

Assisted reproductive technology cycles involving male factor infertility in the United States, 2017–2018: data from the National Assisted Reproductive Technology Surveillance System

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Objective: To describe the prevalence and treatment characteristics of assisted reproductive technology (ART) cycles involving specific male factor infertility diagnoses in the United States.

Design: Cross-sectional analysis of ART cycles in the National ART Surveillance System (NASS).

Setting: Clinics that reported patient ART cycles performed in 2017 and 2018.

Patient(s): Patients who visited an ART clinic and the cycles were reported in the NASS. The ART cycles included all autologous and donor cycles that used fresh or frozen embryos.

Intervention(s): Not applicable.

Main Outcome Measures: Analyses used new, detailed reporting of male factor infertility subcategories, treatment characteristics, and male partner demographics available in the NASS.

Result(s): Among 399,573 cycles started with intent to transfer an embryo, 30.4% ($n = 121,287$) included a male factor infertility diagnosis as a reason for using ART. Of these, male factor only was reported in 16.5% of cycles, and both male and female factors were reported in 13.9% of cycles; 21.8% of male factor cycles had >1 male factor. Abnormal sperm parameters were the most commonly reported diagnoses (79.7%), followed by medical condition (5.3%) and genetic or chromosomal abnormalities (1.0%).

Males aged ≤ 40 years comprised 59.6% of cycles with male factor infertility. Intracytoplasmic sperm injection was the primary method of fertilization (81.7%). Preimplantation genetic testing was used in 26.8%, and single embryo transfer was used in 66.8% of cycles with male factor infertility diagnosis.

Conclusion(s): Male factor infertility is a substantial contributor to infertility treatments in the United States. Continued assessment of the prevalence and characteristics of ART cycles with male factor infertility may inform treatment options and improve ART outcomes. Future studies are necessary to further evaluate male factor infertility. (Fertil Steril Rep® 2022;3:124–30. ©2022 by American Society for Reproductive Medicine.)

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Approximately 50 million couples worldwide have infertility (1–3)—“a disease of the reproductive system defined by the failure to achieve a clinical pregnancy after 12 months or more of regular unprotected sexual intercourse” (4). While research and surveillance efforts have focused mainly on female factor infertility, male factor infertility also contributes substantially to couples’ ability to have children (2). Male factor infertility is defined as “infertility caused primarily by male factors encompassing: abnormal semen parameters or function; anatomical, endocrine, genetic, functional or immunological abnormalities of the reproductive system; chronic illness; and sexual conditions incompatible with the ability to deposit semen in the vagina” (5). The assessment of semen parameters, including sperm concentration, progressive motility, and morphology, is an important part of the diagnostic workup for investigating male fertility status (6).

According to the US National Survey of Family Growth, 9.4% of men (estimated to be approximately 3.8 million men, regardless of marital, cohabitation, or relationship status) aged 25–44 years between 2006 and 2010 reported using a fertility service (7). Despite the large number of males affected by infertility and seeking treatment, there are few published estimates of the prevalence of male factor infertility diagnoses within the United States. Large-scale studies are ultimately needed to identify the specific diagnoses of male factor infertility, beyond semen quality (8).

While there is little information on the prevalence of male factor infertility in the general population, the prevalence of male factor infertility among patients and couples undergoing assisted reproductive technology (ART) treatments is monitored annually. In 1992, the US Congress passed the Fertility Clinic Success Rate and Certification Act. This law requires all fertility clinics in the United States to report detailed information on all ART cycles to the Centers for Disease Control and Prevention (CDC) and for the CDC to publish standardized pregnancy success rates for all fertility clinics in the United States (9). Since 1995, the CDC has reported ART success rates annually on the basis of the latest available data on the type, number, and outcome of ART cycles performed in the US clinics through the National ART Surveillance System (NASS). For more than 2 decades, the data collection tool included up to 8 different female diagnoses that could be selected for each cycle. However, male factor infertility was collected as a single variable to indicate whether male factor infertility was present or absent. Beginning in 2016, the NASS expanded data collection for ART cycles to capture additional information on the type of male factor infertility and male date of birth. The objective of this cross-sectional study was to analyze these data from the NASS to obtain the prevalence of and characterize the

subcategories of male factor infertility cycles performed during 2017 and 2018.

