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Fertility preservation by ovarian tissue transportation and centralized cryobanking for a 20-year old woman with Hodgkin lymphoma

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Abstract:	N/A

Figure 1: Canadian Implementation of the "Hub-and-Spoke" model

Provides access to expert counselling and specialized fertility preservation services while overcoming geographical and systemic barriers, maximizing patient comfort, ensuring timely cancer treatment, and offering a cost-effective and safe solution.

Fertility preservation by ovarian tissue transportation and centralized cryobanking for a 20-year old woman with Hodgkin lymphoma

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Financial statement:

The cost of tissue processing and cryopreservation was covered by Mount Sinai Fertility, estimated at $3,500 CAD. The cost of tissue transportation was covered by First International Courier, estimated at $1,500 CAD.

Competing interests: The authors have no competing interests to declare.

Word count: 1248

Key Points:

- Reproductive risks due to cancer therapy should be discussed with all patients as an integral part of oncology care.
- Ovarian tissue cryopreservation is the only fertility preservation option for patients with ovaries who cannot undergo ovarian stimulation, including children, urgent cases and those living remotely from a fertility centre.
- Ovarian tissue transportation and centralized processing and cryobanking overcome barriers and improve access to care.
- This case demonstrates the feasibility of implementing ovarian tissue transportation and centralized cryobanking in Canada.

Case:

A 20-year-old, G3P2AB1, pediatric cancer survivor presented to her local oncology centre in Southwestern Ontario with right supraclavicular adenopathy. She had a history of Stage IIA Hodgkin lymphoma diagnosed at age 15 and treated with two cycles of OEPA chemotherapy (vincristine, doxorubicin, etoposide and prednisone), achieving complete response. Positron emission tomography-computed tomography revealed multiple lymphadenopathies in the neck and chest above the diaphragm, and biopsy confirmed the diagnosis of relapsed Hodgkin lymphoma, stage IIA. The patient was 8 weeks pregnant at presentation and subsequently underwent a surgical pregnancy termination. She expressed a desire for future fertility and was referred for urgent virtual counselling at an oncofertility centre providing fertility preservation care. We counselled the patient regarding the effects of repeated alkylating-based chemotherapy exposure, the high risk for future infertility and premature ovarian insufficiency, and the various fertility preservation strategies available. Due to the need to initiate immediate salvage chemotherapy and the remote location (380km from Toronto), the patient elected to proceed with ovarian tissue cryopreservation after considering surgical risks, tissue transportation, processing, storage and future transplantation of the ovarian tissue. We coordinated care remotely through a close collaboration with her local oncologist and gynecologist. The patient completed pre-procedure investigations locally, including viral

serology screening to ensure safe tissue handling and storage, and serum anti-mullerian hormone measurement to assess baseline ovarian reserve. A local gynecologist trained in specific oophorectomy techniques for ovarian tissue cryopreservation performed a laparoscopic unilateral oophorectomy using minimal coagulation and delicate tissue handling to preserve follicular viability. The contralateral ovary and both fallopian tubes remained in situ. We arranged for professional courier transportation of the ovarian tissue under continuous temperature monitoring, maintaining 4°C–8°C throughout the 380-km journey to our specialized embryology laboratory. Upon arrival, we stored the tissue overnight at 4°C until the tissue processing could be completed by an embryologist the following day. We completed tissue processing within 23 hours of retrieval, yielding over 60 tissue fragments. Additionally, during processing, we isolated 10 cumulus-oocyte complexes and successfully matured in vitro 8 oocytes that were cryopreserved, providing additional reproductive potential. The patient was discharged home on the day of surgery and started GDP salvage chemotherapy (gemcitabine, cisplatin, dexamethasone) within 6 days. Followed by autologous stem cell transplant with BEAM conditioning (carmustine, cytarabine, etoposide, melphalan) within 3 months. Four months after the procedure, the patient remains well, and no immediate complications related to the fertility preservation procedure or bone marrow transplantation have been reported.

