and the **hands-on training** was provided by RII volunteers in the Rwanda Military Hospital laboratory in Rwanda, in the laboratory in Clovis, CA, and the Merck Indian affiliate laboratory of "More than a Mother" (12).

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or supported training. Trainees also received free access to the American Society for Reproductive Medicine (ASRM) modules in embryology (for laboratory technicians) and endocrinology (for physicians) using 10 ASRM-donated computers. Weekly virtual tutorials were held between the volunteers and Rwandan colleagues. Two Rwandan physicians attended the 2016 ASRM Annual Congress, where teaching sessions in reproductive endocrinology were administered daily by the RII staff. Both physicians participated in the embryo transfer (ET) simulation course (11). Hands-on teaching in embryology, reproductive endocrinology, and minimally invasive gynecologic surgery (MIGS) occurred during ≥7 international visits by the RII team. Merck's "More than a Mother" program (12) provided an additional 3 months of training in India for 2 embryologists and 1 physician. The Women's Specialty and Fertility Center (Clovis, CA) provided 3 weeks of supplementary hands-on laboratory training (Supplemental Figs. 9–15, available online).

Techniques Taught

In-person and electronic classroom didactics included male and female reproductive tract physiology and pathology, including folliculogenesis, menstrual cycle hormone dynamics, and the physiology of the endometrium. Volunteer reproductive endocrinology physicians scrubbed with the OB-GYNs and certified nurse midwives during IVF procedures. Laboratory technicians worked in the laboratory under the tutelage of the RII embryology volunteers and the direct management of investigator C.R. The RII laboratory volunteers were all at the laboratory director or senior embryologist level in the United States. Physicians mastered ovarian stimulation using low-dose regimens, oocyte retrieval, and ET, followed by luteal phase management. Clinical expertise in interpreting test results and hysterosalpingograms (HSGs) was achieved within 3–6 months. The beginnings of performing MIGS involving laparoscopic and hysteroscopic surgeries were achieved after multiple 2-week missions to Rwanda by experienced reproductive medicine surgeons, including investigator K.I. It is understood that IVF and infertility services are not feasible without their intrinsic capability for MIGS. This ensures appropriate triage and adequate preparation of patients through the amelioration of gynecologic pathologies for more effective IVF (Supplemental Table 1, available online).

Embryologists were taught key human laboratory fundamentals, safety, and practical techniques to perform clinical IVF through various modalities (Table 1). Semen analysis and IUI preparation were taught early on. The Rwandan laboratory technicians were accustomed to performing semen analysis as part of their core work as certified laboratory technicians, with their skills advanced to meet the needs of IVF practice. Examples included strict sperm morphology and assessments of sperm from testicular sperm extraction (TESE). Intracytoplasmic sperm injection was introduced in 2018 with the installation of a micromanipulator comprised of parts chosen for portability and easy reassembly in the Rwandan laboratory. Tennis-ball hemispheres under the microscope base were effective in absorbing vibrations, saving substantial funding by not needing a vibration-dampening table. Intense hands-on exercises with immature and unfertilized oocytes were undertaken. In mid-2019, an Integra 3 micromanipulator was purchased at a substantial discount (Research Instruments Ltd. Falmouth Cornwall, UK) and operated with a used Nikon TE2000-S microscope.

Patient Management

Females underwent cycle day-3 ovarian reserve testing, HSG evaluations, physical examinations, and medical histories to determine menstrual normalcy and any abnormalities requiring management. Male partners underwent routine semen analysis and a brief history before acceptance for IVF. However, the 2 urologists at RMH were already booked 1 year in advance with general urology patients, resulting in substantial delays before urological evaluations could be obtained before IVF. This led to adopting pragmatic solutions. One example was a senior OB-GYN with prior experience in IVF to have personally cultivated expertise in TESE, before the involvement of the RII. Urology fellows at the private King Feisal Hospital were given some didactics on male factor infertility and andrology. The more advanced clinical male factor infertility services were only in the early stages by 2020.

Intrauterine Insemination (IUI) Option

Intrauterine insemination was not being used at RMH at the start of the MOU but was introduced during the training phase as techniques in sperm washing were mastered along with catheter use and loading. The dexterity of the Rwandan OB-GYNs at cannulating the internal cervical os was achieved with the use of ultrasound guidance in their IUI procedures. The latter technique enhanced the ability to perform ETs down the line. Experience was gained with low-dose human menopausal gonadotropin (HMG) stimulation for IUI with follicle monitoring using ultrasound alone. Substantial training in risk management was included in the didactics. Strict protocols for cycle cancelation were aimed at reducing multiple births and ovarian hyperstimulation syndrome. Intrauterine insemination was limited to patients with ≥ 1 patent fallopian tube, ≥ 5 million total motile sperm after wash, and an expected follicle of ≥ 17 mm. To limit multiple births, human chorionic gonadotropin was withheld and IUI was canceled when there were >2 follicles ≥ 14 mm in women aged <37 years and ≥ 3 follicles ≥ 14 mm in those aged ≥ 37 years.

