

## Appendix

**Supplemental Table 1.** Opportunities to Integrate Fertility Care into Pediatric and Adult Clinical SCD Practice

Pediatric sickle cell disease care		Adult sickle cell disease care	
Over time, care focus shifts from caregiver to the patient with SCD	Initially focused on caregiver's questions and concerns	Opportunities for fertility preservation, pregnancy, and IVF wane with older age	Adult patient with SCD is primary recipient of counseling & care; partner or family may become secondary participants
	Include fertility preservation, genetic counseling, opportunity for referrals, to address options for future family building		Ovarian reserve testing and semen analysis should be offered
	With each new treatment considered or initiated, include education about treatment-related infertility risks		Complex shared decision making re: hydroxyurea use if azoospermia, oligospermia, DOR or POI identified
	Ethical consideration of children's right to an open future		Higher-stakes fertility preservation for women as ovarian reserve declines.
	Children participate in decision making as is developmentally appropriate		For patients actively trying to conceive, consider standard referral to reproductive specialists or MFM
	In adolescent care, re-visit indications for ovarian reserve measures or semen analysis, invite serial opportunities for discussion of fertility status and fertility preservation		<b>NOTE:</b> People with SCD who are LGBTQ-identified may have additional, distinct indications for fertility preservation or ART

SCD: Sickle Cell Disease; IVF: in vitro fertilization; DOR: Diminished ovarian reserve; POI: premature ovarian insufficiency; ART: Artificial reproductive technologies; MFM: Maternal Fetal Medicine Specialist

## Supplemental Table 2

**Existing international policies governing ART access** National differences in ART coverage will affect the provision of fertility care for people with SCD and their families around the globe. Abbreviations include: ART: Artificial Reproductive Technologies, FPT: Fertility Preservation Treatment, FP: Fertility Preservation, HFEA: Human Fertilization and Embryology Authority IVF: In Vitro Fertilization, ICSI: Intracytoplasmic Spermatic Injection, PGT: Preimplantation Genetic Testing, PGT-M: Preimplantation Genetic Testing for Monogenetic Disorders, PGT-SR: Preimplantation Genetic Testing for Structural Chromosomal Rearrangements, PGT-A: Preimplantation Genetic Testing for Aneuploidy.

<b>North America</b>		
<b>Canada</b>	Governed by	Legislation and guidelines, ART is regulated by the Assisted Human Reproduction Act (2004).
	Policy Level	National and province
	Financial Coverage	Partial – only 4/10 provinces provide financial assistance
	FPT Policy	In Quebec, FPT is covered until 25 or for 5 years for people 21 or older. People who are receiving gonadotoxic treatment or ablation of ovaries or testicles have access to FP. There is no law that requires offering FPT to patients.
	PGT Policy	There is no national policy on PGT. Quebec is the only province with regulations
	IVF/ICSI/Surrogacy Policy	The law prohibits sex selection, hybrid embryos, commercial surrogacy, and trading of sperm and eggs. Single mothers and same-sex couples can access ART.
<b>USA</b>	Governed by	Legislation and guidelines
	Policy Level	National and state
	Financial Coverage	Partial – some states require private insurance
	FPT Policy	As of December 2021, 19 states have passed some type of fertility treatment mandate legislation, with 13 requiring coverage for IVF and 11 requiring coverage specifically for fertility preservation treatment
	PGT Policy	PGT is not regulated, so it can be used for any condition with genetic testing available and is up to the fertility specialist.
	IVF/ICSI/Surrogacy Policy	Marriage is not a requirement. Singles and female same-sex couples can access ART. Surrogacy is allowed.

<b>Europe</b>		<i>Although each country in the EU has its own law regarding ART, the European Society of Human Reproduction and Embryology (ESHRE) Task Force on Ethics and Law acts as a unifying body that provides guidelines. In the UK, the Surrogacy Arrangement Act (1985), the Human Embryology and Fertilization Act (1990), and the Human Reproductive Cloning Act (2001) are the three laws that regulate ART. Fertility clinics must obtain a license from and report to the Human Fertilization and Embryology Authority (HFEA).</i>
<b>Denmark</b>	Governed by...	Legislation and guidelines
	Policy Level	National
	Financial Coverage	Complete coverage through a national health plan.
	FPT Policy	Oocyte cryopreservation is regulated by the law. It is indicated for women < 46 for a medical reason only. It is free for medical reasons.
	PGT Policy	PGT-M and PGT-SR are allowed. PGT-A is only offered within a research protocol approved by an ethics committee.
	IVF/ICSI/Surrogacy Policy	Egg donation is prohibited. Male same-sex couples do not have access to IVF/ICSI. Surrogacy is prohibited.
<b>France</b>	Governed by...	Legislation and guidelines
	Policy Level	National
	Financial Coverage	No costs regarding medications and the laboratory, but patients may have to pay costs related to doctor/medical services.
	FPT Policy	Oocyte cryopreservation is regulated by the law and guidelines. It is indicated for women 18-42 for medical reasons only. It is prohibited for non-medical reasons except for egg donors with no children. It is free for medical reasons.