Discussion:

For reproductive-aged individuals diagnosed with cancer, the prospect of future fertility often becomes a critical concern alongside survivorship[2]. This case illustrates the complex challenges faced by young cancer patients who desire biological children but require urgent treatment that threatens their reproductive potential. Unfortunately, many life-saving interventions, including reproductive organ surgery, chemotherapy, and abdominopelvic radiation, increase the risk of infertility and reproductive endocrine dysfunction[1]. These advancements in cancer treatment and survivorship have led to the development of oncofertility, a discipline that integrates oncology and fertility care to preserve reproductive potential. For individuals with ovaries, the choice of fertility preservation strategy is individualized and depends on patient-specific factors, including age, pubertal and menarchal status, underlying diagnosis, urgency to initiate cancer therapy, baseline ovarian reserve, partnership status, physical and financial access to fertility care, and patient preference (Table 1[3]). The success of fertility preservation procedures in achieving a future live birth is closely tied to the quantity of stored samples and the patient's age at the time of the procedure.

For prepubertal and adolescent patients who cannot undergo ovarian stimulation and whose potential risk of infertility is considered high according to the internationally accepted standardized model for patients undergoing cancer treatment[4], adults younger than 35 years who urgently need to start chemotherapy or patients who have limited access to a fertility clinic, ovarian tissue cryopreservation, declared no longer experimental in 2019[5], is considered the best clinical practice by international fertility and oncology societies[6]. This multi-step procedure involves laparoscopic removal of a whole or part of an ovary, transportation to an expert embryology laboratory for processing, cryopreservation and storage (Figure 1). Processing ovarian tissue in preparation for cryopreservation can also yield mature oocytes that can augment reproductive potential. Ovarian tissue can be stored for over 10 years, and when conception is desired, the tissue is thawed, prepared for transplantation, and auto-transplanted into the patient’s pelvis to restore fertility and endocrine function.

Despite Canadian obstetric and gynecology and fertility societies' clinical guidelines endorsing fertility preservation in cancer patients[7–9], multiple barriers to the delivery of oncofertility care exist[10]. Patient barriers include a lack of awareness and high distress around survival, while healthcare providers' barriers include knowledge gaps and discomfort with discussing infertility risks, leading to low referral rates for counselling and procedures. Barriers at the health care system level include the lack of well-designed and accessible resources to provide urgent oncofertility counselling and the absence of care pathways for coordinating procedures. Funding for fertility preservation procedures also varies by province and can present a substantial barrier to accessing care in provinces where patients must pay out of pocket expenses for this service.

While the ability to perform laparoscopic oophorectomy is readily available in many primary centres, the main practical barrier to equitable access to oncofertility care is that the processing and storage of ovarian tissue require expertise and specialized equipment that are not commonly found in most fertility clinics that perform oocyte or embryo cryopreservation. Centralizing the processing and storage of ovarian tissue in a dedicated cryobank facility offers several advantages, particularly for patients residing in remote areas. Access to care provided by local tissue harvesting, with subsequent safe transportation of the tissue to a central facility, a process shown to be feasible and safe[11]. Given that ovarian tissue cryopreservation is a relatively rare procedure, centralization is also highly cost-effective, as it eliminates the need for maintaining multiple processing sites. Additionally, a centralized cryobank operating in a high-volume setting ensures improved quality control and assurance, as expertise can be concentrated, and standardized procedures can be consistently applied.