In Vitro Fertilization Per Patient Batch

Patients entered a batch on the basis of their enrollment time and completion of the required workup. Initial stimulation protocols were low dose and low cost, using clomiphene citrate 100 mg on days 3–7 and gradually moving to letrozole, which was also readily available. To improve overall responses, initial doses of these oral stimulants were increased by 1–2 tablets per day and extended to day 9. Clinicians canceled approximately half the cycles for suspected ovulation or discordant follicular sizes. After several batches of cycles, HMG at 150 units was added to balance the addition of an antagonist. Once the staff had mastered the use of antagonists, earlier doses of HMG were added to increase the follicular recruitment. At the same time, when more follicles were present, less irrigation was needed, limiting damage to endogenous progesterone (P4) production. In addition, the exogenous P4 dose was raised to 400 mg two times per day per vagina and started earlier, i.e., on the day of retrieval (day 0), rather than day 2 or 3.

The protocol that achieved the success of pregnancies became the one of choice. This was essentially a low-dose protocol for HMG, commencing with letrozole. The intent was to limit costs and serious side effects (13) and protect the limited laboratory staff from the intensity of large numbers of oocytes and subsequent large numbers of embryos, as vitrification was not yet operational during our MOU.

Outcomes Assessed

To monitor progress, deidentified cycle numbers, oocyte retrievals, fertilization, and embryos with high grades on day 3 (7–8 cells, symmetrical blastomeres with $<20\%$ fragmentation) were tabulated. Within each batch, the number of ET procedures was recorded, as were positive blood human chorionic gonadotropin levels and the number of pregnancies with positive heartbeats on vaginal ultrasound.

Cost Analysis

Payment estimates used the government-issued tariff specifying insurers' payments and patients' copayments for covered services at referral hospitals in 2020 (14), using the 2020 currency conversion rate of 1,006 Rwandan francs per USD (15). For infertility services not covered in the tariff, similarly complex covered services were chosen as proxies. To relate payments to births, we considered a program where each woman would have an average of 2 oocyte retrievals and a maximum of 3; and each retrieval would potentially result in a fresh transfer plus a frozen ET 50% of the time.

In view of resource constraints, we modeled outcomes on the basis of patients where available resources might yield the greatest outcomes. Such patients were defined as women aged <35 years with normal ovarian reserve tests, normal uterine cavity, normal endometrium, no significant fibroids or adenomyosis, no hydrosalpinges, no poorly controlled obstetrical risks (e.g., uncontrolled diabetes or a high burden of human immunodeficiency virus), and partners with normal sperm in the ejaculate or a retrieved sperm sample. These criteria parallel those in a risk-sharing program in the United States (16).

To project outcomes, we applied published birth rates from younger patients from 2009 as the time when infertility services were expanding into widespread use (17, 18). We calculated the average IVF payments per delivery on the basis of these studies' conservative and optimistic assumptions regarding women lost to follow-up (Supplemental Text, available online).

RESULTS

Equipment And Physical Facilities

Some of the surgical and laboratory equipment and instruments donated from the United States were initially damaged because of incompatible voltage for use in Rwanda and the use of poor-quality voltage transformers. Emergency electric supplies could be erratic. The 2 "Penguin" AQ incubators, Model No. APM-50DR (Astec Co., Fukuoka, Japan), tolerated these interruptions with minor quality control variations. A collaborative working relationship with the hospital engineers was essential to ensure prompt, expert assistance when needed.

Enhancing Competencies For Infertility Management

Within 6–12 months, Rwandan physicians were performing infertility diagnosis and assessment, and confidently interpreting laboratory results. Technical competence in ultrasound, intrauterine insemination, oocyte retrieval, and ET were attained. Laboratory staff rapidly acquired knowledge in performing basic embryology procedures and standardized semen analyses. After training and initial service function, a complete infertility team began functioning under the

TABLE 2

Staffing involved in establishing the Rwanda Military Hospital infertility center.

Type of professional[a]	No. of international experts	No. of Rwandan staff ever involved	The final No. of dedicated Rwandan staff*
Infertility physicians	4	6	2
Certified nurse midwives (CNMs)	0	6.5	2.5
Operating room (OR) nurses	0	2	1
Embryologists	3	5	2

Note: CNM assisted in the OR procedures; 0.5 CNM denotes CNM with limited skill; OR nurse was skilled at instrumentation for egg retrievals, embryo transfers, and minimally invasive gynecologic surgery (laparoscopy or hysteroscopy).
[a] Final number of the dedicated staff represents the number working during the last year of the memorandum of understanding (MOU).

