SISTER

Sibling oocyte Insemination with frozen Sperm from Third party donors: Evaluation of Reproductive techniques

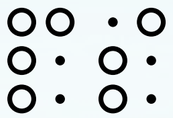
Presenter: Allison A. Eubanks, MD, FACOG
Institution: Walter Reed National Military Medical Center / NIH
Date: March 18, 2026

Disclosures

- Nothing to Disclose

Background & Rationale

Intracytoplasmic sperm injection (ICSI) has helped overcome numerous fertilization challenges:



Low Sperm Count

Poor Motility

Abnormal Morphology

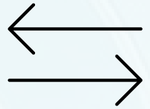
Original indications: Severe male factor infertility

Source: ASRM 2020

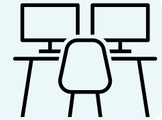
Clinical Practice Gap

Limited evidence for ICSI outside male factor infertility

No ASRM guidance for fertilization method with frozen sperm



Clinical practice varies widely across IVF centers



Unclear benefit of ICSI when frozen sperm parameters are adequate

Sources: ASRM, 2020; Ferraro et al., 2023, Beroukhim et al., 2022, Bolton et al., 2023; Yang et al., 2024; Hunkler et al., 2024

Why Use ICSI with Frozen Sperm?

Concerns with Frozen Sperm

Cryopreservation can impact sperm motility and acrosomal function

Conventional IVF relies on sperm penetration, which may be compromised post-thaw

Rationale for ICSI

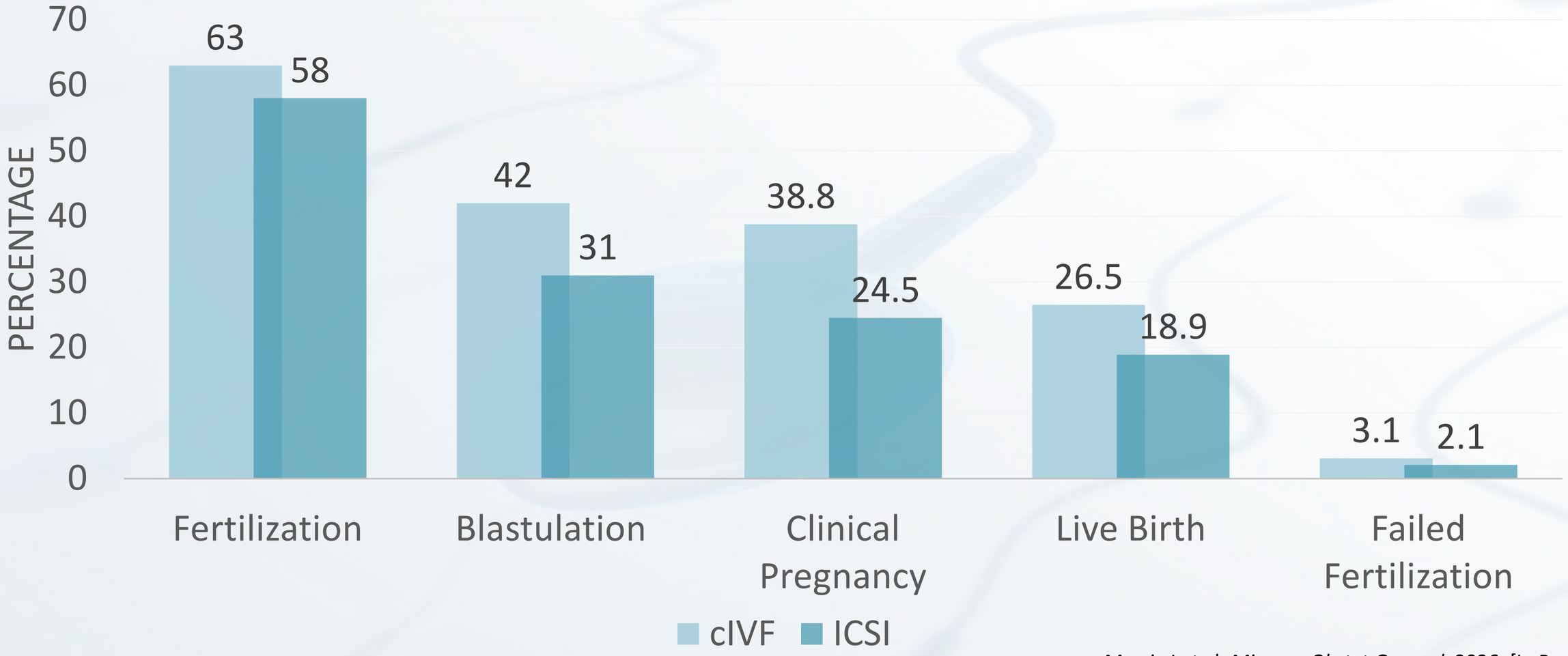
ICSI bypasses these concerns by directly injecting sperm into the oocyte

Improves fertilization rates and reduces the risk of total fertilization failure in some medical diagnoses

Sources: Smith et al., 2019; Johnson et al., 2020; Lee et al., 2021; Yang et al., 2024

Data Question Routine ICSI Use:

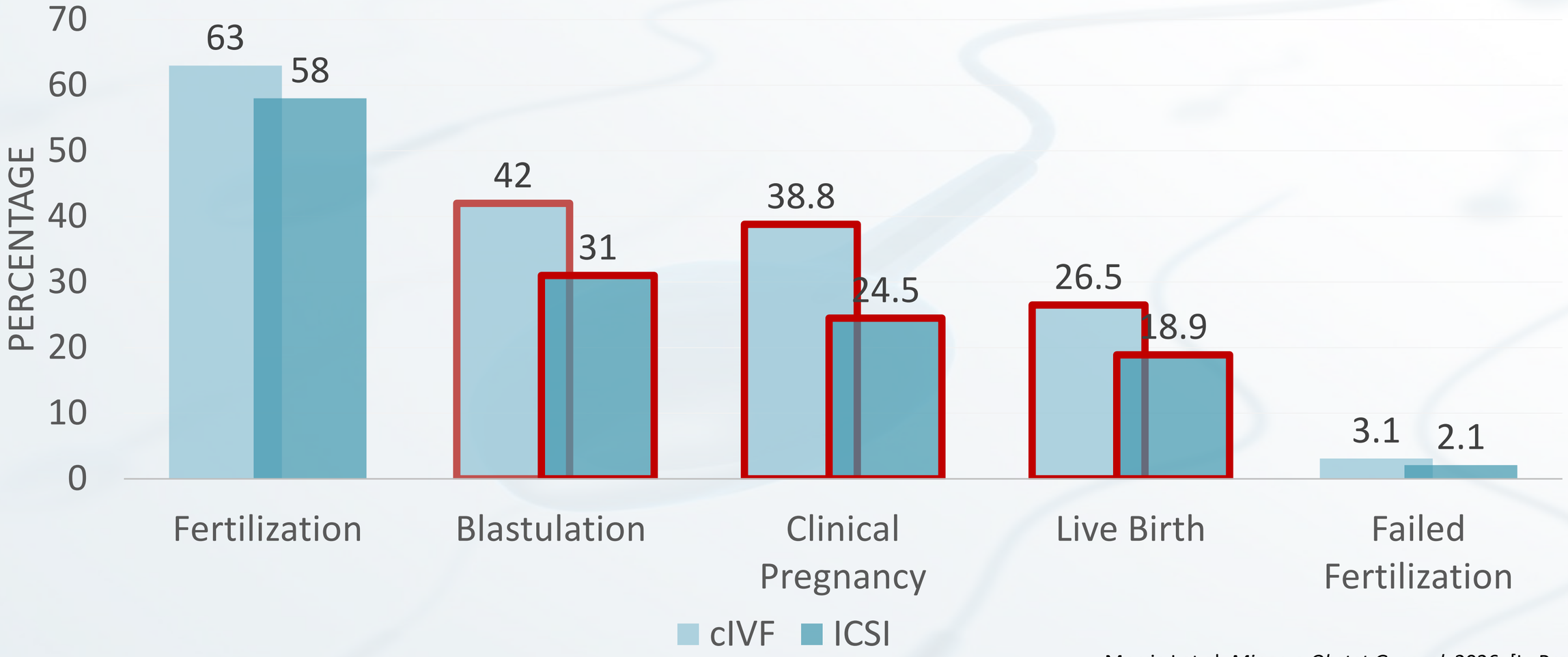
Retrospective US Fertility Study



Morris J et al. *Minerva Obstet Gynecol*. 2026. [In Press].

Data Question Routine ICSI Use:

Retrospective US Fertility Study



Morris J et al. *Minerva Obstet Gynecol*. 2026. [In Press].