This approach is common in many European countries that have established centralized ovarian tissue cryopreservation programs and successfully incorporate tissue transportation across regions. Pioneered by the Danish Network, founded in 1999 with the slogan "the patient stays – the tissue moves," centralization of ovarian tissue cryopreservation in Denmark and southern Sweden, is enabling tissue retrieval locally and transport for processing and storage, leading to multiple live births[12]. One network spanning 125 centres in Germany, Austria, and Switzerland,

consolidates the processing into three main cryobanks, optimizing transportation logistics and achieving multiple live births[13]. Optimizing resources and outcomes, in 2018, the Netherlands merged seven fertility preservation centres into a centralized national program[14]. The UK's centralized cryobank in Oxford follows a "Hub-and-Spoke" model, providing cryopreservation services across England, Wales, and Northern Ireland[15]. Similar centralized models exist in Japan and the US.

This case demonstrates the feasibility of implementing a centralized "Hub-and-Spoke" model for ovarian tissue cryopreservation in Canada. As a proof-of-concept, we successfully delivered specialized oncofertility services through coordinated care pathways that overcome geographical barriers. The hub oncofertility centre provides specialized oncofertility expertise while collaborating with local healthcare teams, as spokes, through a multidisciplinary approach that includes urgent virtual consultations, coordination of local surgical procedures, professional tissue transportation, and centralized expert processing and storage. The described model aims to reduce infertility and reproductive endocrine dysfunction in cancer survivors, minimize the psychosocial impact of infertility, and enhance the quality of life for patients and their families by improving access and coordination of care.

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Fertility pPreservation by oOvarian tTissue tTransportation and ~~Centralized c~~Cryobanking for a 20-year old woman with Hodgkin lymphoma~~in Canada~~

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Competing interests: The authors have no competing interests to declare.

Word count: ~~1229~~1248

Commented [CV1]: Edited for CMAJ style. Can centralized be deleted without changing intended meaning?

Commented [JM2R1]: No. The word "centralized" is very important and part of an internationally recognized concept.
See examples in these publications:
https://pubmed.ncbi.nlm.nih.gov/30733076/
https://www.fertstert.org/article/S0015-0282(25)01800-X/fulltext

Commented [JM3]: Now revised to

Key Points:

- Reproductive risks due to cancer therapy should be discussed with all patients as an integral part of oncology care.
- Ovarian t~~T~~issue c~~C~~ryopreservation is the only fertility preservation option for patients with ovaries who cannot undergo ovarian stimulation, including children, urgent cases and those living remotely from a fertility centre.
- Ovarian tissue transportation and centralized processing and cryobanking overcome barriers and improve access to care.
- This case demonstrates the feasibility of implementing ovarian tissue transportation and centralized cryobanking in Canada.

~~**Summary Box**~~

What is already known about this topic

- Ovarian tissue cryopreservation is the standard fertility preservation method for patients who cannot undergo ovarian stimulation.
- Geographic barriers limit access to specialized oncofertility services in Canada.
- Centralized processing models have been successfully implemented internationally.

What this study adds

- Demonstrates the feasibility of ovarian tissue transportation and centralized processing in Canada.
- Shows specialized fertility preservation care can be delivered remotely through coordinated care pathways.
- Provides proof-of-concept for "Hub-and-Spoke" oncofertility models in Canada.

Commented [CV4]: A summary box is redundant to the key points and is not used for Cases in CMAJ. Therefore, please delete and incorporate any critical points in text or key points.

Your word count right now is 1229. If you need, you can add some of this text to the body of the manuscript.

Commented [JM5R4]: Summary box was added per editor's request in the first revision: "Please include a box with 4–6 summary points that encapsulate the main messages of the article."
If redundant- OK to remove, as all concepts appear in the manuscript.