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supervision of a senior gynecologist with private infertility clinic experience and a supervising embryologist. Table 2 shows the staffing involved in establishing the RMH infertility center, with stratification of international experts and Rwandan staff ever involved. The adjunct staff from the RMH Department of Obstetrics and Gynecology, anesthesia, and ancillary services such as infection control, scheduling, fee collection, and internet technology were also provided by the government through the RMH.

Innovation Unsuccessful And Successful

Table 3 summarizes the steps taken and lessons learned in establishing the RII. Several cost-saving efforts were unsuccessful in the clinical protocol, including reusable oocyte-retrieval needles, handheld syringes for suction pressure, and using clomiphene citrate or letrozole alone for ovarian follicle stimulation. Many cycles had to be canceled owing to the initial avoidance of a gonadotropin-releasing hormone antagonist. Cost-saving efforts coterminus with teaching led to more cancelation, fewer oocytes at retrieval, and lower numbers of high-grade embryos for transfer. The incidence of total absence of oocytes at retrieval and total failed fertilization was higher than the standard experience. Oral dose stimulation led to fewer follicles and therefore aggressive irrigation at retrieval. The luteal phase regimen, therefore, demanded higher doses of P4.

Other adaptations were more successful: reusable trocar and cannula set for MIGS, water for sonolucency rather than gel-based substances; and coadministration of letrozole with low-dose HMG, which helped reduce the amount of HMG per stimulation. Reliance was made on ultrasound alone for follicle tracking without routine blood estradiol (19). Overall, despite the initial lack of pregnancies, ongoing pregnancies occurred with time (Fig. 1).

Outcomes

Table 4 shows IVF cycle outcomes from September 2018 through December 2020. Despite the extensive experience of the international RII staff, the learning curve to reach ongoing IVF pregnancies was prolonged. Seven batches of patients, >1.5 years, and >88 cycle starts occurred before a single ongoing pregnancy was established. This profound delay understandably lowered both staff and patient morale. Concurrent analyses indicated that improvement could be achieved through better yield of mature oocytes and improved management of the luteal phase.

Cost Analysis

The projected cost to insurers and families of 1 oocyte retrieval with a fresh transfer and a frozen ET 50% of the time was 1,521 USD, consisting of 654 USD for medications and 867 USD for all services (Table 5). Costs to insurers and families of 2 oocyte retrievals would average 3,042 USD per woman. The conservative and optimistic projected payments per delivery would be 5,156 and 4,540 USD, respectively. These amounts would not include government funding of personnel salaries, utilities, and capital amortization (Supplemental Tables 1–6 and Supplemental Figs. 16–17, available online).

DISCUSSION

Early results showed low retrieval rates, reduced fertilization, and therefore, low ET rates. Our analysis of each batch of patients as well as hands-on management pointed to high cancelation rates for suspected ovulation, low numbers of follicles from pure oral stimulants, high failed oocyte retrievals, and high total failed fertilization. With more follicles available, fewer retrievals resulted in 0 oocytes. It was also opined that when we had sufficient oocytes instead of just 1 or 2 for most cycles, there would be fewer total failed fertilization.

Corrections for these deficits led to the introduction of low-dose HMG followed by an antagonist. This was first introduced sequentially with oral agents followed by HMG, which added much to the cost and initially limited some patients from treatment. The HMG also added to the concerns for ovarian hyperstimulation syndrome. Such risk avoidance was a primary tenet of our philosophy when introducing a new technology in a low-resource area.

The early pregnancy success rates were low, even by historical standards. There were 5 (5.7%) chemical pregnancies from the 88 starts in 2019. However, once we corrected for premature ovulation and learning curve issues with oocyte retrieval, 6 pregnancies from 41 starts and 24 transfers were achieved in 2020, 5 of which were ongoing (20% ongoing pregnancy rate per transfer). We also improved luteal support with an earlier start of P4 and at higher doses. The luteal phase

TABLE 3

Summary of steps taken, and lessons learned when establishing the Rwanda Infertility Initiative (RII).