Study Objective & Design

FOCUS

OBJECTIVE	Compare fertilization and embryo development between conventional IVF and ICSI in frozen donor sperm cycles
NULL HYPOTHESIS	Blastulation rates do not differ between fertilization methods when sperm parameters are adequate

ENSURING FEASIBILITY

DESIGN	Prospective, **randomized sibling - oocyte trial**
SETTING	Single Large IVF Center
PARTICIPANTS	Women undergoing IVF with frozen donor sperm
STUDY ARMS	50% ICSI | 50%conventional IVF

Study Eligibility Parameters

INCLUSION CRITERIA

In-Cycle Eligibility

Normal Ovarian Reserve:
AMH > 1ng/mL, AFC > 10

No Male Factor Infertility:
Post- wash motility ≥ 50%, concentration ≥5M

Pre-Cycle Eligibility

Adequate Follicular Response at Trigger:
⩾ 5 follicles- ≥17mm (≥15mm)

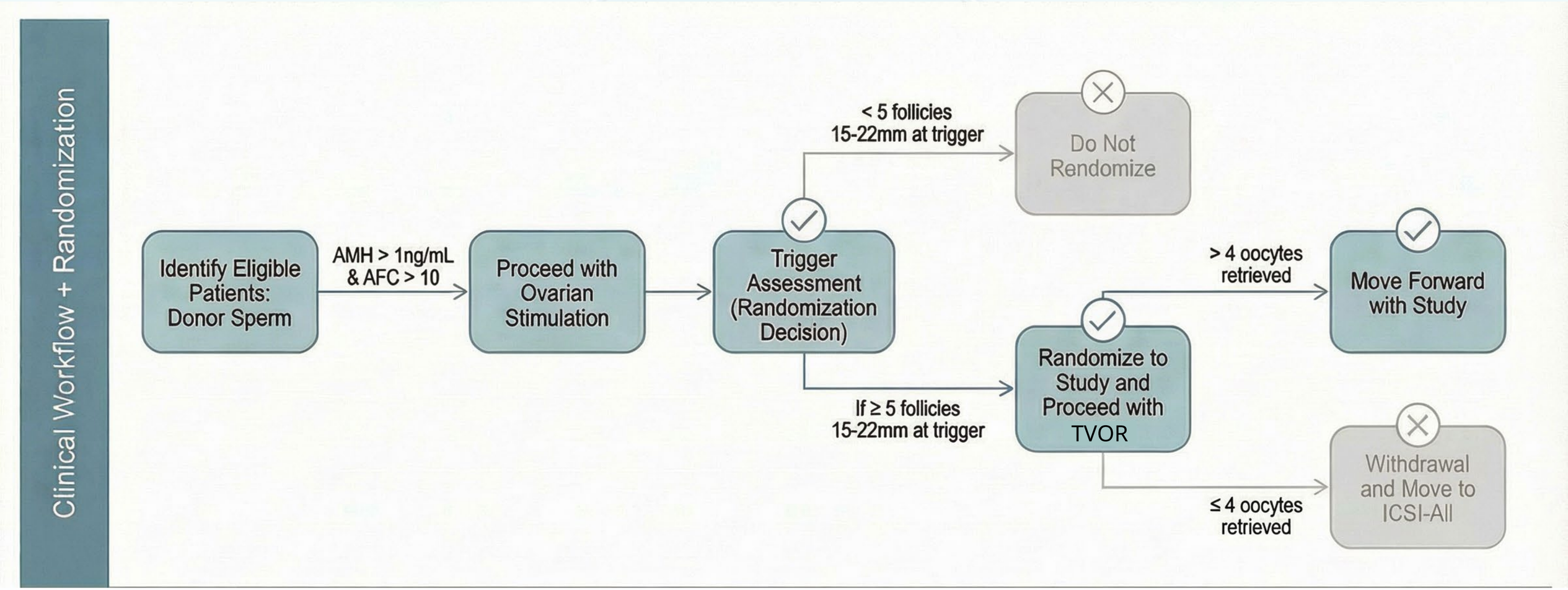
Adequate oocyte yield at retrieval:
> 4 oocytes retrieved

EXCLUSION CRITERIA

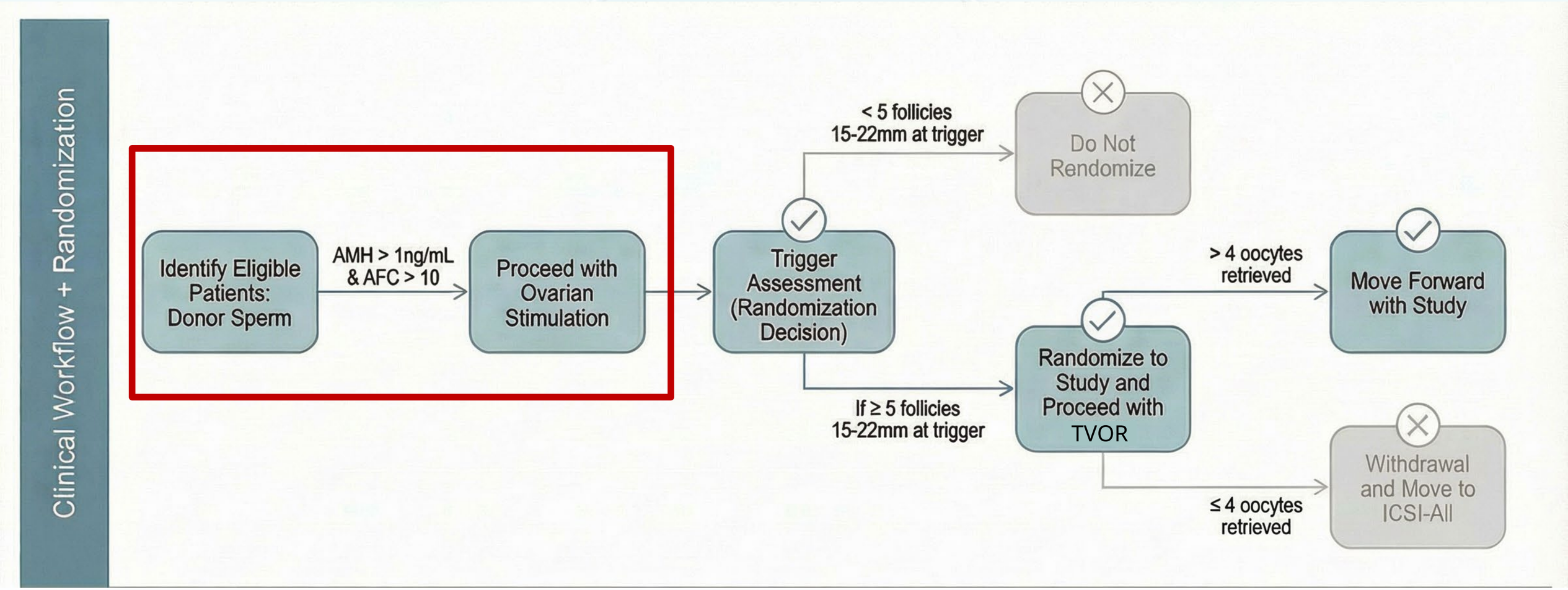
Prior Poor Ovarian Response: < 4 MIIs retrieved in prior cycle

Uterine Factor Infertility: Submucosal fibroids, adenomyosis, or other structural pathology

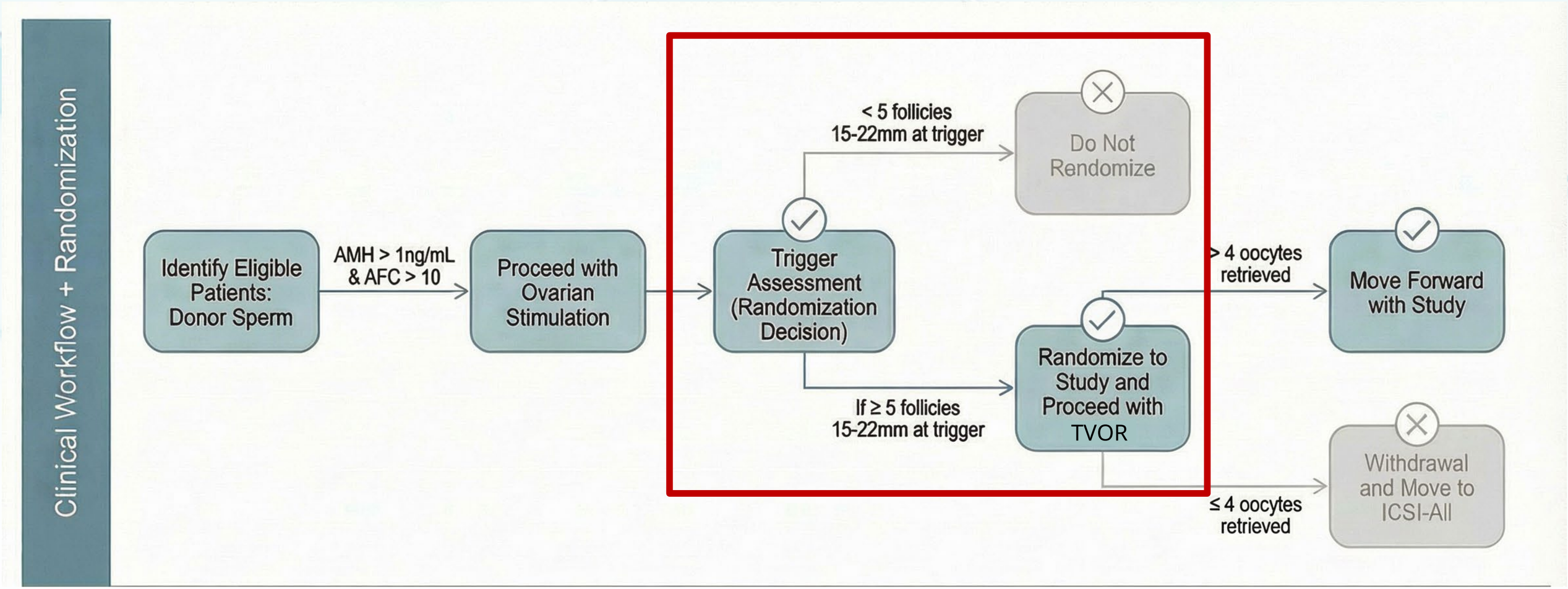
Methods: Clinical Randomization Workflow