MATERIALS AND METHODS

Data Source

Since 2011, at least 97% of all ART cycles in the United States were reported by ART clinics to the CDC’s NASS annually, including patient demographics, medical history, diagnosis, clinical parameters, and outcomes (10, 11). Until 2016, clinics reported male factor infertility as a reason for using ART in the NASS as a simple dichotomous “yes/no” variable. Beginning in 2016, male factor infertility has been reported in 4 subcategories: medical condition; genetic or chromosomal abnormality; abnormal sperm parameters; and other male factor. More than 1 diagnosis or reason for using ART can be reported for each cycle. Abnormal semen parameters was defined as any reporting of the following: obstructive azoospermia, the complete absence of sperm from the ejaculate that may result from epididymal, vasal, or ejaculatory duct pathology; nonobstructive azoospermia, the complete absence of sperm in the ejaculate due to testicular failure, varicoceles, or chromosomal abnormalities such as Y-chromosome microdeletions or karyotypic abnormalities (e.g., Klinefelter syndrome); moderate oligozoospermia, semen with a low concentration of sperm, defined as between 5 and 15 million spermatozoa per mL; severe oligozoospermia, defined as <5 million spermatozoa per mL; low sperm motility, defined as less than the laboratory norm, typically <40%; or low sperm morphology, defined as less than the laboratory norm, typically <4%.

The 2016 male factor cycle data were excluded from analysis because of inconsistent data reporting in the first reporting year. Typically, clinics require a transition period from the notification of change in how they are to collect data to implement changes to the recording of cycles. We used SPSS version 27 to examine the 2017 and 2018 data for the prevalence of differing male factor infertility diagnoses stratified by patient and treatment characteristics. The results presented are a percentage of known data. Characteristics that were missing data (>5%) were male age (13.4%), male race/ethnicity (37.0%), sperm source (61.2%), sperm status (67.9%), and intracytoplasmic sperm injection (ICSI) (10.6%). Although sperm source and status had substantial missingness, we included them in the results because both are important factors in male factor infertility.

Study Population

The patient characteristics included male age, male race/ethnicity (non-Hispanic White, non-Hispanic Black, Hispanic, non-Hispanic Asian, and other race), sperm source (partner, donor, patient, or mixed), sperm status (fresh, frozen, or

mixed), female age, and concurrent female diagnosis (tubal factor, ovulation disorder, diminished ovarian reserve, endometriosis, uterine factor, other factor, unexplained factor, and no female diagnosis). Other race includes non-Hispanic multirace, non-Hispanic Native Hawaiian, non-Hispanic Pacific Islander, non-Hispanic American Indian, and non-Hispanic Alaska Native. The individuals providing sperm for the cycle (sperm source) were grouped into 4 categories and defined as follows: “partner” is when the female patient’s male partner serves as the source of sperm; “donor” is when the female patient or couple uses donor sperm; “patient” is when the male is the primary patient and uses donor eggs or embryos with a gestational carrier; and “mixed” could be any combination of partner, donor, and/or patient as a sperm source. The treatment characteristics included ICSI, preimplantation genetic testing (PGT), and single embryo transfer (SET). This study was approved by the Institutional Review Board at the CDC.

RESULTS

In 2017–2018, among 399,573 cycles with the intent to transfer an embryo reported in the NASS, 121,287 (30.4%) reported male factor infertility as a reason for ART. Of these, “male factor only” was reported in 16.5% of cycles, and both male and female factors were reported in an additional 13.9% of cycles. Among cycles with a male factor infertility diagnosis, 21.8% had >1 male factor. Abnormal sperm parameters (79.7%) were the most commonly reported male factor infertility diagnoses, followed by medical condition (5.3%) and genetic or chromosomal abnormalities (1.0%); other male factor was reported in 17.6% of cycles with male factor infertility (Fig. 1). Abnormal sperm parameters were further divided into subcategories: azoospermia (11.1%); oligospermia (37.5%); low motility (30.8%); and low morphology (41.4%). Among the cycles with a low morphology diagnosis, 83.3% had >1 male factor infertility diagnosis.