Case:

A 20-year-old, G3P2AB1, pediatric cancer survivor ~~from Southwestern Ontario~~ presented to her local oncology centre in Southwestern Ontario with right supraclavicular adenopathy. ~~The patient~~ She had a history of Stage IIA Hodgkin lymphoma diagnosed at age 15 and treated with two cycles of OEPA chemotherapy (vincristine, doxorubicin, etoposide and prednisone), achieving complete response. Positron emission tomography-computed tomography revealed multiple lymphadenopathies in the neck and chest above the diaphragm, and biopsy confirmed the diagnosis of relapsed Hodgkin lymphoma, stage IIA. The patient was 8 weeks pregnant at presentation and ~~had undergone~~subsequently underwent a surgical pregnancy termination at XX weeks. ~~The patient~~She expressed a desire for future fertility and was referred for urgent virtual counselling at an ~~Oncofertility~~ oncofertility ~~Centre~~ centre providing fertility preservation care. We counselled the patient regarding the effects of repeated alkylating-based chemotherapy exposure, the high risk for future infertility and premature ovarian insufficiency, and the various fertility preservation strategies available. Due to the need to initiate immediate salvage chemotherapy and the remote location (380km from Toronto), the patient elected to proceed with ~~Ovarian~~ ovarian t~~T~~issue c~~C~~ryopreservation after considering . ~~We counselled the patient regarding~~ surgical risks, tissue transportation, processing, storage and future transplantation of the ovarian tissue. ~~The patient signed appropriate consents and waiver forms.~~ We coordinated care remotely through a close collaboration with her~~the~~ local oncologist~~y~~ and gynecologist~~y teams~~. The patient completed pre-procedure investigations locally, including viral serology screening to ensure safe tissue handling and storage, and serum a~~A~~nti-~~Mullerian~~ mullerian h~~H~~ormone measurement to assess baseline ovarian reserve. A local gynecologist trained in specific oophorectomy techniques for ovarian tissue cryopreservation performed a laparoscopic unilateral oophorectomy using minimal coagulation and delicate tissue handling to preserve follicular viability. The contralateral ovary and both fallopian tubes remained in situ. We arranged for professional courier transportation of the ovarian tissue under continuous temperature monitoring, maintaining 4°C–8°C throughout the 380-km journey to our specialized embryology laboratory. Upon arrival, we stored the tissue overnight at 4°C until the tissue processing could be completed by an embryologist the following day ~~to~~

Commented [CV6]: Please define acronym.

Commented [JM7R6]: This is the standard name of this chemotherapy protocol; the medications are listed in parentheses in their most common form.
Can also be substituted with the longer version: vincristine sulfate (Oncovin), etoposide phosphate, prednisone and doxorubicin hydrochloride (Adriamycin)

Commented [CV8]: Clusters of enlarged lymph nodes? Is 'lymphadenopathies' a diagnostic term?

Commented [JM9R8]: Yes, this is the plural version of the word Lymphadenopathy.
Mentioned in this publication:
https://pubmed.ncbi.nlm.nih.gov/20069473/

Commented [CV10]: At what GA was the pregnancy termination?

Commented [JM11R10]: The same time, at 8 weeks.

Commented [CV12]: How does viral serology screening ensure safe handling and storage?

Commented [JM13R12]: Screening providers of eggs, sperm and reproductive tissue for viral serology is a standard protocol and indicated by the Assisted Human Reproduction Act (Canadian Law):
Infectious Disease Agents
At the time of initial testing, all sperm and ova donors must be tested for the presence of the following infectious disease agents, as listed in clause 2.3.3 of the Directive:
a.Human Immunodeficiency Virus (HIV) -1 and -2;
b.Hepatitis C Virus (HCV);
c.Hepatitis B Virus (HBV);
d.Human T-cell Lymphotropic Virus (HTLV) -1 and -2 (sperm donor only);
e.*Treponema pallidum* (syphilis);
f.Cytomegalovirus (CMV) (sperm donor only);
g.West Nile Virus (WNV), if the donation is made during the time of year when WNV is potentially transmissible to humans in the donor's country of residence, or if in the preceding 56 days, a donor has lived in or travelled to an area where WNV is endemic;
h.*Chlamydia trachomatis*; and
i.*Neisseria gonorrhoeae*.
From:
https://www.canada.ca/en/health-canada/programs/consultation-safety-sperm-ova-regulations/document.html#a15

Commented [CV14]: Correct?

