

# A Retrospective Review of IUI Clinical Outcomes following Semen Collection in the ProteX™ versus a Standard Specimen Cup

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**OBJECTIVE:** While intrauterine insemination (IUI) using freshly ejaculated, prepared semen combined with ovarian stimulation of the female partner remains a first-line treatment for infertility, it has a relatively low success rate (approximately 15% per cycle). An obvious rate-limiting step in the success of the process is the quality of the male partner's semen. Traditionally, clinics have used a standard specimen cup (SSC) for specimen collection, a cup designed for 25-150 mL of urine, not the 2-5 mL of a standard semen sample. The objective of the present study was to compare a new sperm collection device (NSCD — ProteX), explicitly designed to maximize available sperm by providing a collection environment that supports sperm function, to the SSC

**DESIGN:** Retrospective study of IUI cycles in which a NSCD was compared with those using the SSC.

**MATERIALS AND METHODS:** Retrospective data from 338 patients undergoing IUI for six months after the clinic switched semen collection device to the NSCD were compared to the previous six-month period using the SSC. All samples were treated using standard lab procedures post-collection. Data collected included male and female partner's age, female partner's method of ovarian stimulation, initial and post-processing semen parameters, including volume, concentration, motility, and total motile count.

**RESULT:** Female partners ranged in age from 21-48, with means of 34.8 vs. 35.4 (SSC vs. NSCD, respectively). In contrast, there were differences between the groups for method of ovarian stimulation. However, the majority of patients in each group were treated with Clomid or Letrozole (> 80%). Males' ages were similar (36.7 vs. 36.8). However, men collecting in the NSCD had higher volumes (2.2 vs. 2.5 mL; P < 0.008), motile cells (48.3 vs 53.0 mil; p < 0.001) and total motile counts (73.0 vs 91.3; P < 0.005). While both groups had initial pregnancy rates of 12%, 90% of the pregnancies resulting from sperm collected in the NSCD continued to heartbeat versus 70% in the SSC (P < 0.02).

**DISCUSSION:** This retrospective study suggests that ongoing pregnancy rates may be improved by producing semen samples in a more physiologic collection container with a measured amount of culture media (NSCD), that is designed to provide healthier cells for reproductive procedures. These findings agree with earlier animal studies.