Step	Action	Benefits	Barriers encountered*	Lessons learned**
1.	Met with government leaders.	Important collaboration from the top.	High turnover, new officials not equally supportive.	Establish agreements and ensure an active MOU for the duration of the project.
2.	Not for profit, RII launched.	Easier for cash donors and equipment companies to donate to Rwanda. RII with a US address enabled good passthrough to Rwanda for foreign donations.	Some companies would not ship to countries where their equipment had no approval. RII is not registered within Rwanda. Presented a problem with a government institution such as the RMH.	Important to recognize the benefits of registration of nonstate institutions in the host country. Need to learn the host country's regulations. Host country health care law would be helpful.
3.	Signed MOU with Hospital Commandant and the RII	Enthusiastic support from the top.	The head of the hospital was replaced 5 times during our work.	Signed agreements are needed and are better than goodwill.
4.	Used English as the primary language for communication.	English is required at Rwandan schools; there are 4 official languages in Rwanda: Kinyarwanda, English, French, and Swahili.	Accent intonation and cultural differences sometimes hampered reciprocal understanding.	Consider an on-site translator where the translation is not edited to the host's expectations. Patient-friendly documents (e.g., consents) to be made in advance
5.	Met with physicians and established reciprocal proficiencies.	Essential, in view of the importance of proficiency standards in IVF	Poor inventory management. Equipment borrowed at will by other departments, minimal accountability	The IVF unit with its adjacent OR to have a manager responsible for the facility, upkeep, and inventory of equipment and instruments Consider the OR nurse manager from RII to train RMH staff and new manager on equipment inventory.
6.	MIGS plan developed contemporaneously with IVF training.	MIGS with hands-on training geared toward fertility enhancement proved beneficial.	Other duties interrupted training. Available equipment poorly managed. Repairs not coordinated to demands of a visiting MIGS surgeon.	Training (OB-GYNs) in MIGS takes a protracted exposure to this surgery. Consider a chosen OB-GYN for a 6–9-mo fellowship.***
7.	Cost-sensitive IVF training implemented.	Good flow of medical training in low-dose, low-cost IVF protocols, and endocrinology	Minor language challenges. A senior physician trained elsewhere had poor buy-in on lower-cost protocols. Low-cost protocols are blamed as the cause of the initial absence of success. Fewer follicles resulting from low-dose stimulation required more retrieval expertise	Additional work, with citation reprints needed for buy-in to low-dose, reduced-cost approaches. Separate the hands-on retrieval and transfer training with an application of low-dose techniques.

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TABLE 3

Continued.

Step	Action	Benefits	Barriers encountered*	Lessons learned**
8.	Certified nurse midwives (CNMs) training.	Clinically astute, some with many years of experience with the reproductive process. Easy to train. Adapted well to advanced physician assistants.	Minor language challenges. Myths regarding fertility are not clearly understood by the RII team, therefore difficult to debunk. Myths included issues of coital frequency, abstinence, work attendance during IVF, and supplemental potions.	Preparedness of possible cultural myths with the use of patient consent and instruction for debunking. Special training is needed for the CNMs to help patients with the emotional aspects of failed treatments.
9.	Training pathology technicians to IVF laboratory protocols by the IVF laboratory director	Experience working in a laboratory and training on the same equipment they were accustomed to. Some were quick to learn with good dexterity.	Employment agreements in the pathology laboratory created tensions. Some laboratory personnel had poor hygiene, dental care, and home circumstances, causing concern for contamination. Staff turnover, traffic accidents, and hampered training progress.	Awareness of possible interdepartmental conflict when staff is pulled from another department. Example: demands on batching of IVF patients limited routine pathology night schedules.
10.	In vitro fertilization laboratory equipment Donated	Good condition of donated equipment. Standard equipment (e.g., centrifuges, pH meters, and others) could be borrowed. Military hospitals, when willing, mobilized the best available equipment in the country.	Voltage transformers were needed for some equipment, some of which were below standard, resulting in some equipment damage.	Allocation of funding needed for highest quality transformers. Acquire permission to work with the US Embassy to obtain proficient technology and equipment.
	Upgrades and replenishment.	Laboratory equipment and consumables needed importation. Military hospitals exerted some influence on expediting customs procedures.	Huge shipping costs are often out of proportion to low-resource environments. Customs issues not fully resolved. Vigilance is required to avoid unexplained delays at customs.	Volunteer staff allocated some portions of equipment to hand luggage. Baggage fees are often less than shipping fees. Hospital procurement staff to be identified and procedures clarified. Graft awareness is needed.
11.	IVF Consumables Donated	Donated consumables enabled quick ramp-up of IVF procedures	Hospitals are initially reluctant to contribute to consumables. RII had a poor understanding of fiscal procedures for a new division in the maternity department.	Donated funds may delay the learning curve of the host's fiscal skills to establish upfront fiscal arrangements for consumables and unexpected items.
	Purchased	Initially purchased in United States and Europe, which facilitated product identification. The airport is logistically close to the IVF laboratory.	Temperature control of media presented challenges. East Africa supplier in Kenya: costly shipping, limited product choice.	Ensure the most expeditious and safe transport. Batch patients to assist in price, quantity, and shelf-life discipline.

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TABLE 3

Continued.