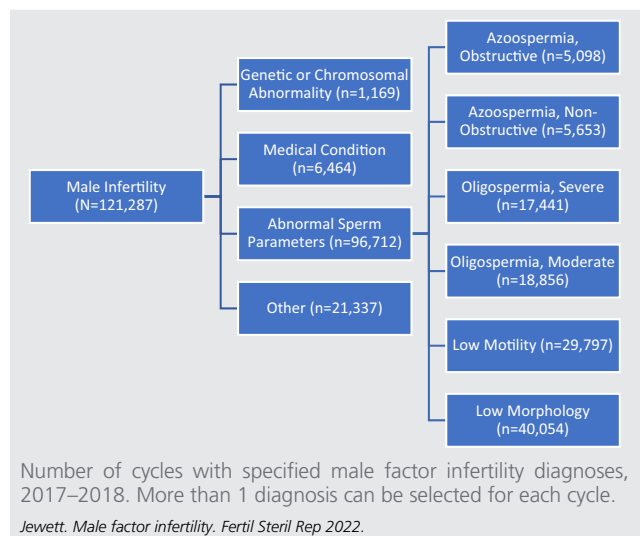
Age and Race/Ethnicity

The age distribution among males with male factor infertility was as follows: 33.0% for the age of <35 years; 36.8% for the age of 35–40 years; 24.7% for the age of 41–50 years; and 5.5% for the age of >50 years. Males aged ≤40 years accounted for most male factor infertility cycles across every subcategory of male factor infertility diagnosis (range, 61.9%–85.0%), except for obstructive azoospermia in which 56.7% were ≥41 years of age (Table 1). Non-Hispanic White males were most often represented in all male factor subcategories (range, 67.0%–82.3%).

Sperm Source and Status

For cycles with a male factor and known sperm source, 93.6% used partner sperm, 5.7% used donor sperm, and <1% used male patient or mixed sperm. Donor sperm were used in 36.5% of cycles with a nonobstructive azoospermia and 37.1% of cycles that had a genetic or chromosomal abnormality. All other male factor diagnoses mostly used partner sperm: medical condition (89.7%); obstructive azoospermia (92.0%); severe oligospermia (95.7%); moderate oligospermia

FIGURE 1



(98.5%); low motility (97.8%); low morphology (98.6%); and other male factor (84.2%).

For male factor infertility cycles with a known sperm status, fresh sperm were used in 81.2% of cycles, frozen sperm were used in 18.1%, and <1% was mixed. Most cycles that had a medical condition (58.8%), severe oligospermia (84.1%), moderate oligospermia (94.0%), low motility (90.5%), low morphology (94.3%), and other male factor (65.6%) used fresh sperm. Frozen sperm were used most often in cycles with a genetic or chromosomal abnormality (70.8%), obstructive azoospermia (69.7%), and nonobstructive azoospermia (74.7%).

Female Partners

Approximately half (48.3%) of cycles with male factor infertility had female partners aged <35 years, and 12.0% had female partners aged >40 years (Table 1). The ART cycles with male factor infertility related to genetic or chromosomal abnormality had the highest percentage of female partners aged <35 years (61.0%). Among the 121,287 cycles with male factor infertility, 55,528 (45.8%) also had at least 1 female diagnosis. Diminished ovarian reserve was the most commonly reported female diagnosis associated with male factor infertility subcategories: medical condition (22.8%); genetic or chromosomal abnormality (13.5%); obstructive azoospermia (18.2%); nonobstructive azoospermia (15.1%); severe oligospermia (17.7%); moderate oligospermia (20.2%); low motility (21.9%); low morphology (23.8%); and other (23.6%).

ART Treatment

Intracytoplasmic sperm injection was the primary method of fertilization in cycles with a male factor infertility diagnosis (82.7%) and within all male factor subcategories: abnormal sperm parameters (84.0%); medical condition (78.8%); genetic or chromosomal abnormality (76.6%); and other male factor (72.7%) (Table 1).

TABLE 1

Characteristics, diagnoses, and treatment among ART users with male factor infertility, National ART Surveillance System 2017–2018, United States^a.

