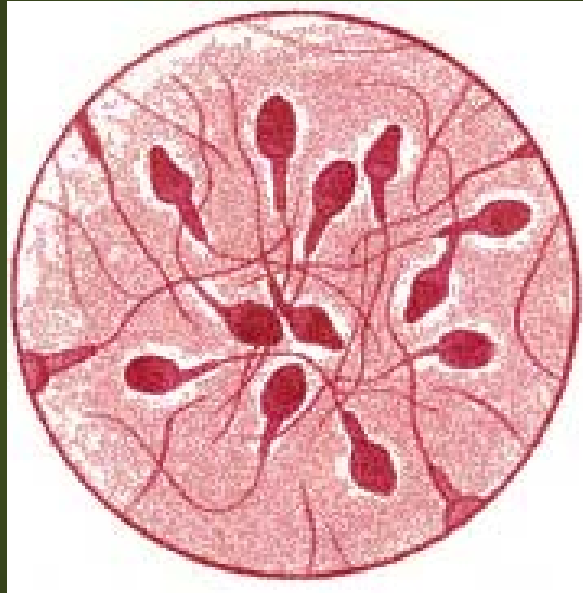


The Implications *of the* New WHO Guidelines *for* Sperm Analysis



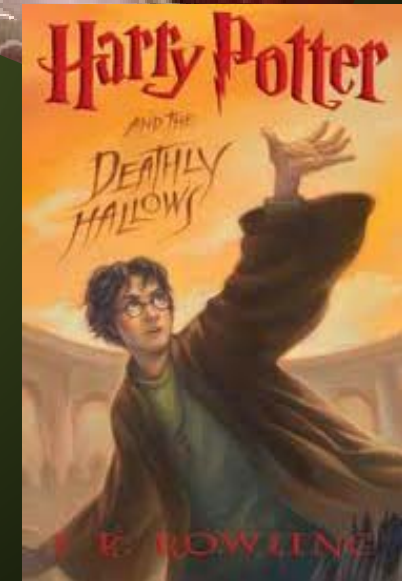
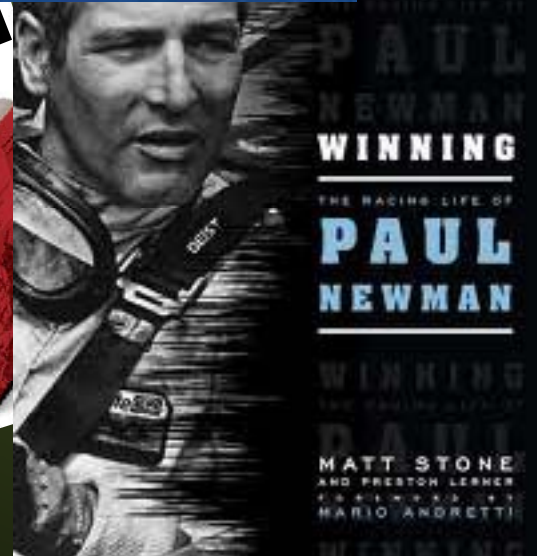
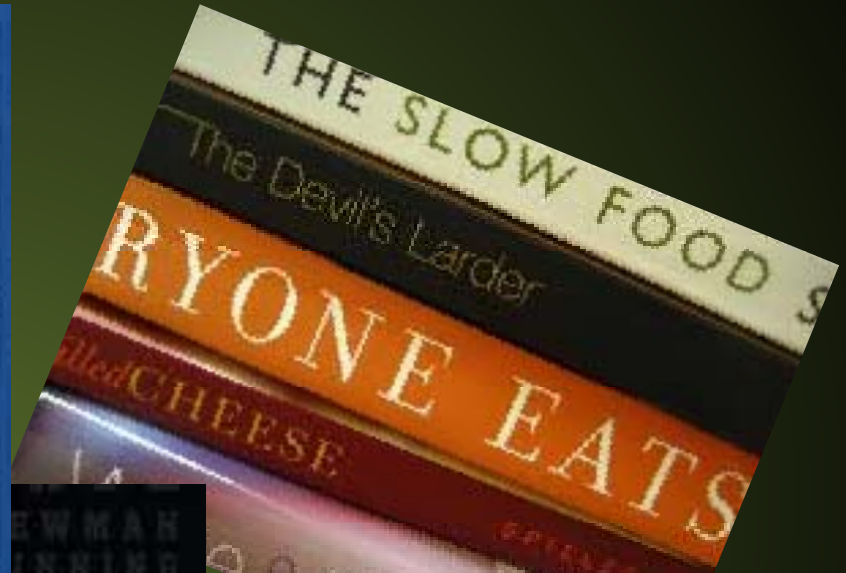
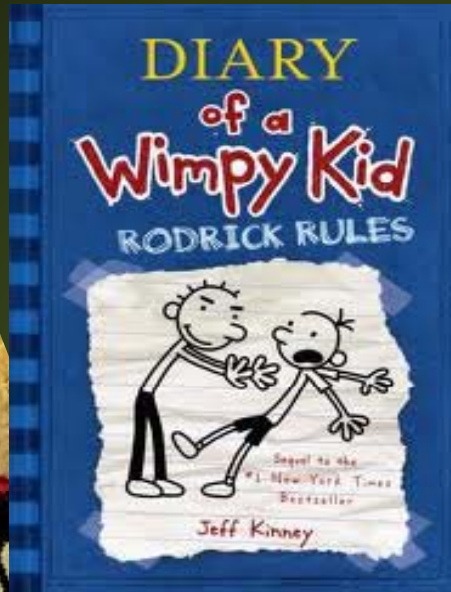
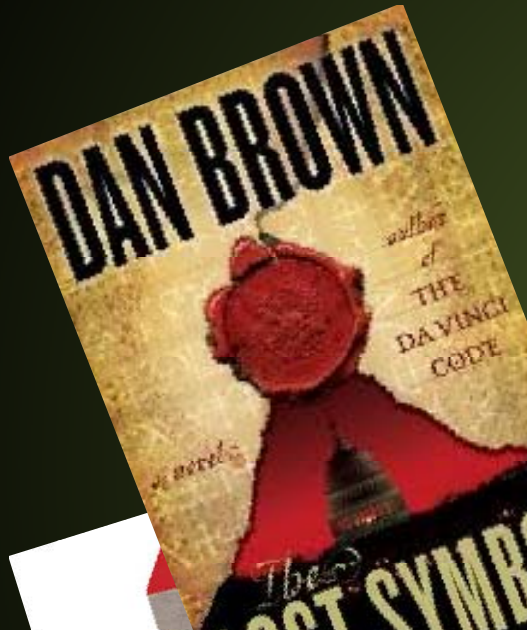
Paul Turek MD, FACS, FRSM
Director, The Turek Clinic