Commented [JM15R14]: Yes.

~~align with embryology laboratory working hours~~. We completed tissue processing within 23 hours of retrieval, yielding over 60 tissue fragments. Additionally, during processing, we isolated 10 cumulus-oocyte complexes and successfully matured in vitro 8 oocytes that were cryopreserved, providing additional reproductive potential. The patient was discharged home on the day of surgery and started GDP salvage chemotherapy (gemcitabine, cisplatin, dexamethasone) within 6 days. Followed by autologous stem cell transplant with BEAM conditioning (carmustine, cytarabine, etoposide, melphalan) within 3 months. ~~To date~~Four months after the procedure, the patient remains well, and no immediate complications related to the fertility preservation procedure or bone marrow transplantation have been reported.

Commented [CV16]: Please define.

Commented [JM17R16]: This is the standard name of this chemotherapy protocol, with medications listed in parentheses in their most common form. Can also be replaced with: gemcitabine, dexamethasone, platinol)

Commented [CV18]: Please define.

Commented [JM19R18]: This is the standard name of this chemotherapy protocol, with medications listed in the parentheses in their most common form. Can also be replaced by the longer version if more appropriate: BCNU (carmustine), etoposide, cytarabine (Ara-C), and melphalan

Commented [CV20]: Please say exactly how many months following her last cycle of chemo or since the procedure.

Commented [JM21R20]: Procedure occurred on March 7th, and I called her for follow up in July 14th. Thus updated at 4 month after the procedure, 1 month after last course of chemo (BMT in June).

Commented [CV22]: Can you also provide more specific information about her cancer status?

Commented [JM23R22]: She just completed her BMT when I spoke with her, thus still followed up to confirm if in full remission, but reported no immediate complications (also confirmed with her primary oncologist).

Discussion:

~~Advancements in medical care in children, adolescents and young adults with malignancy~~ have ~~enhanced survival and long-term health outcomes.~~ For reproductive-aged individuals diagnosed with cancer, the prospect of future fertility often becomes a critical concern alongside ~~survivorship~~[2]. This case illustrates the complex challenges faced by young cancer patients who desire biological children but require urgent treatment that threatens their reproductive potential. ~~Quality of life, especially parenting biological children upon recovery, has emerged as a crucial element of survivorship.~~ Unfortunately, many life-saving interventions, including reproductive organ surgery, chemotherapy, and abdominopelvic radiation, increase the risk of infertility and reproductive endocrine dysfunction[1]. These advancements in cancer treatment and survivorship have~~is~~ led to the development of oncofertility, a discipline that integrates oncology and fertility care to preserve reproductive potential. For individuals with ovaries, the choice of fertility preservation strategy is individualized and depends on patient-specific factors, including age, pubertal and menarchal status, underlying diagnosis, urgency to initiate cancer therapy, baseline ovarian reserve, partnership status, physical and financial access to fertility care, and patient preference (Table 1[3]). The success of fertility preservation procedures in achieving a future live birth is closely tied to the quantity of stored ~~materials~~ samples and the patient's age at the time of the procedure.

For prepubertal and adolescent patients who cannot undergo ovarian stimulation and whose potential risk of infertility is considered high according to the internationally accepted standardized model for patients undergoing cancer treatment[4], adults younger than 35 years who urgently need to start chemotherapy or patients who have limited access to a fertility clinic, ovarian tissue cryopreservation ~~(OTC)~~, declared no longer experimental in 2019[5], is considered the best clinical practice by international fertility and oncology societies...[6]. This multi-step procedure involves laparoscopic removal of a whole or part of an ovary, transportation to an expert embryology laboratory for processing, cryopreservation and storage (Figure 1). Processing ovarian tissue in preparation for cryopreservation can also yield mature oocytes that can augment reproductive potential. Ovarian tissue can be stored for

Commented [CV24]: This sentence is a bit vague, and readers may not immediately connect this adult patient to children and adolescents with cancer and their need for cryopreservation.