Characteristics	Medical condition	Genetic/ chromosomal abnormality	Azoospermia, obstructive	Azoospermia, nonobstructive	Abnormal sperm parameters					
					Oligospermia, severe ($< 5 \times 10^6$)	Oligospermia, moderate (5×10^6 – 15×10^6)	Low motility ($< 40\%$)	Low morphology ($< 4\%$)	Other	
Number of cycles with male infertility diagnosis, N = 121,287	n = 6,464	n = 1,169	n = 5,098	n = 5,653	n = 17,441	n = 18,856	n = 29,797	n = 40,054	n = 21,337	
Male demographics of ART users with a male factor infertility diagnosis										
Age of male partner or male patient ^b	<35	31.4%	44.5%	17.1%	36.1%	37.2%	34.9%	32.3%	35.7%	25.7%
	35–40	38.3%	40.6%	26.2%	34.3%	35.2%	37.9%	37.5%	38.0%	36.2%
	41–50	25.3%	13.2%	40.3%	24.1%	22.1%	23.0%	24.5%	22.7%	30.0%
	>50	5.1%	1.8%	16.4%	5.5%	5.5%	4.2%	5.7%	3.6%	8.1%
Male race/ethnicity ^c	Non-Hispanic White	74.3%	82.3%	78.2%	71.5%	70.4%	72.5%	69.5%	70.9%	67.0%
	Non-Hispanic Black	6.4%	3.5%	7.8%	8.9%	10.3%	8.1%	8.5%	7.9%	7.5%
	Non-Hispanic Asian	12.3%	9.2%	5.6%	11.4%	9.8%	10.2%	12.8%	12.8%	16.5%
	Hispanic	6.4%	4.2%	7.6%	7.4%	8.3%	8.1%	8.3%	7.5%	7.6%
	Other race	0.5%	0.8%	0.7%	0.8%	1.2%	1.0%	0.9%	1.0%	1.5%
Male factor infertility diagnosis and sperm characteristics										
Sperm source ^d	Partner	89.7%	61.2%	92.0%	61.9%	95.7%	98.5%	97.8%	98.6%	84.2%
	Donor	9.6%	37.1%	7.5%	36.5%	3.7%	1.3%	1.8%	1.2%	15.4%
	Patient	0.7%	1.7%	0.4%	1.6%	0.6%	0.2%	0.4%	0.2%	0.4%
	Mixed	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Sperm status ^e	Fresh	58.8%	28.8%	30.1%	24.0%	84.1%	94.0%	90.5%	94.3%	65.6%
	Frozen	40.8%	70.8%	69.7%	74.7%	14.5%	5.5%	8.9%	5.1%	33.8%
	Mixed	0.5%	0.3%	0.2%	1.3%	1.4%	0.5%	0.6%	0.5%	0.6%
Male factor infertility diagnosis and female patient age group and female factor infertility										
Female patient/partner age	<35	47.2%	61.0%	46.5%	53.2%	53.6%	49.9%	48.2%	48.5%	40.8%
	35–37	23.1%	21.8%	23.3%	22.4%	22.3%	23.9%	23.5%	23.3%	23.4%
	38–40	17.2%	11.1%	17.4%	15.4%	14.5%	15.1%	16.2%	16.7%	18.4%
	41–42	6.9%	3.5%	7.0%	4.6%	5.5%	6.0%	6.3%	6.1%	7.6%
	>42	5.6%	2.1%	5.8%	4.3%	4.1%	4.9%	5.5%	5.3%	8.0%
	No female partner	0.2%	0.5%	0.0	0.1%	0.1%	0.1%	0.3%	0.1%	1.8%
Female infertility diagnosis ^f	Tubal factor	5.9%	3.7%	4.0%	3.7%	5.3%	8.8%	8.2%	11.2%	6.4%
	Ovulation disorder	11.5%	12.0%	8.0%	10.4%	13.4%	15.6%	16.3%	19.4%	10.8%
	Dim ovarian reserve	22.8%	13.5%	18.2%	15.1%	17.7%	20.2%	21.9%	23.8%	23.6%
	Endometriosis	4.3%	2.7%	3.4%	3.9%	3.9%	5.9%	5.7%	7.2%	5.5%
	Uterine factor	5.9%	2.6%	4.5%	4.2%	4.9%	5.3%	6.9%	9.1%	5.3%

Jewett. Male factor infertility. Fertil Steril Rep 2022.

TABLE 1

Continued.