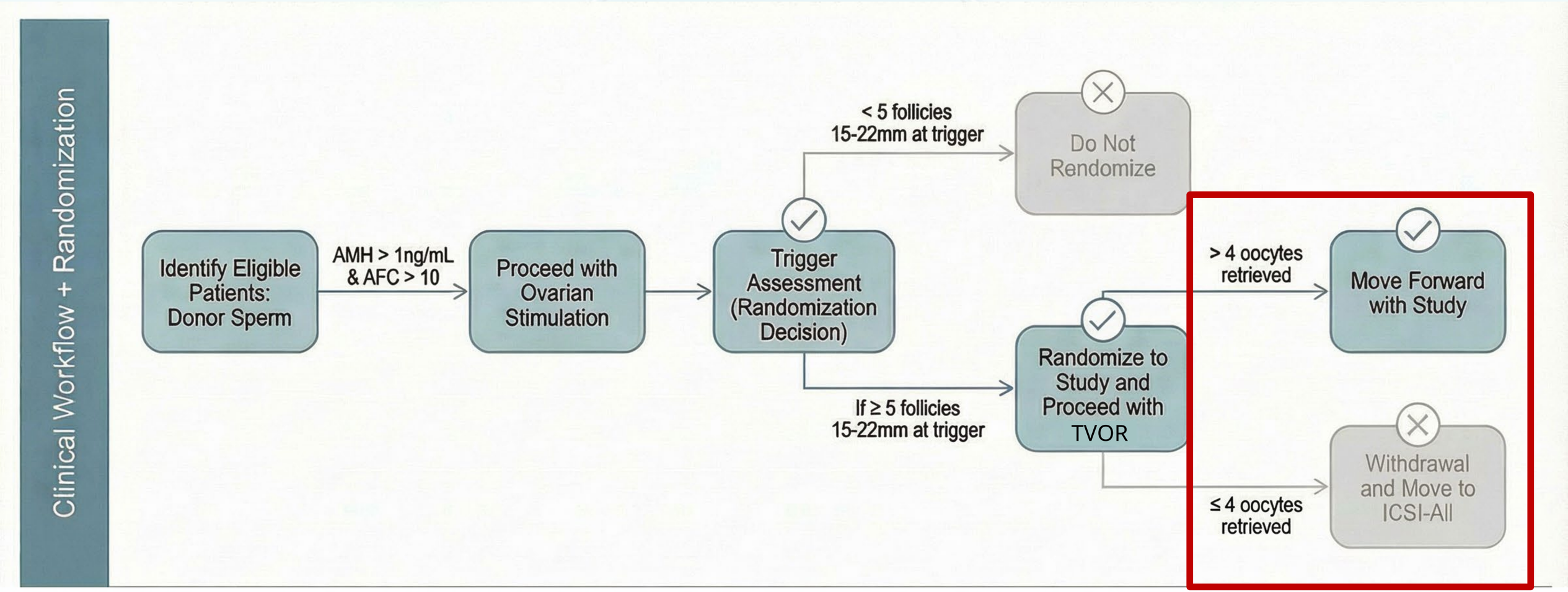
Methods: Clinical Randomization Workflow



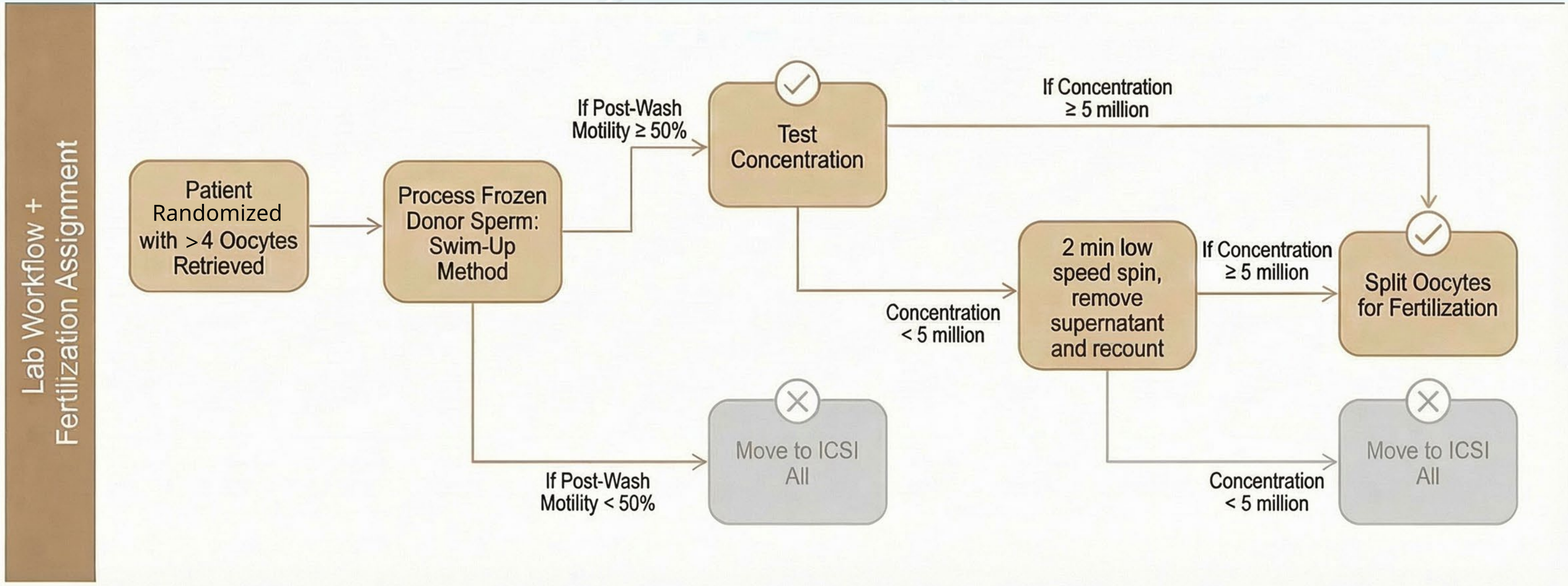
Methods: Clinical Randomization Workflow



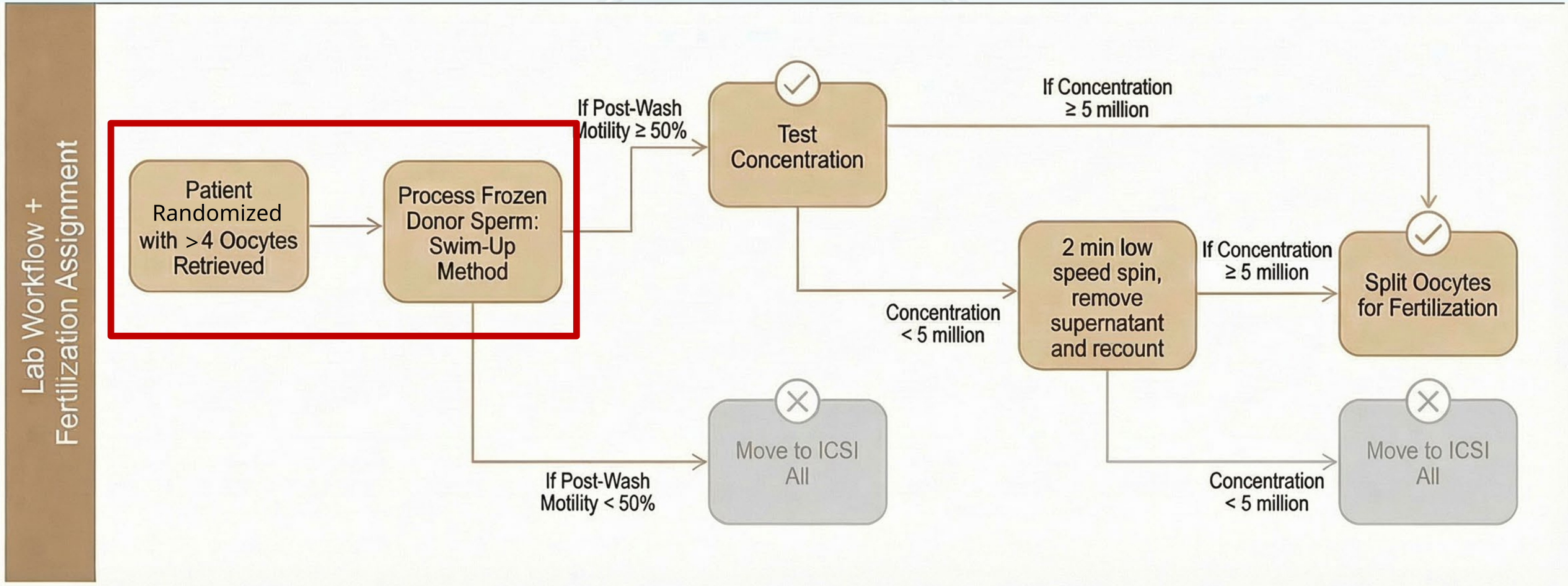
Methods: Clinical Randomization Workflow