Step	Action	Benefits	Barriers encountered*	Lessons learned**
12.	Ensure adequate hospital building and infrastructure dedicated to IVF.	New premises reasonably adapted to the needs of the IVF center.	Some materials (e.g., flooring) needed replacement. Several episodes of depleted clean water tanks; bottled water was used as standby. Roof leakage required temporary tarp fixes. Air conditioning needed development.	Ensure the existence of laboratory infrastructure and air handling according to the standards of the host country; if not available, use standards published by ESHRE or ASRM.
13.	Electronic communications were adopted for training in between in-person missions.	Frequent low-cost Zoom meetings were effective. WhatsApp, currently at no cost, was useful. The use of a cell phone camera helped in long-distance teaching of follicular monitoring and embryo grading.	Frequent Wi-Fi service disruption.	Spend money on dedicated quality Wi-Fi within the laboratory, clinic, and OR. Be aware of other nonprofit groups often working within the same institution who may have instituted powerful Wi-Fi and information technology to avoid duplication.
14.	The identified major need for ICSI.	Many more patients could be served. Micromanipulation equipment was donated and training was easier than expected.	Andrology and genetics support are limited. Intracytoplasmic sperm injection increased the costs of consumables but costs cheaper than failed fertilization per live birth.	Severe male factor infertility may be prevalent and so consider introducing ICSI as soon as feasible. Consider collaboration with other (e.g., private) hospitals when needed.
15.	Attempt to introduce cryopreservation.	With limited budget-focused training on fresh IVF cycles. Laboratory staffs are not so overwhelmed.	Difficulty aligning solutions with vitrification procedures and equipment. Confusion by in-house production of media vs. branded products. Free training by suppliers to Kenya was not aligned with cost-efficient freezing devices purchased. Suppliers not engaged in concepts of low cost vs. simple discount.	Need a dedicated analysis of best practices to align equipment costs, laboratory space, alarm system, and technician training. Electronic data management is a priority to avoid incorrect identification of embryos. Avoidance of abandoned frozen embryos remains a challenge. The host country may best devise solutions after dialogue with RII.
16.	Third-party reproduction.	The need exists but is a low priority. Family often eager to donate gametes or to provide surrogacy. Host senior staff well-informed of legal procedures, such as court-order-supported surrogacy requests.	Conflicts developed between the visiting RII volunteers vs. the in-house host participants e.g., psychosocial aspects not reciprocally appreciated. MDs did their cursory social work.	In-depth sharing of socio-cultural traditions (patients and the community) is needed. Host country social workers or psychologists should be identified to become trained and dedicated to IVF and reproductive health teams. Social worker's report to be part of the protocol.

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TABLE 3

Continued.

Step	Action	Benefits	Barriers encountered*	Lessons learned**
17.	Long-term quality and performance standards.	Essential in providing and maintaining the highest standards of care, both clinically and in the laboratory.	The fluidity of leadership and staff arrangements hampered long-term planning.	Include long-term planning in the initial contract.
18.	MOU expired, in 2020.	Host country experts assume responsibility. National basic health care insurance laws are well developed. Rwandan health insurance policies have inherent opportunities for cross-subsidies.	No long-term monitoring is feasible. National healthcare to determine what infertility service is covered and what is not (e.g., third-party reproduction).	Share plans for sustainability with the host country. Example: engage experts to advise on cost-effective and affordable practices for national health service.

Note: * Anticipated and unanticipated; ** ideal, but often not feasible; *** for example, Institut de Recherche contre les Cancers et l'Appareil Digestif (IRCAD) [Research Institute against Digestive Cancer]. The host country is the country where the technology is being established and where it will remain. ASRM = American Society for Reproductive Medicine; ESHRE = European Society of Human Reproduction and Embryology; ICSI = intracytoplasmic sperm injection; IVF = in vitro fertilization; MD = medical doctor; MIGS = minimally invasive gynecologic surgery; MOU = memorandum of understanding; OB-GYN = obstetrician-gynecologist; OR = operating room; RII = Rwanda Infertility Initiative; RMH = Rwanda Military Hospital.

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was also less hampered by reducing the need for irrigation, as the intraoperative oocyte numbers had become ample (Fig. 1). Other considerations for reduced pregnancies per transfer were latent tuberculosis and nonuniversal assessment of the endometrial cavity using hysteroscopy. Saline sonohysterography was hampered by the cost of catheters vs. hysteroscopy, which was paid for by some insurers.