Characteristics	Abnormal sperm parameters									
	Medical condition	Genetic/ chromosomal abnormality	Azoospermia, obstructive	Azoospermia, nonobstructive	Oligospermia, severe ($< 5 \times 10^6$)	Oligospermia, moderate (5×10^6 – 15×10^6)	Low motility ($< 40\%$)	Low morphology ($< 4\%$)	Other	
Other related to fertility	25.7%	31.0%	23.8%	18.8%	18.7%	22.4%	25.2%	32.4%	40.7%	
Unexplained	0.0	0.1%	0.0	0.1%	0.1%	0.1%	0.2%	0.1%	0.2%	
No female factor	37.5%	46.5%	50.8%	52.6%	44.6%	32.9%	28.5%	13.6%	31.5%	
Percentage of male infertility cycles that were canceled, used ICSI, PGT, and number of embryos transferred										
Canceled cycles	—	2.7%	3.0%	3.6%	2.3%	2.8%	2.9%	2.9%	7.1%	
ICSI performed ^g	No	21.2%	23.4%	16.0%	23.8%	14.4%	15.0%	14.9%	27.3%	
	Yes	78.8%	76.6%	84.0%	76.2%	85.6%	85.0%	85.1%	72.7%	
PGT performed	No	69.3%	64.1%	76.2%	78.6%	78.9%	76.7%	75.9%	72.0%	
	Yes	30.7%	35.9%	23.8%	21.4%	21.1%	23.3%	24.1%	28.0%	
Number of embryos transferred	1 (SET)	71.9%	74.2%	65.1%	63.7%	63.6%	65.6%	64.3%	65.8%	
	2	24.2%	23.7%	31.3%	32.7%	32.9%	31.3%	32.2%	30.6%	
	3+	3.9%	2.1%	3.6%	3.6%	3.5%	3.1%	2.7%	3.6%	

Note: ART = assisted reproductive technology; Dim ovarian reserve = diminished ovarian reserve; ICSI = intracytoplasmic sperm injection; PGT = preimplantation genetic testing; SET = single embryo transfer.

^a Missing values were $< 5\%$ unless noted below; the percentages shown are a proportion of known data.

^b Age of male partner or male patient had 13.4% missing values.

^c Male race/ethnicity had 37.0% missing values. Other race includes non-Hispanic multirace, non-Hispanic Native Hawaiian, non-Hispanic Pacific Islander, non-Hispanic American Indian, and non-Hispanic Alaska Native.

^d Sperm source had 61.2% missing values.

^e Sperm status had 67.9% missing values.

^f More than 1 diagnosis can be selected for each cycle.

^g ICSI performed had 10.6% missing values.

Jewett. Male factor infertility. Fertil Steril Rep 2022.

Preimplantation genetic testing was used in 26.4% of cycles with a male factor infertility diagnosis and varied by subcategory: genetic or chromosomal abnormality (35.9%); medical condition (30.7%); abnormal sperm parameters (range, 21.1%–31.2%); and other male factor (28.0%).

Single embryo transfer was used in 66.8% of cycles with a male factor infertility diagnosis and varied by subcategory: genetic or chromosomal abnormality (74.2%); medical condition (71.9%); abnormal sperm parameters (66.6%); and other male factor (65.8%).

DISCUSSION

Among all patients and couples undergoing ART in the United States between 2017 and 2018, the overall prevalence of male factor infertility was 30.4%. Male factor infertility was the only listed reason for ART in 1 of every 6 cycles. For most cycles with male factor infertility, the male was reported as being aged ≤ 40 years, and abnormal sperm parameters were the most commonly reported in approximately 80% of cycles with a male factor infertility diagnosis.

Although the age of the female is a significant factor in infertility, increasing male age may impact semen parameters and, therefore, decrease the likelihood of pregnancy (8). In this study, most cycles with male factor infertility involved males aged ≤ 40 years. Our results indicate that almost half of male factor infertility cycles included at least 1 female diagnosis and approximately half of cycles with male factor infertility had female partners aged < 35 years.

Because a semen analysis, which measures sperm concentration, progressive motility, and morphology, is the basic and most often used strategy to assess male factor infertility, it follows that abnormal sperm parameters were the most commonly reported factors associated with male factor infertility (6). However, a semen analysis does not provide a comprehensive assessment of male factor infertility. Nearly 1 in 5 cycles reported “other male factor.” Approximately half of the “other male factor” cycles are missing an explanation in the NASS data; the other half have several different explanations that need to be explored in future analyses. The assessment of male factor infertility beyond abnormal sperm parameters will provide a better understanding of the causes of male factor infertility.

In this study, male race and ethnicity information was missing from more than one third (37.0%) of male factor infertility cycles. On the basis of the reported data, most patients who seek care from fertility clinics are non-Hispanic White people despite the evidence that people of color are disproportionately affected with adverse outcomes of infertility (12). Studies show that socioeconomic factors, lack of access, and delayed access likely contribute to people of color not receiving infertility services (12). Efforts are needed to improve reporting of race and ethnicity in the NASS surveillance data to better understand who is receiving infertility treatment, the reasons for treatment, and the outcomes of treatment.