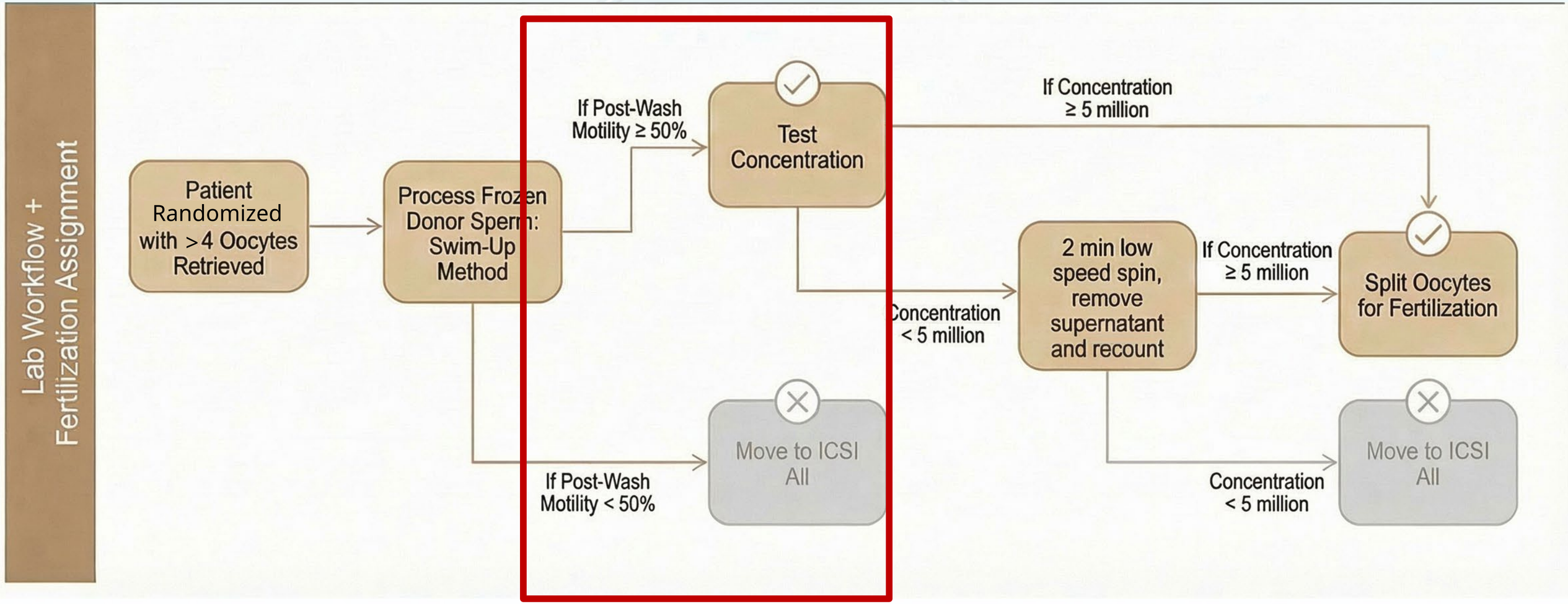
Methods: Laboratory Workflow



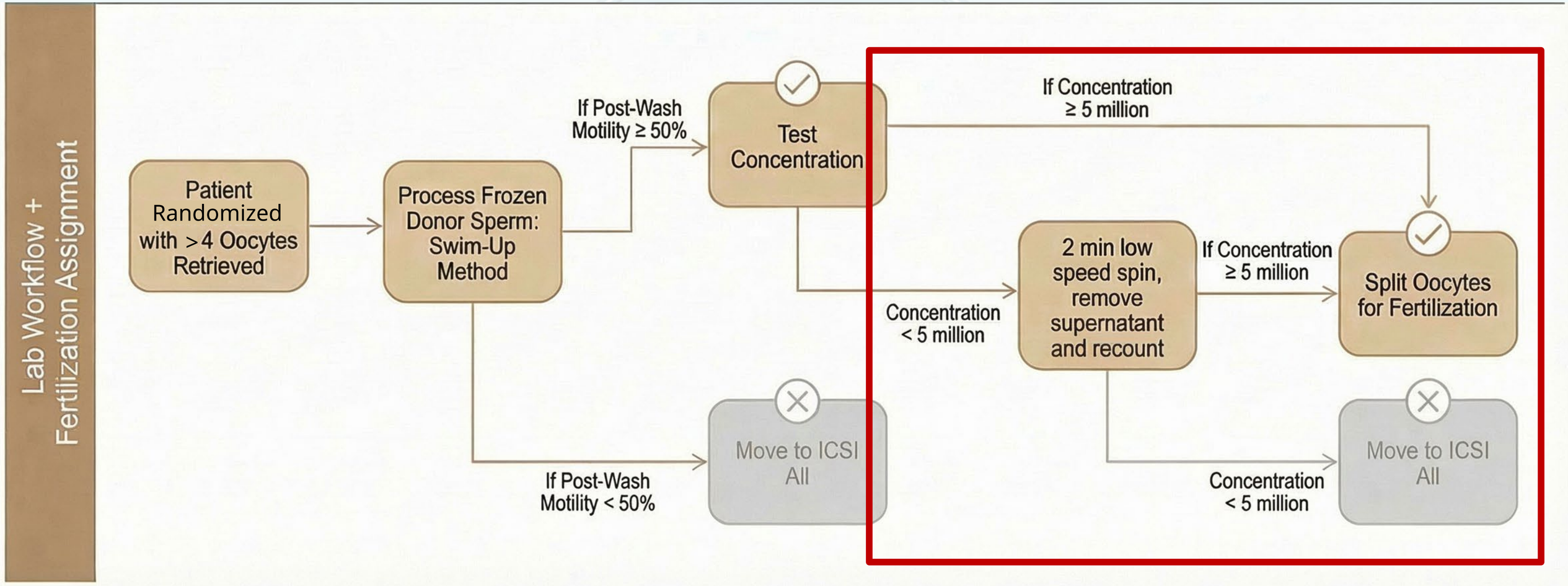
Methods: Laboratory Workflow



Methods: Laboratory Workflow



Methods: Laboratory Workflow



Methodology

RANDOMIZATION

Sibling-oocyte method balances inter-patient variability

STATISTICAL ANALYSIS

- Oocyte-level blastulation
  - Logistic regression with GEE
- Patient level
  - Chi-squared and student t-test
- Controlling for maternal age

Power Calculation

ASSUMPTIONS

ALPHA

Alpha = 5% (Z=1.96)

POWER

Power = 80% (Z=0.84)