**DISCLOSURES:** S.D. Prien is the inventor and serves as scientific consultant to Reproductive Solutions.

**FUNDING:** ProteX were provided by Reproductive Solutions.

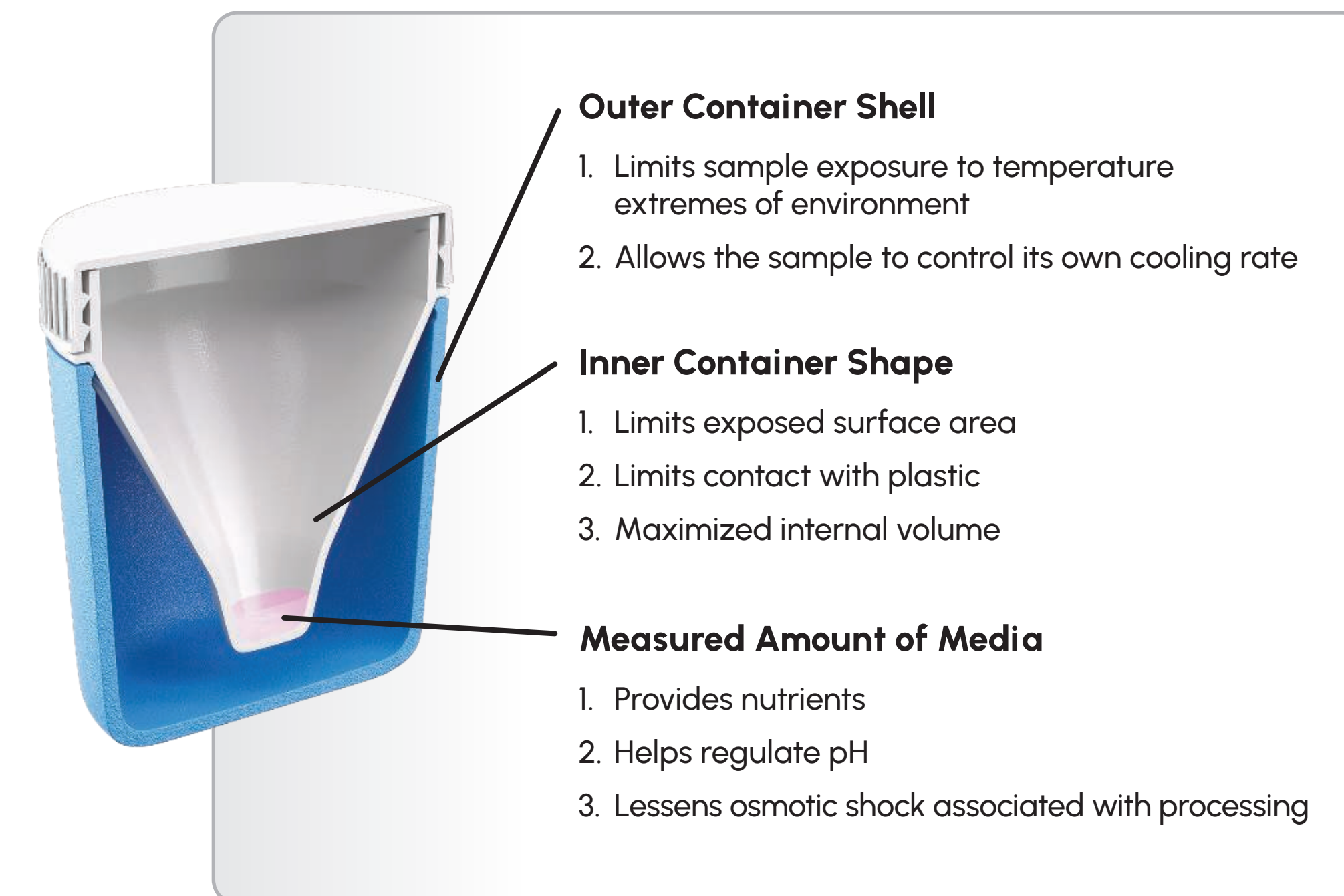
## INTRODUCTION

It is well established that one-in-eight couples desiring children will suffer some form of infertility. While assisted reproductive technologies (ARTs) are considered the "gold standard" for infertility treatment, intrauterine insemination IUI is still commonly used as the initial treatment in most clinics. While IUI success rates have remained relatively constant over the last 40 years (reported in the literature as between 12-16%), it remains a popular option with the patient due to the low expense compared to ARTs.

IUI requires the collection and processing of semen samples with the goal of producing the largest pool of spermatozoa possible at the time of insemination. While some improvements have been made in the sperm wash media, the basic technique has remained unchanged for several decades. This includes the sample being produced into a standard specimen cup (SSC) designed to collect 50-100 milliliters of urine.

Intrinsically, it is evident that the collection of a sample into an SSC presents an environment unlike the introduction of sperm into the vagina. While the SSC does produce samples that result in pregnancy, it is far from an ideal collection device for semen. The ProteX collection device was specifically designed for the collection of human semen samples and the preservation of healthier spermatozoa. The device (Figure 1) was designed to minimize the shock to sperm at collection. The cup design 1) maximizes the volume into the smallest exposed surface area, allowing the sample to maintain its own temperature for more extended periods of time, 2) insulates the cup from extremes in environmental temperature and slowing the cooling curve to about a third of a degree per minute, 3) provides a measured amount of media which helps to stabilize pH, provide nutrients and regulated early osmoregulation. Numerous previous laboratory and animal-based studies demonstrate the design supports better sperm health as demonstrated by improved semen parameters and increased pregnancy rates (animal studies only). A small FDA approved trial proved the equivalence of the device with the SSC and designation as an FDA class I/class II device, allowing entrance into the marketplace. The present study represents a review and comparison of the ProteX to the SSC when used for semen collection.