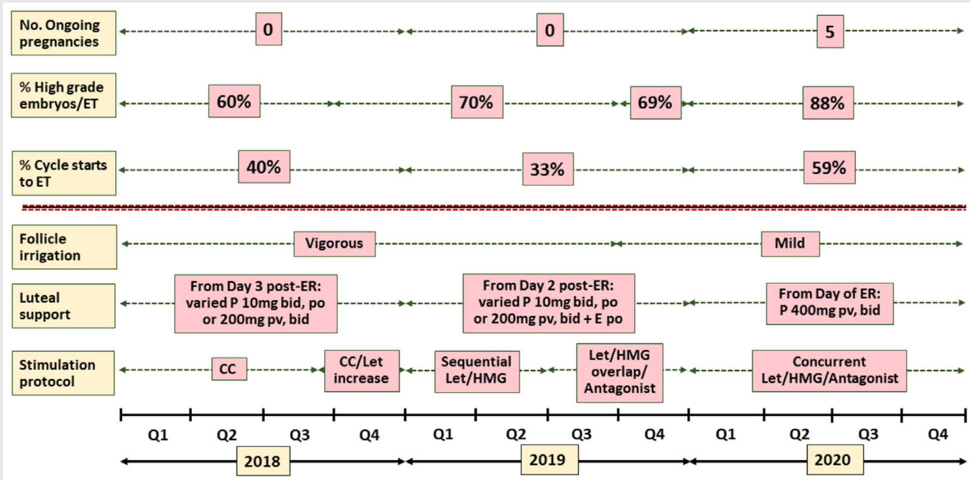
Male factor infertility was found to be common, as previously reported (20), along with many cases of obstructive azoospermia and severe oligospermia. Indeed, TESE was performed by the senior Rwandan gynecologist in response to the limited-resource environment well appreciated by the host physicians. It became easier for the fertility gynecologist to learn and adopt the TESE procedure than to have the challenge of the 1-year waiting list for urologic evaluation.

We found it pragmatic to introduce intracytoplasmic sperm injection instrumentation and training before other technologies such as embryo cryopreservation. The RII approach was proof of principle for fresh IVF first, with the introduction of cryopreservation later. Inherently, initial low oral dose stimulation led to fewer embryos suitable for cryopreservation. Furthermore, a training program along with identity security using computer technology, which is considered mandatory in a cryopreservation program, was challenging because we lacked an electronic data capture system. Our stepwise approach differed from the Walking Egg Model (21, 22), in which IVF computer technology was front-loaded in the planning stages.

Cryopreservation of embryos is, of course, important, especially in the application of elective single ET and for further lowering the costs of IVF services. In regard to costs, we studied the role of the intravaginal culture device, INVOcell (Invo Bioscience, Sarasota, Ll) (23). The unit price was ≥100 USD, plus other consumable costs added to each case. Crude accounting suggested more cost efficiency with a standard donated incubator. The INVOcell is still a consideration for the future as a backup for power or equipment failures. The van Blerkom CO_2 chemical reaction in a closed glass tube and battery-operated heating bath platform (24) is fascinating (the Walking Egg), but it was easier for us to work with the existing medical-grade CO_2 and emergency power backup available at the hospital center.

Global health partnerships, especially North-South partnerships that address an increase in access to care in low- and middle-income countries, need to adhere to global guidance and ensure sustainability (i.e., "without colonization" or through "decolonization") of health programs and service development, education, and training (25). In particular, fertility care and infertility services have been neglected in many parts of the world. In the mid-1980s, global public health efforts had been asked by governments and global donors in reproductive health to reprioritize infertility and instead emphasize the unmet need for unintended pregnancies and the impact of sexually transmitted diseases (including human immunodeficiency virus) on maternal and reproductive health (26). However, a renewed global movement to address the integration of infertility public health care services began in 2008 within the WHO, together with the ASRM, the International Committee Monitoring

FIGURE 1



Timeline of activities at Rwanda Military Hospital. CC = clomiphene citrate; ER = egg retrieval; ET = embryo transfer; HMG = human menopausal gonadotropin; Let = letrozole; P po = dydrogesterone; P pv = progesterone.

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Assisted Reproductive Technologies, the International Federation of Fertility Societies, and other dedicated foundations and continues to build momentum as it is defined by the WHO as an essential service (27). One of the most challenging components, however, is the establishment and sustainability of developing infertility public health services in low- and middle-income countries. As described here, this sustainable infertility service was successfully established in Rwanda through a North-South partnership, that is, through a collaborative endeavor between the RII and RMH. To better ensure long-term sustainability for all who require access to infertility services, we suggest first developing greater fertility awareness and care within primary health care centers and establishing referral systems to the clinical service established at the RMH. Finally, we suggest forming additional clinical services in academic settings and private-public partnerships.

Before RII engagement, a general OB-GYN clinic at RMH existed with multiple attending physicians but no specialized training in infertility treatment or reproductive endocrinology. During our training missions, the opportunity for individualized growth through continuity of care with dedicated physicians was limited. The attending physicians (IVF trainees) could be also on the obstetric emergency roster during the IVF schedule and clinic time. When the specialty infertility clinic began, patients arrived at the clinic with scan results from remote hospitals, including HSGs and other reports, temperature charts, laparotomy statements, arrays of results from various hormonal panels, and a semen analysis.