EXPECTATIONS

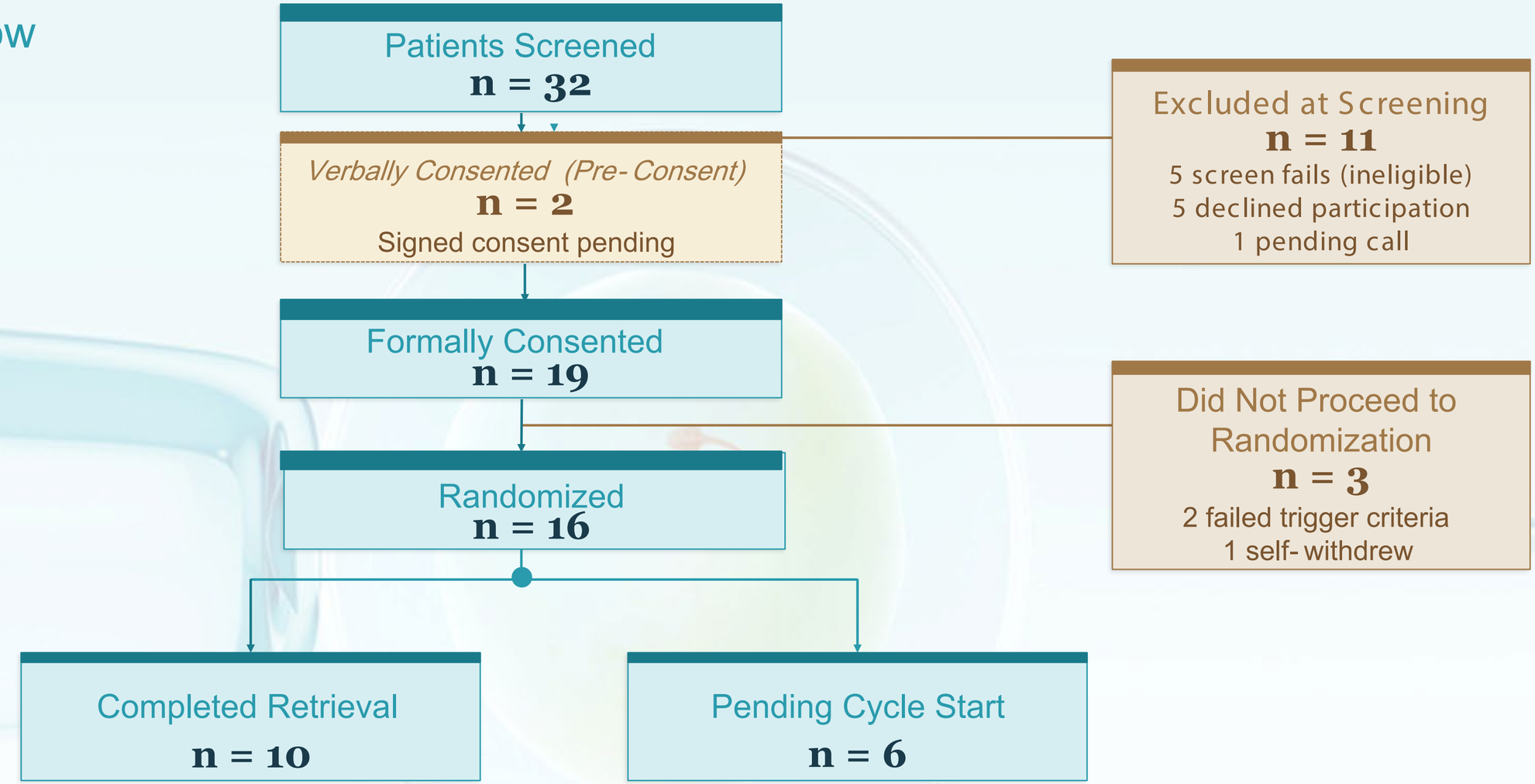
- Estimated blastulation proportion in ICSI group: 31%
- Estimated blastulation proportion in IVF group: 42%
- Intrapatient Correlation = 0.2
- Expected cluster size (# of eggs per patient) = 15

NUMBERS NEEDED

- Final N oocytes per group = **712 oocytes**
- Final total oocytes needed = **1424 oocytes**
- For 15 eggs/patient = **95 patients**