**FIGURE 1.** Design and concept of the ProteX device.



**TABLE 1.** Demographic data and semen parameters from the review of 695 cycles using the ProteX (n=338) or Standard Specimen Cup (SSC; n=357) for semen collection and use in IUI. Data with a P value of < 0.05 are considered statistically different.

|   | ProteX<br>n=338 | STD (+/-) | SSC<br>n=357 | STD (+/-) | P value |
|---|-----------------|-----------|--------------|-----------|---------|
| Age   | 37.6            | 5.6       | 37.8         | 5.7       | 0.618   |
| Days of Abstinence                          | 2.4             | 2.1       | 2.1          | 1.6       | 0.051   |
| Time from collection to arrive in lab - min | 37.6            | 42.9      | 33.8         | 24.0      | 0.152   |
| Time from Arrival to start of process - min | 8.4             | 10.0      | 9.3          | 6.8       | 0.183   |
| Processing time                             | 28.2            | 9.7       | 27.0         | 8.9       | 0.104   |
| Total Elapsed timer - min                   | 72.7            | 48.4      | 70.0         | 25.7      | 0.328   |
| Initial Volume - mL                         | 2.5             | 1.4       | 2.2          | 1.2       | 0.008   |
| Initial Concentration mil/mL                | 75.3            | 68.1      | 68.8         | 2.6       | 0.162   |
| Initial Motility (%)                        | 53.0            | 13.5      | 48.3         | 14.9      | 0.001   |
| Initial Total Motile mil                    | 91.3            | 94.1      | 73.0         | 77.0      | 0.005   |
| Final Volume - mL                           | 0.5             | 0.8       | 0.5          | 0.2       | 0.280   |
| Final Concentration mil/mL                  | 88.4            | 73.6      | 92.3         | 80.0      | 0.525   |
| Final Motility (%)                          | 57.4            | 31.8      | 53.7         | 20.3      | 0.069   |
| Final Total Motile mil                      | 25.0            | 22.0      | 25.0         | 24.4      | 0.871   |

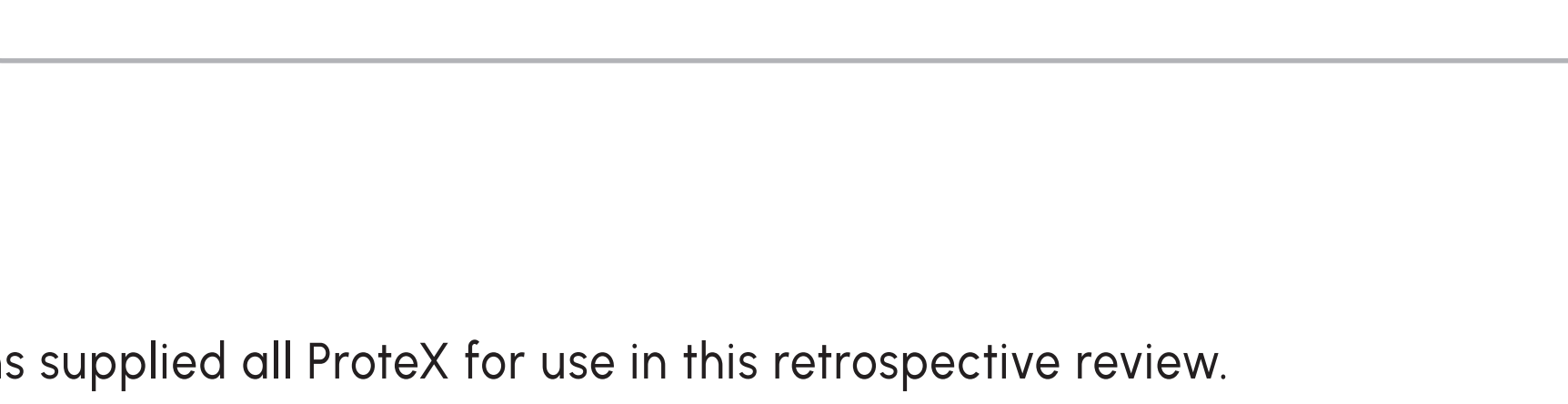
**TABLE 2.** Demographic data and stimulation Protocols of 695 women receiving semen collected in either a ProteX (n=338) or Standard Specimen Cup (SSC; n=357) for use in IUI. Data with a P value of < 0.05 are considered statistically different.