Can you start with a sentence that is more focused on this case (ie. a reproductive aged person now undergoing urgent treatment for cancer but desiring fertility). You can then follow this sentence with a sentence about survivorship and adolescents and children. (ie. and this also impacts adolescents and children)

Commented [JM25R24]: Thank you for this comment, now revised for better readability

Commented [CV26]: Reference for this statement?

Commented [JM27R26]: Now added a reference.

Commented [CV28]: Reference for this statement?

Commented [JM29R28]: Now added a reference.

Commented [CV30]: The reference in the Table needs to occur as it appears in the text. Instead of 1, it would be 2. Please include it in the manuscript reference list and not on the Table file. You can include the reference superscript in the title of the Table.

Commented [JM31R30]: Now corrected and reference added in the text.

Commented [CV32]: Is there another word that can be used? Stored samples?

Commented [JM33R32]: Yes, OK to replace with stored samples. I chose the word "materials" to collectively include oocytes, embryos and reproductive tissues (ovarian tissue).

Commented [CV34]: Please state by whom.

Commented [JM35R34]: By international professional societies (oncology and fertility alike). Later in the text all the Canadian guidelines are cited as most relevant to local reader.

~~many~~ over 10 years, and when conception is desired, the tissue is thawed, prepared for transplantation, and auto-transplanted into the patient's pelvis to restore fertility and endocrine function.

Despite ~~a~~ Canadian obstetric and gynecology and fertility societies clinical guidelines endorsing fertility preservation in cancer patients[7–9], multiple barriers to the delivery of oncofertility care exist[10]. Patient barriers include a lack of awareness and high distress around survival, while healthcare providers ~~report~~ barriers ~~associated with~~include knowledge gaps and discomfort with discussing infertility risks, leading to low referral rates for counselling and procedures. Barriers at the ~~organizational~~ health care system level include the lack of well-designed and accessible resources to provide urgent oncofertility counselling and the absence of care pathways for coordinating procedures. F~~On the healthcare system level, f~~unding for fertility preservation procedures also varies by province and ~~presents a~~can present a substantial barrier to accessing care in provinces where patients must pay out of pocket expenses for this service.

While the ability to perform laparoscopic oophorectomy is readily available in many primary centres, the main practical barrier to equitable access to oncofertility care is that the processing and storage of ovarian tissue require expertise and specialized equipment that are not commonly found in most fertility clinics that perform oocyte or embryo cryopreservation. Centralizing the processing and storage of ovarian tissue in a dedicated cryobank facility offers several advantages, particularly for patients residing in remote areas. Access to care provided by local tissue harvesting, with subsequent safe transportation of the tissue to a central facility, a process shown to be feasible and safe[11]. Given that ovarian tissue cryopreservation ~~OTC~~ is a relatively rare procedure, centralization is also highly cost-effective, as it eliminates the need for maintaining multiple processing sites. Additionally, a centralized cryobank operating in a high-volume setting ensures improved quality control and assurance, as expertise can be concentrated, and standardized procedures can be consistently applied.

This approach is common in many European countries that have established centralized ovarian tissue cryopreservation~~OTC~~ programs and successfully incorporate tissue transportation across

Commented [CV36]: Up to how many years exactly?

Can you revise the sentence to, "Ovarian tissue can be stored for roughly XX years…"

Commented [JM37R36]: This is a great question that has no clear answer, similar to eggs and embryos, we don't know how long these can be stored. There are documented cases of re-transplantation leading to pregnancies after 15 or 20 years. So technically there is no known expiration date.
I suggest saying "over 10 years" , as this time frame is very well established, and will be most relevant for young people- for example the 3yo child we froze tissue for, might not return before 30 years of storage have passed…

Commented [CV38]: Is it connected to the fallopian tube (asking for all of us non-surgeons…)?