TABLE 4

No. of in vitro fertilization (IVF) cycles performed with outcomes.

Batch date	No. of cycles started	Drug(s) used	No. of cycles having an embryo transfer	No. of cycles with ≥1 high-grade embryo	Pregnancies
September 2018	28	CC	14	8	0
November 2018	50	Let or CC	17	13	0
2018 Subtotal	**78**		**31**	**21**	**0**
March 2019	31	Let or CC	3	2	0
July 2019	20	Let and HMG sequential	6	4	0
September 2019	9	Let, HMG sequential, and ant	4	2	0
December 2019	28	Let, HMG, and ant	16	12	5 Chemical
2019 Subtotal	**88**		**29**	**20**	**5**
March and April 2020	11	Let, HMG, and ant	7	3	1 Ongoing
July and August 2020	16	Let, HMG, and ant	9	9	1 Ongoing
December 2020	14	Let, HMG, and ant	8	7	1 Chemical 3 Ongoing
2020 Subtotal	**41**		**24**	**19**	**6**
TOTAL	**207**		**84**	**60**	**11**

Note: CC = clomiphene citrate 50 mg tablets: 100 mg per day, days 3–7); hCG = human chorionic gonadotropin (5,000 units SQ); HMG = human menopausal gonadotropin; Let = letrozole (2.5 mg tablets, 2 tablets per day, days 3–7 instead of CC); Let-HMG sequential (letrozole 5 mg per day, days 3–7, HMG 150 IU per day, day 7 until hCG 10,000 units trigger); Let, HMG, Ant (letrozole, 5 mg tablets per day, days 3–7, HMG 150 IU per day, day 3 until hCG trigger); antagonist (0.25 mg sq per day when the lead follicle is 14 mm); bolded numbers are yearly subtotals.

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TABLE 5

Cost of average in vitro fertilization (IVF) retrieval in women < 35 years by the type of insurance, payer, and service (USD).

	Mutuelle insurance			Other patients			All patients			
Type of service	**Insurance**	**Family**	**Subtotal**	**Insurance**	**Family**	**Subtotal**	**Insurance**	**Family**	**Total**	**%**
Consultations	$13	$1	$15	$25	$15	$41	$19	$8	**$28**	**2%**
Diagnostic services	$104	$10	$114	$199	$119	$318	$151	$65	**$216**	**14%**
Medications	$16	$638	$654	$417	$237	$654	$217	$438	**$654**	**43%**
Procedures (fresh)	$100	$333	$434	$248	$404	$653	$174	$369	**$543**	**36%**
Vitrification	$24	$2	$26	$85	$49	$134	$54	$25	**$80**	**5%**
Total	$257	$985	$1,242	$975	$825	$1,799	$616	$905	**$1,521**	**100%**
Row %	21%	79%	100%	54%	46%	100%	40%	60%	100%	

Note: Half of the retrievals are assumed to generate a frozen embryo, and frozen embryos would be used before another fresh retrieval. The exchange rate was 1,006 RWF per USD (15). Bolded values are total for that row and that row as a percentage of total cost across all rows.

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As with many low- and middle-income countries globally, knowledge of general reproductive endocrinology was equivalent to that of a generalist gynecology expert without specialization in advanced infertility treatment. Staff physicians often invoked the pathology written reports for guidance on semen analysis and HSG. Hormone results were interpreted without regard to the menstrual cycle or clinical picture. An HSG report would be regarded as "normal" when both tubes were open without much reference to the uterine cavity itself. Hysterosalpingograms scans themselves were seldom studied. Laparotomy was the surgical approach of choice when, for example, investigating tubal disease or treating a stable ectopic pregnancy. Nevertheless, the dedicated work by the Rwandan clinicians also managing the full array of benign and malignant gynecologic diseases was a testament to their ability to enhance competency in infertility as well.

For some patients, MMI paid the previously mentioned private clinic cost of 5,000 USD per IVF cycle, with complex cases referred to India at higher costs. Few Rwandans were eligible, and most could not afford these services. Clearly, an alternative approach at reduced cost and allowing broader access to care in Rwanda was required. This was reached through collaboration among all stakeholders. The formation of RII, coupled with the donation of time, equipment, and infrastructure, ultimately resulted in an infertility clinic and IVF laboratory integrated within the RMH maternal health facility. As an indication of demand, as soon as this plan was integrated and clinic doors opened for care, the RMH witnessed the arrival of hundreds of people seeking care, outstripping the capacity of the clinic to receive new patients.