|                         | ProteX<br>n=338 | STD (+/-) | SSC<br>n=357 | STD (+/-) | P value |
|-------------------------|-----------------|-----------|--------------|-----------|---------|
| Age                     | 35.5            | 5.6       | 34.8         | 5.7       | 0.078   |
| Ovarian Stimulation (%) |                 |           |              |           | 0.008   |
| Natural Cycle           | 8.9             |           | 5.0          |           |         |
| Clomid                  | 29.0            |           | 38.4         |           |         |
| Letrozole               | 54.1            |           | 49.0         |           |         |
| COH                     | 4.7             |           | 6.4          |           |         |
| Tamoxifen               | 3.3             |           | 1.1          |           |         |

**TABLE 3.** Early outcome of IUI treatment cycles of 695 IUI cycles using either a ProteX (n=338) or Standard Specimen Cup (SSC; n=357) for semen collection. Data with a P value of < 0.05 are considered statistically different.

|               | ProteX<br>n=338 | SSC<br>n=357 | P value |
|---------------|-----------------|--------------|---------|
| Positive Beta | 40              | 43           | 0.235   |
| Sac           | 36              | 32           | 0.07    |
| Heartbeat     | 36              | 30           | 0.02    |

**FIGURE 2.** Early Pregnancy outcome of an IUI study comparing the ProteX to the standard specimen cup for semen (SSC) collection. Columns within an event (pregnancy test, sac development, heartbeat) with different superscripts are different at the P < 0.02 level.



## MATERIALS & METHODS

- The ProteX was incorporated into the clinic's IUI program in June 2021, using the device with the recommended inclusion of a measured amount of the lab's standard sperm wash media.
- These data were to be compared to those patients undergoing IUI during the previous six month.
- Due to the Pandemic, patients could collect in the clinical facility or at home. However, the collection location was not available for this study.
- Limited demographic data were collected for both the male and female partner.
- The semen sample was prepared for IUI using standard laboratory procedures.
- Data were collected on pre-and post-preparation semen parameters, including volume, concentration/mL, % motility, and total motile counts (millions).
- Pregnancy data collected included; initial pregnancy tests, sac development pregnancies, and pregnancy reaching heartbeat.

## RESULTS

- Data from a total of 695 cycles, 338 ProteX and 357 Standard Specimen Cup collections, were reviewed.
- As stated above, patients were given the option of collecting in the clinic or at home. While data on location was not given, the average time between the collection and start of processing was similar in both groups (TABLE 1; P = 0.183), suggesting equivalent numbers in both groups collected in both locations.
- TABLE 1 provides the demographic data from the male patients. These data were similar between both groups (P = 0.681).
- TABLE 2 provides the demographic and the data for the female patients. It was noted this was an older population with a mean age of 35.3 years. There was also a trend toward the women treated with the ProteX collected sperm to be older (P = 0.078) than those collected treated with sperm collected in the SSC.
- There were differences in the stimulation regimens of the women in the study (P < .008), with more women in the SSC group receiving Clomid and more women in the ProteX going through natural cycles.
- Samples collected in the ProteX demonstrated higher initial volumes (P < 0.008), motilities (P < 0.001) and total motile cells (P < 0.005) compared to the SSC.
- There were a total of 83 positive pregnancy tests recorded in the study population (TABLE 3), 43 in the SSC (12.0%) and 40 in the ProteX (11.8%).
- While these initial pregnancy tests were similar in both groups (P = 0.235), there was a trend (P = 0.078) toward more patients reaching sac development and a higher number of patients reaching heartbeat (P < 0.02) when using the ProteX as the collection device (FIGURE 2).

