

CONCLUSION

While the majority of laboratories in the United States have adopted WHO 5 reference range criteria, a large percentage (36.5%) still use other criteria 6 years after the WHO 5 criteria were published. This variability could result in a male patient being characterized as “fertile” in one center and “subfertile” in another, leading to inconsistencies in treatment, and potentially shifting the burden of the infertility workup and interventions to the female. This discrepancy is particularly relevant given that, contrary to earlier standards, the WHO 5 criteria were developed from a population of normal, fertile males and did not contain infertile males. The current lack of consensus amongst laboratories in SA reference ranges could thus substantially impact the management of the male patient and his partner, simply depending on where they seek treatment. While large regional studies are needed to develop region-specific reference ranges, more consistent adoption of existing reference values would help to standardize the categorization of males and the subsequent approach to couples experiencing infertility.

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EDITORIAL COMMENT



The inconsistent adoption of the WHO 5th edition (2010) semen analysis reporting standard by laboratories is a huge problem in clinical andrology. Although the study by [First author last name] and colleagues has a few methodological shortcomings, its simple design is particularly effective at conveying the magnitude of this widespread problem. For those in a reproductive medicine specialty practice it will not be surprising, but for the rest of the urology community it will be staggering to see that over a third of US laboratories are performing semen analyses according to decades-old standards.¹

While the WHO 5th edition standard is not perfect, it is the best and most current standard adopted by laboratories and reproductive centers worldwide to characterize a semen analysis on the spectrum of normal fertility. To that point, it is important to understand that these “reference ranges” do not represent fertile (normal) versus infertile (abnormal) in the same way that a white blood cell count can either be normal or represent an abnormal leukocytosis. Rather, the lower limit of normal for each parameter is in fact the 5th percentile of men with normal fertility, therefore indicating where on the continuum of normal fertility a particular semen parameter may be. Unfortunately, while a complete blood count result from another laboratory can easily and reliably be interpreted by a clinician, we cannot always say the same about a semen analysis. There are multiple

reasons for this, with one of the primary reasons being inconsistent laboratory reporting.

Prior to the most recently published reference range in the WHO 5th edition (2010), the second most recent edition (1999) is now approaching 20 years old. It is not invalid to report a result alongside an outdated reference range; however, when labs do not follow the most current standard of reporting, it represents a “red flag” to the clinician that the lab may not only perform semen analyses infrequently, but also, more importantly, may be out of touch with modern andrology assessment techniques. The resulting drawback is particularly evident with sperm morphology, which went through a significant change when Kruger strict morphology was adopted for the 5th edition. The light microscopy version of morphology assessment, which was part of the 1999 and earlier WHO reference standards, is now obsolete and relatively useless to clinicians. Nevertheless, this change in morphology reporting is likely a factor in why some laboratories have not adopted the most current standard.

Not only are nonconforming labs out of touch and potentially less accurate, but results reported by such labs can lead to mischaracterizations of patients’ reproductive potentials, missed diagnoses, and ultimately can heighten the barriers to male reproductive care. It is about time that CLIA-certified laboratories be required to conform to modern reference values in reporting semen analyses in order to maintain compliance.

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Reference

1. Place reference for present study (currently unknown): “Inconsistent Adoption of World Health Organization V (2010) Semen Analysis Reference Ranges in the United States Six Years After Publication”.

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AUTHOR REPLY

We appreciate the reviewer's comments regarding our manuscript. The inconsistent adoption of WHO V (2010) semen analysis reference ranges can result in numerous unintended consequences, including inconsistencies in the diagnosis and treatment of male factor infertility depending simply on the location of the patient's evaluation. Patients commonly express confusion and dismay when being categorized as “normal” at one center and “infertile” at another, and this scenario can also result in uncertainty on the part of physicians unfamiliar with the field of reproductive medicine. We agree with the reviewer that more consistent adoption of contemporary WHO semen analysis reference ranges would greatly help rectify this situation and provide patients and clinicians alike with great clarity. However, we suspect that a primary reason for the inconsistent adoption of the WHO V reference ranges is the fact that these values do not represent a true boundary between the “fertile” and “infertile” states. Rather, these values are arbitrary cut-points selected at the 5th centile value for each parameter, derived from data from an international cohort of fertile males. Given the fact that the contemporary reference values are not derived to differentiate fertile from infertile men, many centers continue to use the older reference ranges because they feel that they do a better job discriminating fertility from infertility. Until reference ranges that more clearly separate these two groups are implemented, inconsistent adoption will likely persist. Unfortunately, given the high degree of overlap in semen analysis values for fertile and infertile men, we suspect that such reference ranges will not be generated any time soon.

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