In addition to Rwanda's successful system of *mutuelles* (community-based insurance), other financing models for low-income countries are promising. Vouchers have proved efficacious in financing a package of pregnancy-related services (28). Vouchers are generally awarded to targeted recipients through an objective screening process (e.g., low-income pregnant women from a designated geographical area). An analogous system could be developed to allocate vouchers for infertility treatment on the basis of medical (e.g., better prognosis) and social (e.g., genocide survivors) criteria. Donors that support reproductive health might recognize the importance of infertility treatment and fund some vouchers. These might be supported also through some combination of philanthropy, reallocating existing government revenues, or innovative earmarked funding. Such sources include "sin" taxes (alcohol and tobacco) or novel funding (e.g., fines from automatic traffic cameras). The knowledge that such funding would benefit a socially useful cause might increase acceptability and contribute to safer behavior.

High-level commitments by RMH, MMI, and the Ministry of Health were critical to ensuring this initiative's viability. Pragmatic approaches to solving challenges are paramount for success. These included: a decision to allocate a portion of the RMH maternal health building; committing resources for international experts; seconding experienced staff from other departments; and procuring drugs by RMH, when feasible, before the batch of patient consultations (Table 4). The procurement of building materials or furnishings involved a unique resource-sharing business understanding, where available supplies (such as from a local church) were relinquished on the diligent request of the hospital with these being returned when the supply chain was so provided.

Unfortunately, other issues were more difficult: some patients could not afford the injectable medications and opted for the weaker oral ones or skipped the cycle. Other challenges encountered were both at the policy and program levels. At the policy level, continued limited funding and modest priorities for infertility services had been responsible for constrained services. At the program level, some administrative tasks were allocated to the most experienced personnel available, such as the clinicians. This highlights the need for programs such as this to have a range of specialized managers to improve overall efficiency. Examples of inefficiencies included doctors needing to find an operating stool, thereby delaying a procedure, and a lack of a clinical manager to troubleshoot obstacles such as patients being cut off from enrollment by the scheduling office.

Changes in hospital leadership at RMH (5 leaders in 5 years) required continued and renewed advocacy for infertility care. Some physicians moved into the private sector because of the lack of implementation of public health sector retention mechanisms. Such mechanisms include pay-for-performance arrangements. Indeed, to ensure the retention of trained staff, the adaptation of Rwanda's performance-based financing system, binding contracts, or other strategies will be needed (29, 30). Support for staff retention and continuous training of new physicians in this field will be necessary for long-term sustainability. Currently and moving forward, national regulations and professional society guidance concerning infertility practices will require continuous refinement, reporting, and monitoring.

High patient volumes at the RMH infertility clinic signaled an enormous unmet need for access to care for infertility services. Such services are needed in low- and middle-income settings and, when incorporated within maternity hospitals, ensure early antenatal care and a continuum of health care for mother and child. Our experience shows that the integration of infertility services within a low-resource setting is possible with the following prerequisites: multi-stakeholder commitment; infrastructure; social health protection mechanisms; medical products and equipment; health information systems; training programs and staff retention mechanisms; and quality assurance monitoring. Infertility diagnostics and treatment should be part of primary health care, designed to achieve universal health coverage.

By the end of 2020, when the RII and RMH leadership and staff completed their MOU obligations, the infertility clinic had become fully functional. Continued development should ensure its sustainability by making it an autonomous financial unit within the hospital. However, a national strategic plan for fertility care will be required to establish priorities, guidelines, regulations, monitoring of quality care, and a national registry for reporting outcomes to ensure continued monitoring of public and private clinic practices. Designing a patient-friendly and rapid transfer system from health centers to the RMH clinic and establishing a decentralized system for diagnostic assessments at the district hospital level to refer cases with clear management plans will be helpful. Notably, algorithms for fertility care will require constant revision, as will future national referral systems—from primary health care centers to centralized infertility services in regional teaching hospitals.

CONCLUSION

During the 5-year MOU between RII and RMH, the RII initiative worked together with key national Rwandan stakeholders and followed a health system building framework to successfully establish affordable and sustainable infertility services in the public sector. Despite inevitable challenges along the way, success was achieved through an ethical, respectful, functional, and cooperative engagement within this North-South partnership, recognizing that flexibility, personnel training, and self-sufficiency were all paramount to ensuring sustainability. We hope that our report will encourage future North-South, as well as South-South, partnerships to work with policymakers and in-country maternal public health services to develop integrated fertility care and infertility services. Such approaches will best ensure a continuum of high-quality care throughout early pregnancy, as well as continued maternal and child health.

Our analysis of real-world data showed that a reduced-cost protocol for fertility care and IVF cycle management is feasible in a low-income country. Low-income countries, such as Rwanda, may fund infertility treatment and IVF treatments for eligible younger patients.

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