Commented [JM39R38]: No, the tissue can be placed in multiple location in the pelvis, but not physically attached to the tube. If the tissue is in anatomic proximity to the tube, such as the contralateral ovary or pelvic sidewall, then ovulated oocytes can be picked-up by functioning tube and facilitate a spontaneous pregnancy. According to international reports 50% of the pregnancies following transplantation are spontaneous, while the rest require fertility treatment. I did not go into these details due to the limited nature of this report.

Commented [CV40]: Please state which guideline committee.

Commented [JM41R40]: The SOGC- obstetrics and gynecology, and CFAS- fertility professional societies' guidelines are cited in 7 to 9 citations.

Commented [CV42]: Reference for this sentence? If not, consider rewording to 'provider barriers include…" rather than 'report'.

Commented [JM43R42]: Revised.

Commented [CV44]: health care systems level? It seems like this organization would have to be organized on a provincial health care systems level.

Commented [JM45R44]: Yes, agree with this change, revised.

Commented [CV46]: Would patients be paying out of pocket in some provinces? Can you name which ones?

Commented [JM47R46]: The only province that covers OTC is Quebec. All the other provinces either do not have any coverage for fertility care/fertility preservation, or do not include OTC under covered procedures (like Ontario). I submitted a formal business case to the Ontario Fertility Program- advocating for coverage for OTC as a standard of care procedure.
I think that the publication of this manuscript will play an important role and will help advocate for provincial

Commented [JM48R46]: I like the way you rephrased this sentence. Suggest keeping as is.

regions. Pioneered by the Danish Network, founded in 1999 with the slogan "the patient stays – the tissue moves," centralization of ovarian tissue cryopreservation~~OTC~~ in Denmark and southern Sweden, is enabling tissue retrieval locally and transport for processing and storage, leading to multiple live births[12]. ~~The FertiPROTEKT Network,~~One network spanning 125 centres in Germany, Austria, and Switzerland, consolidates the~~OTC~~ processing into three main cryobanks, optimizing transportation logistics and achieving multiple live births[13]. Optimizing resources and outcomes, in 2018, the Netherlands merged seven fertility preservation centres into a centralized national program[14]. The UK's centralized cryobank in Oxford follows a "Hub-and-Spoke" model, providing cryopreservation services across England, Wales, and Northern Ireland[15]. Similar centralized models exist in Japan and the US.

This case demonstrates the feasibility of implementing a centralized "Hub-and-Spoke" model for ovarian tissue cryopreservation in Canada. As a proof-of-concept, we successfully delivered specialized oncofertility services ~~to a remote patient~~ through coordinated care pathways that overcome geographical barriers. The hub o~~O~~ncofertility c~~C~~entre provides specialized oncofertility expertise while collaborating with local healthcare teams, as spokes, through a multidisciplinary approach that includes urgent virtual consultations, coordination of local surgical procedures, professional tissue transportation, and centralized expert processing and storage. T~~By improving access to care, t~~he described model aims to reduce infertility and reproductive endocrine dysfunction in cancer survivors, minimize the psychosocial impact of infertility, and enhance the quality of life for patients and their families by improving access and coordination of care.

Commented [CV49]: You would have to spell out this acronym. Therefore, I suggest this edit.

Commented [JM50R49]: This is not an acronym, but rather a blend word combining Fertility (Ferti) and the German spelling for Protection (Protekt) - that was chosen as the brand name for the German fertility network.
But-- I am OK with this change if you feel better aligns with CMAJ style.

Commented [CV51]: Remote suggests geographically remote (ie very rural, hard to get to). Can you use a different adjective?

Commented [JM52R51]: If you think that this is inappropriate I am OK with removing the word remote altogether. As the highly specialized nature of this service is relevant to anyone who does not live close to our centre, even if they are not "rural", for example a patient in London, or Ottawa, cannot be considered rural, but they lack the access to this service if they don't physically come to us. The proposed model allows for ANY patient in Canada (not only in Ontario) to enjoy this service, without traveling long distances or delaying their cancer care.