Study Progress and Feasibility: Enrollment Underway

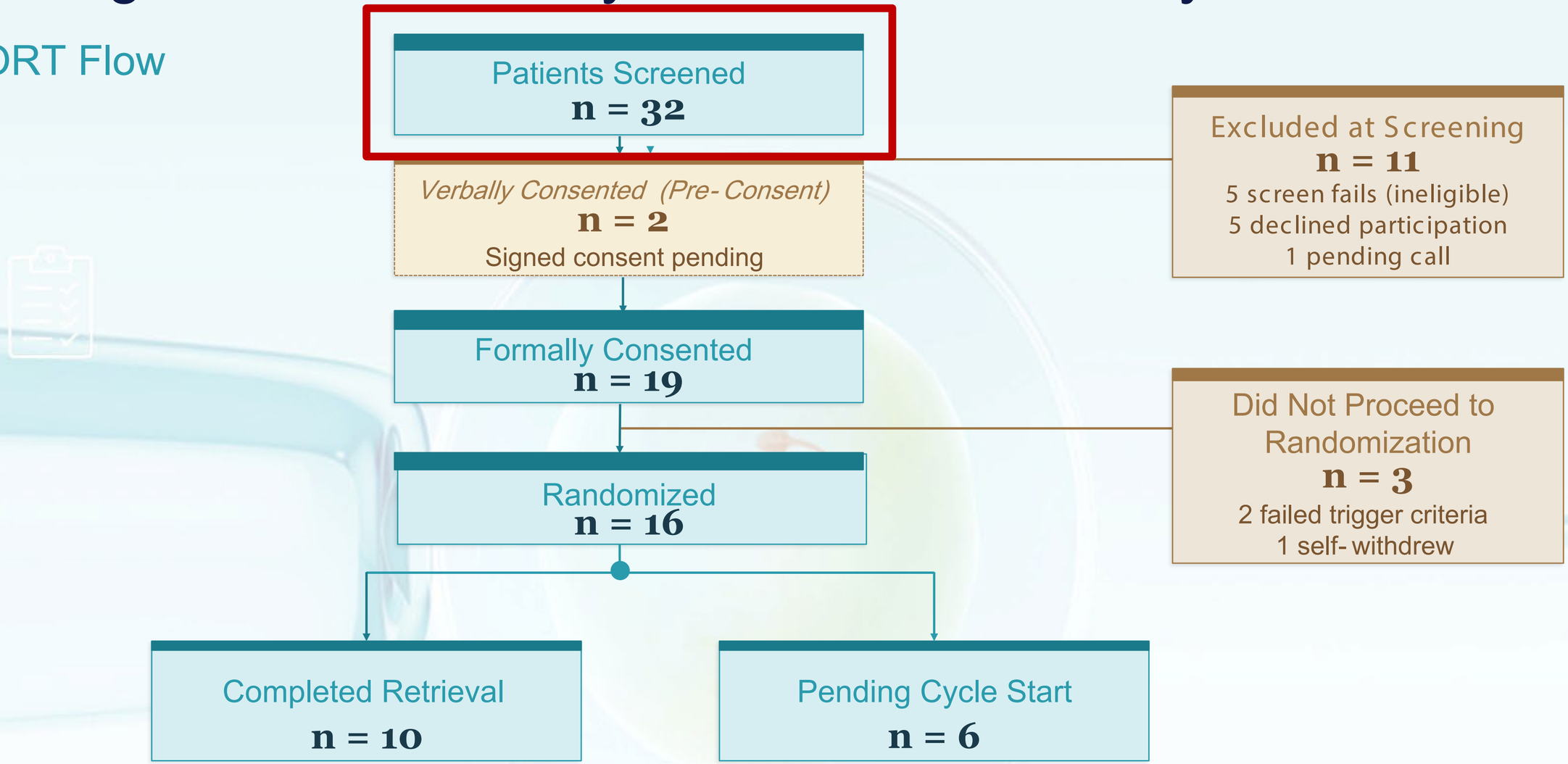
CONSORT Flow



Enrolled / Progressing Pre-Consent (Verbal) Excluded / Withdrawn

Study Progress and Feasibility: Enrollment Underway

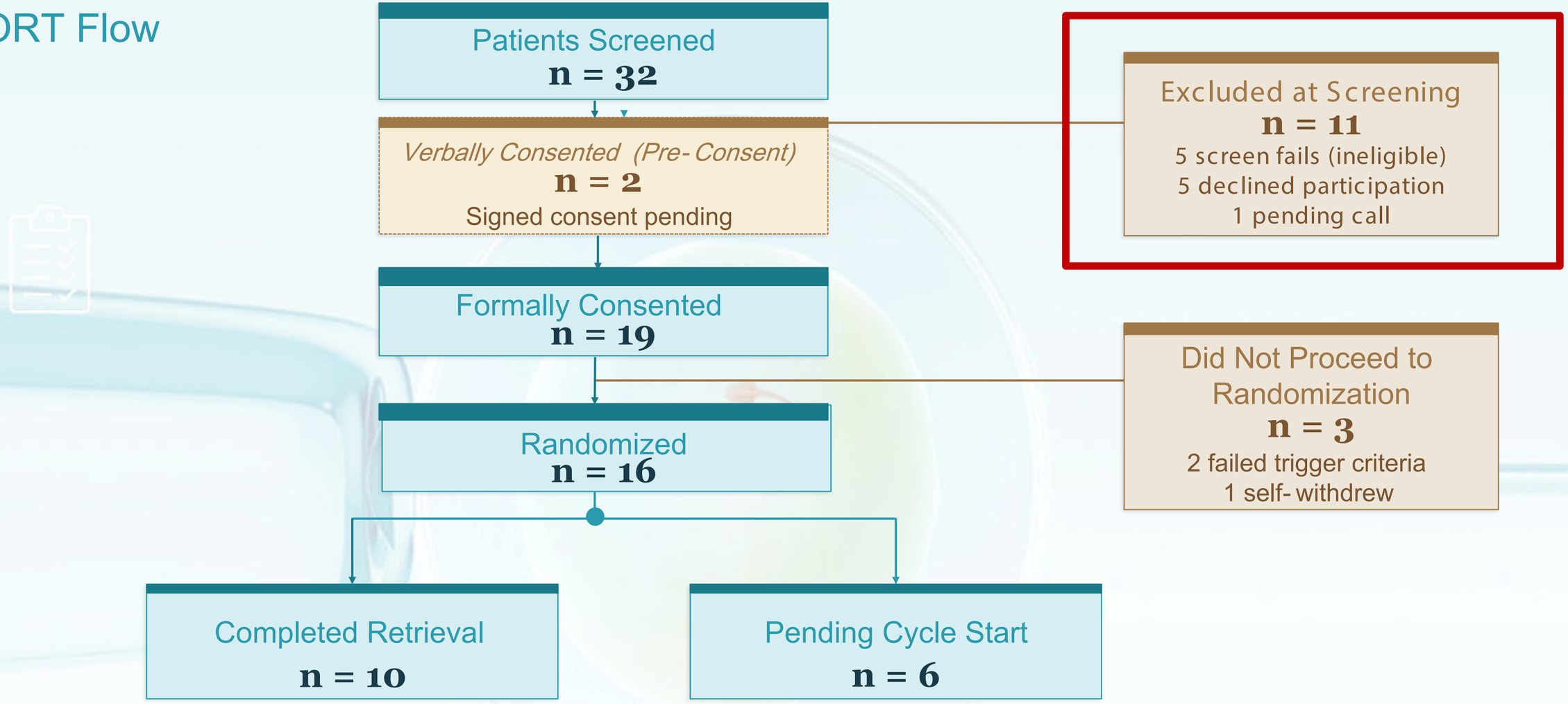
CONSORT Flow



Enrolled / Progressing Pre-Consent (Verbal) Excluded / Withdrawn

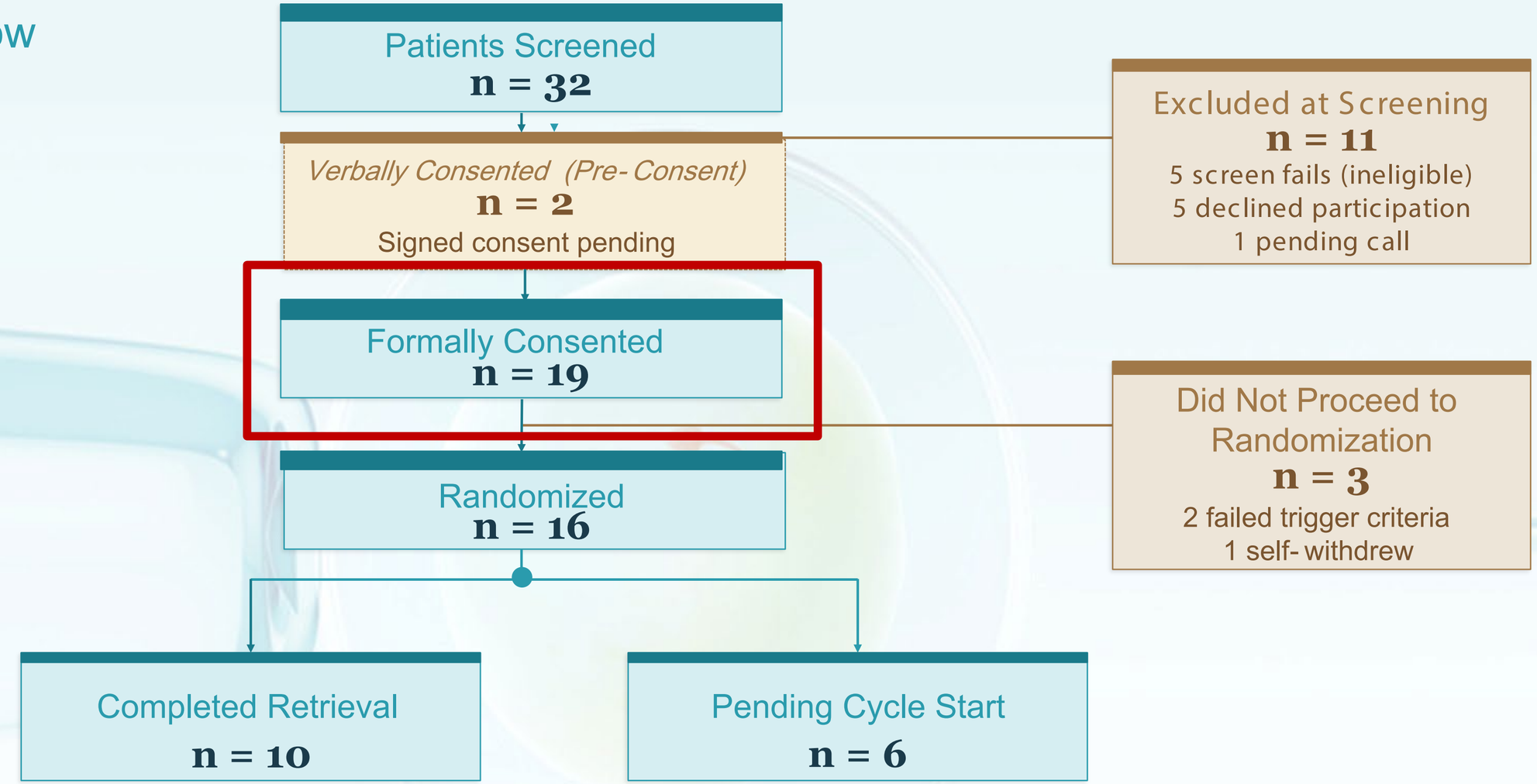
Study Progress and Feasibility: Enrollment Underway

CONSORT Flow



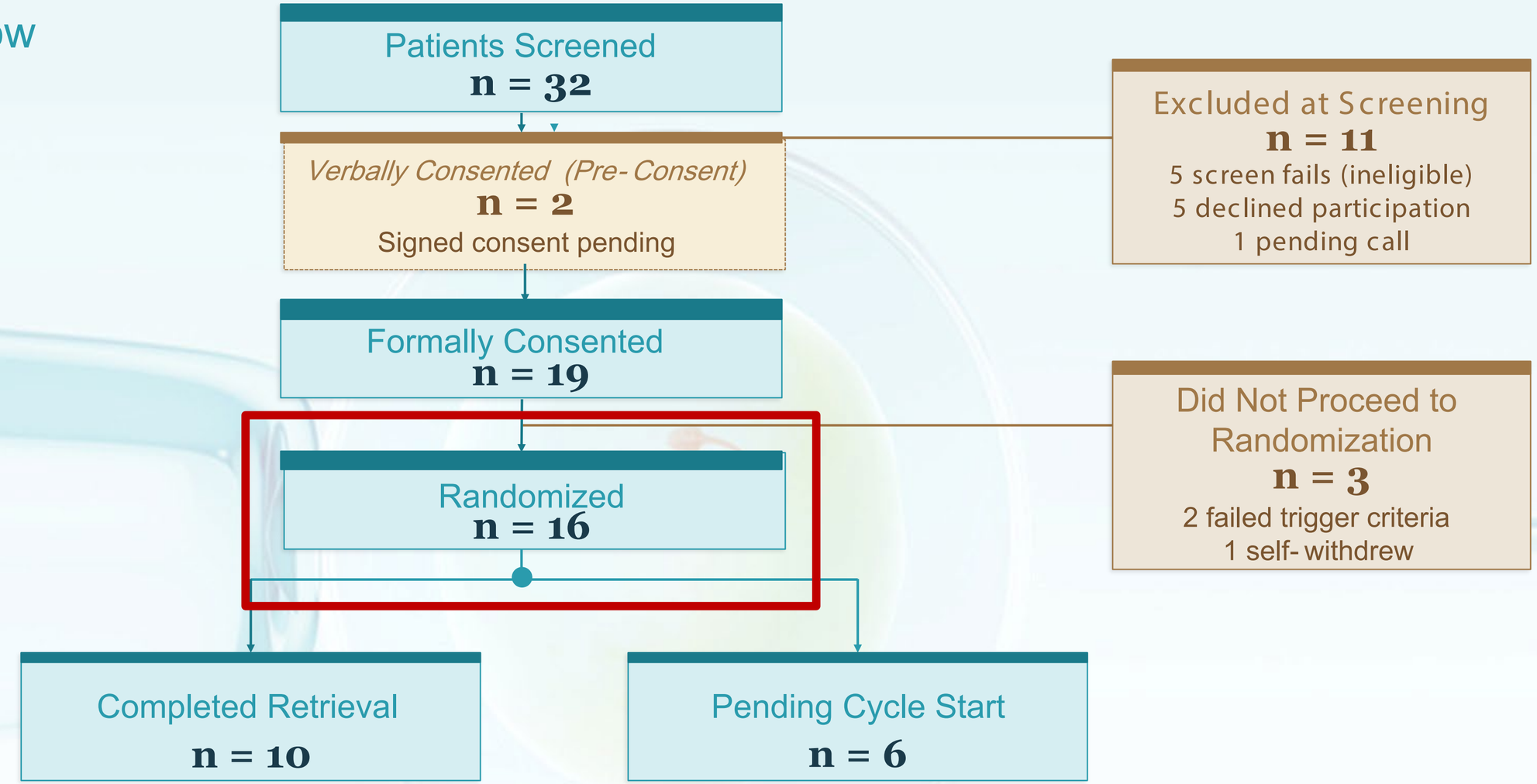
Study Progress and Feasibility: Enrollment Underway