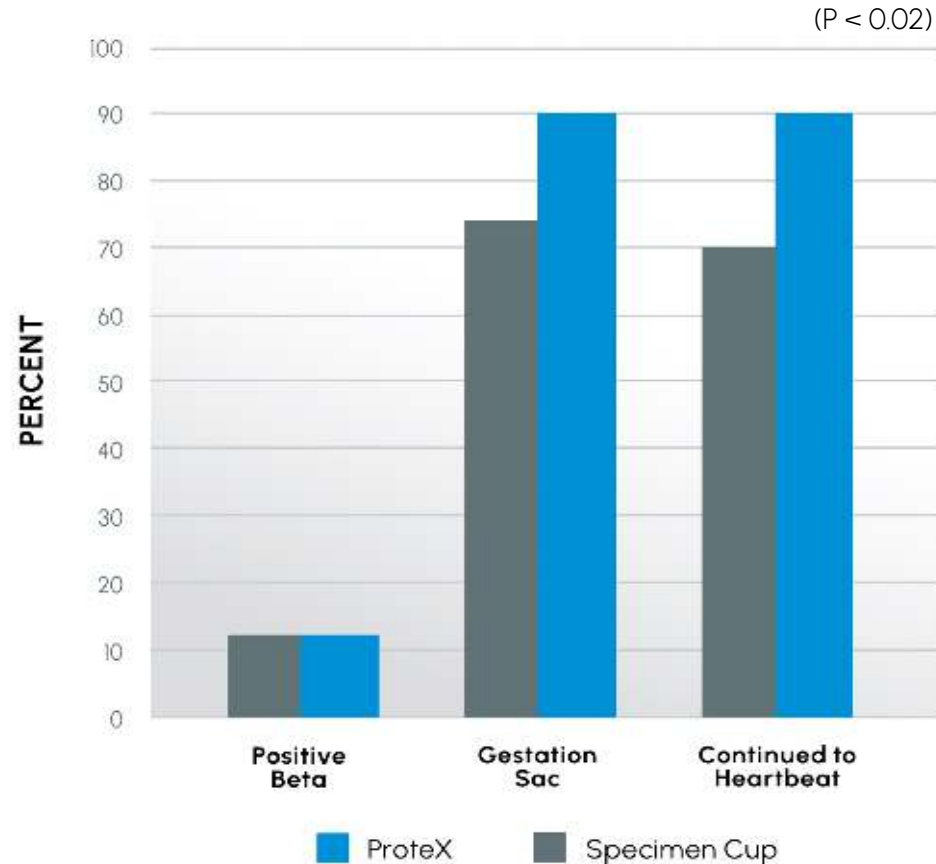
## DISCUSSION

- Data from this study involving almost 700 patients supports earlier small-scale studies.
- Semen quality from samples collected in the ProteX demonstrated better initial parameters than those collected in the SSC.
- It is unclear why the large difference in initial volumes. However, it is possible it is the patients in the ProteX group were less stressed concerning transport times and produced better samples.
- As in an earlier smaller trial, initial pregnancy data suggest more pregnancies continue on to heartbeat when the ProteX is used in the collection.
- Collectively these data suggest sperm collected in the ProteX may be in better physiological and biochemical condition than those collected in the SSC. This suggests healthier sperm may result in healthier pregnancies, and if all pregnancies in this trial reach delivery, a 20% higher take-home baby rate in this study.
- Even with the large number of couples participating, the 83 pregnancies are still a relatively low number, and further study will be needed to confirm these results.

**ACKNOWLEDGMENTS** Reproductive Solutions supplied all ProteX for use in this retrospective review.

# IUI clinical trial data views

Up to **29% increase in pregnancies reaching heartbeat** with couples using ProteX. (P < 0.02)



|   | ProteX      | STD         | SSC         | STD         | P value      |
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| <b>Initial Motility (%)</b>                 | <b>53.0</b> | <b>13.5</b> | <b>48.3</b> | <b>14.9</b> | <b>0.001</b> |
| <b>Initial Total Motile mil</b>             | <b>91.3</b> | <b>94.1</b> | <b>73.0</b> | <b>77.0</b> | <b>0.005</b> |
| Final Volume - mL                           | 0.5         | 0.8         | 0.5         | 0.2         | 0.280        |
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Source: S.D Prien<sup>1</sup>, Z. Williams<sup>2</sup>, E. Forman<sup>2</sup>. (2022). A Retrospective Review of IUI Clinical Outcomes following Semen Collection in the ProteX™ versus a Standard Specimen Cup. American Association of Bioanalysts — poster session. <sup>1</sup>Reproductive Solutions, Dallas, TX. <sup>2</sup>Columbia Center for Fertility, Columbia University, NY.

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