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Table 1: Fertility preservation strategies in individuals with ovaries

Strategy	Procedure involves	Advantages	Limitations
Embryo Cryopreservation	• 2-3 weeks of ovarian stimulation • Injectable medications administration • Multiple visits for blood draws and ultrasounds to monitor response • vaginal approach procedure • fertilization of oocyte by sperm, in the lab, and freezing of embryos	Well-established success rates: 35.3% live birth rate	• Only in post-pubertal patients • Delays cancer therapy • Requires sperm provider • Limits reproductive autonomy • Access – requires physical proximity to a fertility clinic
Oocyte Cryopreservation	• 2-3 weeks of ovarian stimulation • Injectable medications administration • Multiple visits for blood draws and ultrasounds to monitor response • vaginal approach procedure • freezing of unfertilized oocytes	Well-established success rates: 25.8% live birth rate	• Only in post-pubertal patients • Delays cancer therapy • Access – requires physical proximity to a fertility clinic
Ovarian Tissue Cryopreservation	• Surgery – Laparoscopic oophorectomy • Transportation of tissue • Processing and storage of ovarian tissue	• Pre and post-pubertal patients (<35y) • No delay in cancer therapy • No physical proximity to fertility clinic • Restores endocrine and fertility functions • Well-established success rates: 32.3% live birth rate (in international centres)	• Requires surgery (at time of harvesting and again at time of re-transplantation) • No live births reported in Canada • Requires unique OTC expertise

- For patients requiring pelvic radiation, ovarian and/or uterine transposition can be offered.
- Live birth rates from a meta-analysis comparing the success of oocytes, embryo, and ovarian tissue cryopreservation[3]

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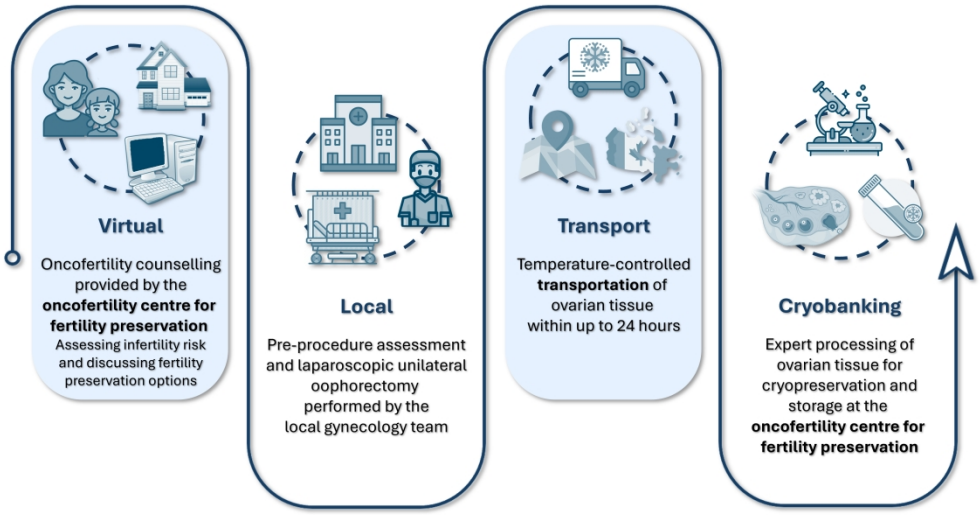

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Author Contributions Statement

JM conceived the study, established the ovarian tissue transportation and centralized cryobanking program, provided oncofertility counseling and coordinated patient care, wrote the original draft, and led the revision process. ME processed the ovarian tissue, coordinated care, and contributed to manuscript review. MS performed the surgical procedure and reviewed the manuscript. EMG supervised the project and reviewed the manuscript. All authors reviewed and approved the final manuscript for publication.