CONSORT Flow



Study Progress and Feasibility: Enrollment Underway

CONSORT Flow



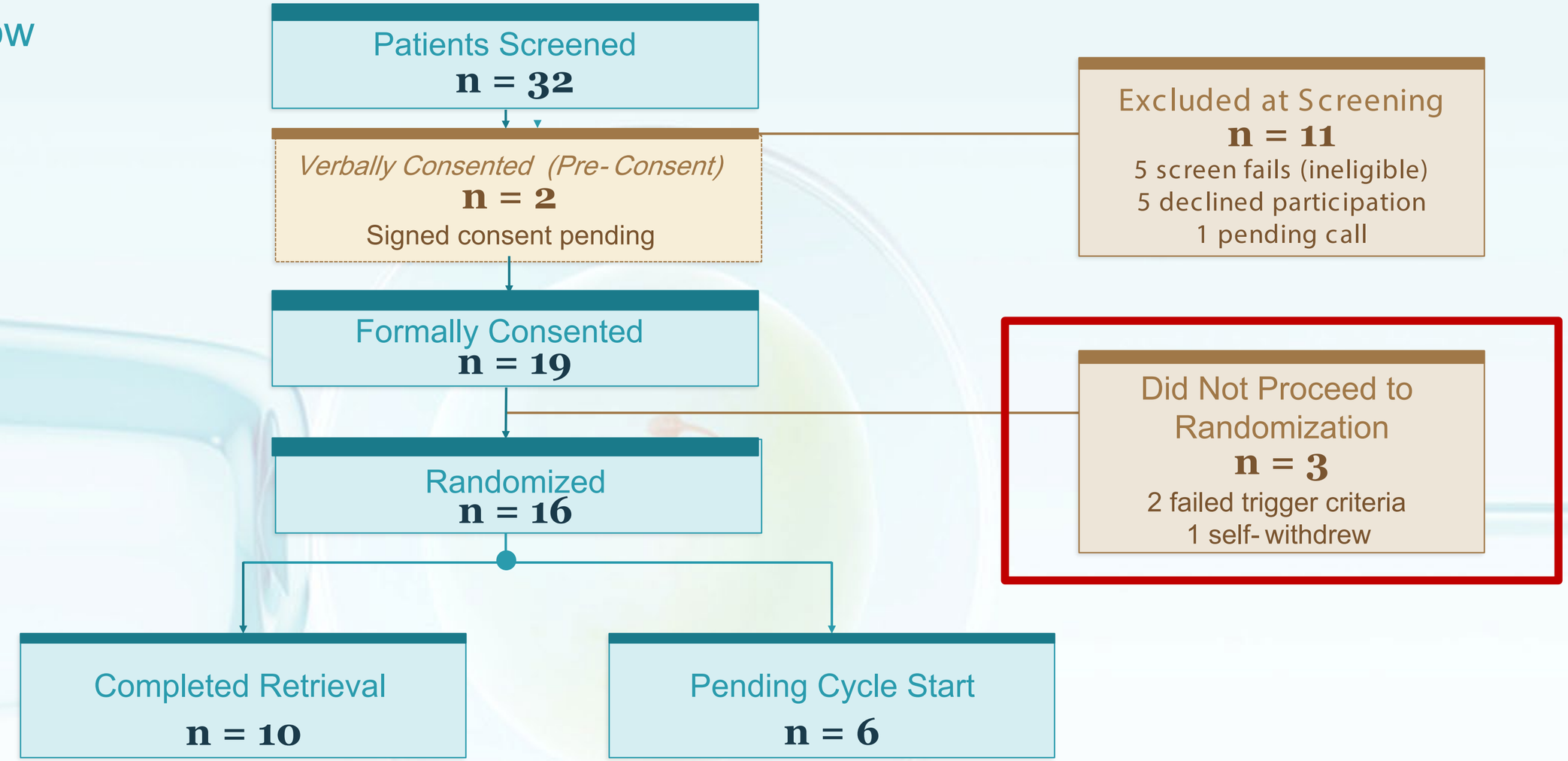
Enrolled / Progressing

Pre-Consent (Verbal)

Excluded / Withdrawn

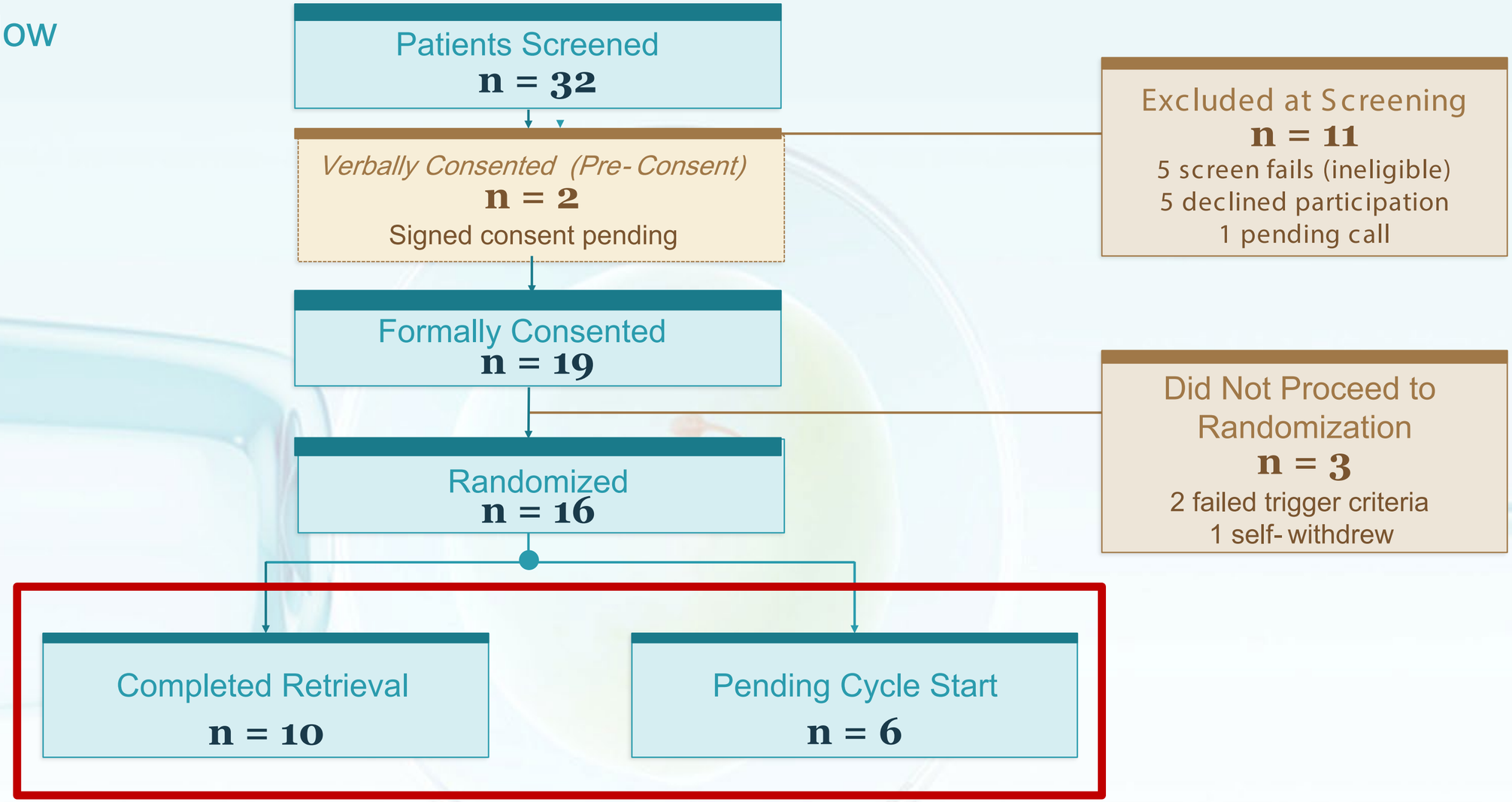
Study Progress and Feasibility: Enrollment Underway