The treatment parameters examined in this study were the use of PGT, ICSI, and SET in the context of male factor infertility. Preimplantation genetic testing was used in approximately one quarter of cycles with a male factor infertility

diagnosis and used more often in cycles in which the male partner reported a genetic or chromosomal abnormality. This higher rate of PGT use among cycles with a genetic or chromosomal abnormality was expected given the benefit of PGT in the setting of known parental genetic abnormalities (13). Intracytoplasmic sperm injection is recommended by the American Society for Reproductive Medicine and the Society for Assisted Reproductive Technology for couples with male factor infertility or who are using PGT among other indications (14). Intracytoplasmic sperm injection was the primary method of fertilization in cycles with a male factor infertility diagnosis. Despite the lack of evidence showing ICSI as beneficial to non-male factor infertile couples, clinics have been performing ICSI in most male and non-male factor cycles (15). In this study, ICSI was used in $> 80\%$ of all male factor infertility cycles reported in the United States. The use of SET has been increasing, and preliminary reports show that the clinical pregnancy rates after SET in male factor infertility are not significantly different from those of other types of infertility (16). Female age and the use of PGT are the primary factors that determine the number of embryos to transfer during ART (17). Male factor infertility appears to be less of a factor in the decision about the number of embryos to transfer, unless poor-quality sperm contribute to poor-quality embryos (13). Single embryo transfer, used in approximately two thirds of cycles with male factor infertility, is noted as a strategy to reduce multiple births due to ART and improve outcomes (18).

Prior research on male factor infertility has not been able to describe the prevalence and characteristics of specific male factor infertility diagnoses for several reasons; before 2016, the surveillance of male factor infertility among ART users was only reported as a dichotomous “yes/no” and surveillance mainly focused on the female patient (19). Social constructs have perpetuated infertility as a female issue (20), which may decrease the tendency of males to seek care. This report contains the analysis of approximately 98% of ART cycles performed in the United States (10, 11) and, therefore, is highly representative of all ART cycles performed. However, this study had 3 main limitations. First is the substantial number of responses categorized as unknown or missing, particularly for sperm status, sperm source, and race and ethnicity. Male factor infertility cycles had varying but substantial proportion of missing responses for male age (13.4%), male race and ethnicity (37.0%), sperm source (61.2%), sperm status (67.9%), and ICSI (10.6%). Readers should use caution when interpreting the results of the indicators with increased missingness. Further assessment is needed to understand why clinics are not collecting and/or reporting these missing data. Second, analysis was conducted at cycle-level data and is not patient-based. Therefore, patients may be counted more than once because a patient can have > 1 cycle during the 2-year period. Finally, as with any study using surveillance data, the accuracy of data is limited by the clinic data entry. However, the CDC conducts an annual quality control process called validation whereby medical records are compared with data entry in the NASS to ensure that data reporting is accurate. Approximately 8% of clinics are validated each year. According to the latest validation of the

2018 Assisted Reproductive Technology Surveillance Report (11), the discrepancy rate for male factor infertility was 5.4%. Furthermore, male factor infertility was underreported because in most discrepancies, male factor was found in the medical record but not reported in the NASS.

These data highlight the importance of recognizing and addressing male factor infertility as an important contributor to overall infertility and the use of ART. These findings also demonstrate the importance of collecting detailed information about male factor infertility among ART cycles to better understand the populations impacted. In addition, policies such as insurance coverage for infertility care may consider the inclusion of male factor infertility (21).

Improving infertility surveillance by collecting additional data from the male partner in the NASS was one of the recommendations of the National Public Health Action Plan for the Detection, Prevention, and Management of Infertility (22). The subsequent expansion of male factor infertility surveillance and this study are the first steps in understanding the breadth and depth of male factors contributing to the success or failure of ART. Future studies using the NASS data are necessary to further evaluate patients by diagnosis that go beyond semen parameter status. Future research may also include a statistical comparison of male factor vs. non-male factor infertility as well as comparisons of male factor infertility diagnoses between men evaluated by a reproductive endocrinologist and those evaluated by a urologist to better understand the differing perspective of the 2 disciplines. Although the surveillance of male factor infertility has improved in the last few years, there are several opportunities for additional improvement, such as decreasing missingness to better analyze a more complete collection of data on male demographics, sperm source characteristics, and treatments. Improved surveillance can assist in the identification of male factor infertility and the improvement of interventions for infertile couples.

CONCLUSION

In conclusion, male factor infertility is a substantial contributor to infertility treatments in the United States. Additional research focusing on male factor infertility is warranted. Continued assessment of the prevalence and characteristics of ART cycles with male factor infertility may inform treatment options and improve ART outcomes.

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