	PGT Policy	PGT is authorized by the public health code for couples who have a high probability of having a child with an incurable heritable disease. The couple must have another child or relative with the disease. PGT-A is prohibited.
	IVF/ICSI/Surrogacy Policy	Only heterosexual couples have access to 3 <sup>rd</sup> party egg or sperm donation. There is no numerical age limit on ART access. “Normal reproductive age” is decided by the multidisciplinary staff of the center, with consent from the couple.
<b>Germany</b>	Governed by...	Legislation and guidelines
	Policy Level	State
	Financial Coverage	Coverage varies based on private and statutory insurance
	FPT Policy	Oocyte cryopreservation is regulated by the law and guidelines. It is indicated for women 20-49 for medical and non-medical reasons. It is not funded.
	PGT Policy	PGT is allowed within strict limits.
	IVF/ICSI/Surrogacy Policy	Singles and male same-sex couples do not have access to ART. For insurance coverage, couple must be married, woman is 25-40 and man is 25-50, and the egg and sperm are theirs. Egg cell donation, surrogate motherhood and elective single embryo transfer are prohibited.
<b>UK</b>	Governed by...	Legislation and guidelines
	Policy Level	National - governed by the Human Fertilization and Embryology Authority (HFEA)
	Financial Coverage	Partial insurance coverage – IVF is free for women under 40.
	FPT Policy	Oocyte cryopreservation is regulated by the law and guidelines. There are no age or medical restrictions for freezing. It is free in the NHS for medical reasons.
	PGT Policy	PGT is regulated by the HFEA, which has a list of approved conditions including sickle cell anemia.
	IVF/ICSI/Surrogacy Policy	No restrictions on who can access IVF/ICSI with 3 <sup>rd</sup> party donations. Marriage not a requirement. Singles and female same-sex couples can access ART. Surrogacy is allowed.

<b>Asia</b>		<i>In India, ART is regulated mostly by guidelines. There was very recent legislation that was passed. The Surrogacy (Regulation) Act (2021) prohibits commercial surrogacy. New Assisted Reproductive Technology (Regulation) Act (2021) regulates ART clinics and labs. In Saudi Arabia, ART is regulated by the Law of Units of Fertilization, Utero-Fetal, and Infertility Treatment.</i>
<b>India</b>	Governed by...	Guidelines and very new legislation
	Policy Level	National and state boards
	Financial Coverage	None
	FPT Policy	Standard FPT options are oocyte and embryo cryopreservation and gonadal shielding offered to women 15-45. Standard options for men include sperm cryopreservation and gonadal shielding. FPT is not covered by insurance.
	PGT Policy	PGT for non-medical sex selection is prohibited.
	IVF/ICSI/Surrogacy Policy	Marriage is not a requirement. Singles and female same-sex couples are permitted to use ART. New Surrogacy (Regulation) Act 2021 prohibits commercial surrogacy. New Assisted Reproductive Technology (Regulation) Act 2021 regulates ART clinics and labs.
<b>Saudi Arabia</b>	Governed by...	Legislation
	Policy Level	National and private clinics
	Financial Coverage	Varies – government subsidizes ART for couples with primary or secondary infertility, only 1 child, female < 43. Services from private clinics is not covered by insurance.
	FPT Policy	FPT is offered only to married, different-sex couples. FPT options include cryopreservation of sperm, embryos, and oocytes. This is offered mostly to people without cancer, as people with cancer are not educated about their options.
	PGT Policy	PGT is offered only to married, different-sex couples for severe genetic conditions.

	IVF/ICSI/Surrogacy Policy	Only those with a curable medical problem or evidence of poor fertility have access to ART. Couple must be married.
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<b>Africa</b>		<i>In Ghana and Nigeria, no laws that regulate ART. Fertility treatment practices vary based on the private clinic.</i>
<b>Ghana</b>	Governed by...	Guidelines
	Policy Level	Private clinics
	Financial Coverage	None. Some people who have private insurance through an international company can get costs reimbursed.
	FPT Policy	The Accra Fertility Center offers cryopreservation of extra embryos. For males, they offer semen analysis and cryopreservation.
	PGT Policy	The Ruma Fertility and Specialist Hospital Limited is the only IVF clinic in Ghana that offers PGT for women over 35 and for couples who are both carriers of sickle cell trait.
	IVF/ICSI/Surrogacy Policy	Some clinics offer ART with donor sperm and oocytes and surrogacy.
<b>Nigeria</b>	Governed by...	Guidelines
	Policy Level	Varies by clinic, some follow the United Kingdom's HFEA
	Financial Coverage	None
	FPT Policy	The Nordica Fertility Center offers oocyte and embryo cryopreservation as well as sperm banking.
	PGT Policy	The Nordica Fertility Center offers PGD for inheritable diseases, sex selections, and frequent miscarriage due to a genetic disease.
	IVF/ICSI/Surrogacy Policy	All fertility treatments are provided only for married, different-sex couples.