CONSORT Flow

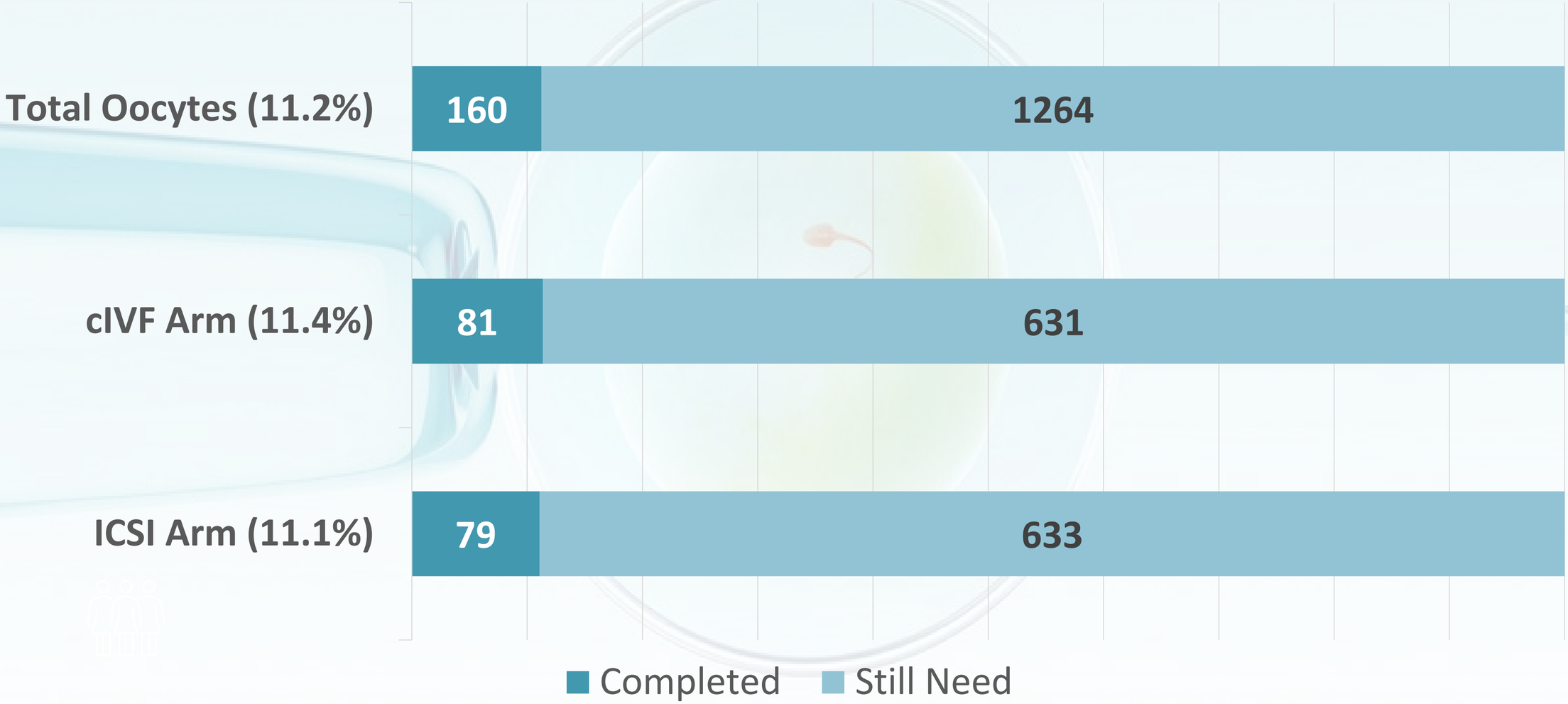


Study Progress and Feasibility: Enrollment Underway

CONSORT Flow



Progress Towards Power



Project Timeline

OCT 25- DEC 26	OCT 25 – DEC 26	DEC 25 – MAR 27	JAN 27- APR 27	APR 27-JUL 27
Patient recruitment & enrollment 8 pts/month	Oocyte retrieval, insemination, and embryo culture	Follow-up for early clinical pregnancy outcomes	Data cleaning and statistical analysis	Manuscript preparation and submission

Award Budget Overview

Laboratory Consumables $2000	• ICSI micropipettes • Culture dishes and media • Embryo handling supplies
Statistical Analysis $1200	• Statistical Software License
Participant Recruitment & Coordination $6800	• Recruitment outreach to clinical teams • Study advertising materials

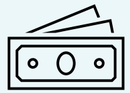
Potential Impact on IVF Practice and Cost

… And, if ICSI is unnecessary in these cases, we can:

Addressing a critical gap in ART

Reduce unnecessary ICSI usage (~$1,500–$2,000 per cycle)

Minimize risks associated with micromanipulation



Improve cost-effectiveness of ART treatments and potentially outcomes

Thank you to the mentors and support for this project

- Dr. Phillip Romanski
- Dr. Kate Devine
- Dr. Micah Hill
- SGF Research Team
- SGF Embryology –CO, Rockville, WR
- Dr. Kerry Flannagan
- Dr. Jing Wu

Supplementary Slides

Semen Parameters

Post-wash progressive motility ⩾50%
Concentration ⩾5 million

Rationale

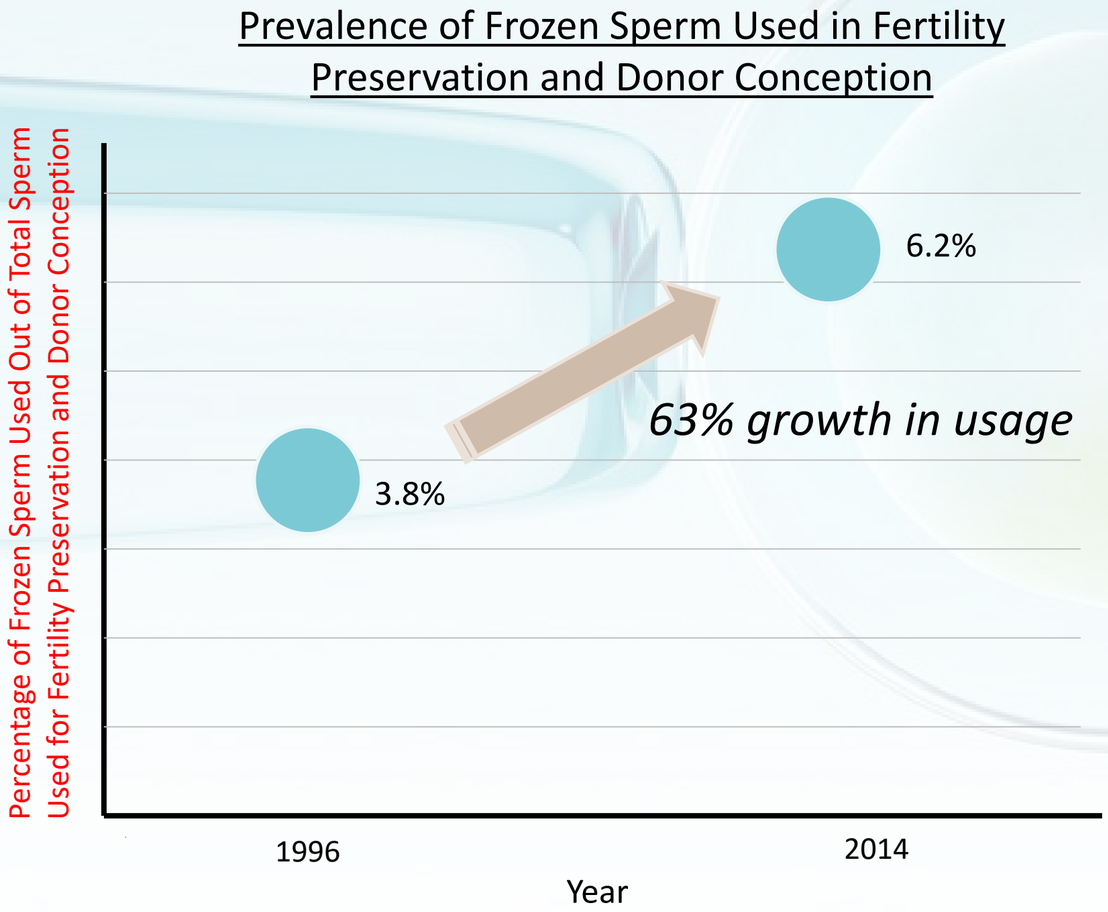
- Ensures adequate sperm availability for physiologic fertilization
- Aligns with standard embryology lab thresholds for conventional IVF
- Below thresholds → convert to ICSI to minimize fertilization failure

Supporting Evidence

- RCT data support use of conventional IVF when ⩾2 million progressively motile sperm are available post-preparation
- Treatment allocation frameworks suggest IVF is appropriate when total motile sperm counts and motility are within normal ranges
- Studies of frozen-thawed sperm demonstrate preserved fertilization and live birth rates with conventional IVF despite modest reductions in motility

(Xie et al., 2024; Torra-Massana et al., 2023; Sciorio & Fleming, 2024; Berntsen et al., 2025)

Background & Rationale



Frozen sperm use is increasing for fertility preservation and donor conception

Better cryopreservation, increasing donor by choice households, increasing frozen sperm for non- medical reasons

Sources: Gerkowicz et al., 2018; Wang et al., 2023; Paffoni et al., 2024; Patel et

Budget Category	Description	Total Cost
Consumables for ICSI	Micromanipulator pipettes, microinjection dishes, ICSI-specific culture media for 2 oocytes per patient	$2,850
Consumables for Conventional	Standard culture dishes, insemination media for 2 oocytes per patient	$713
Embryologist Labor	Time for ICSI (~10 min/oocyte) and conventional insemination (~3 min/oocyte) for 4 oocytes per patient	$2090
Statistical Software	Software license for advanced data analysis (e.g., SPSS or SAS)	$1,200
Personnel Training	Training for lab personnel on protocol standardization for randomization and culturing	$1,000
Quality Control Materials	Specialized materials for embryo tracking, labeling, and monitoring to ensure trial integrity	$2,000
Participant Recruitment & Coordination	Recruitment outreach to clinical teams Study advertising materials	$6800

- clinic engagement
- recruitment outreach
- provider/nurse education
- study awareness materials
- light refreshments for recruitment meetings