Critique *of the* New WHO Reference Values: How Will They Affect *Our* Practice?

1. Review of WHO 2010 reference ranges
2. Published buzz about the new reference ranges
3. Buzz among SSMR members about the new reference ranges
4. Summary

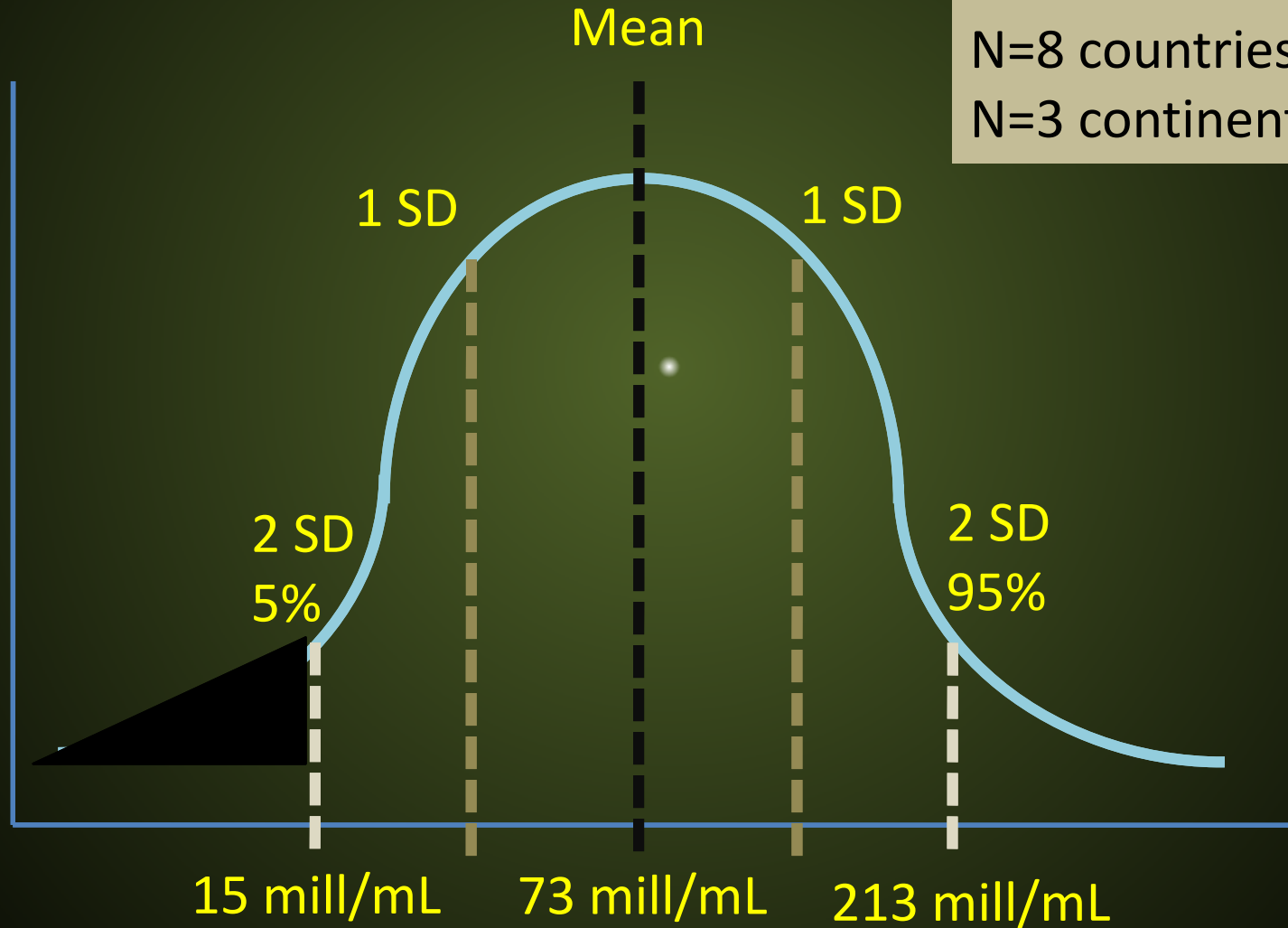


Think of This *as a* Book Review

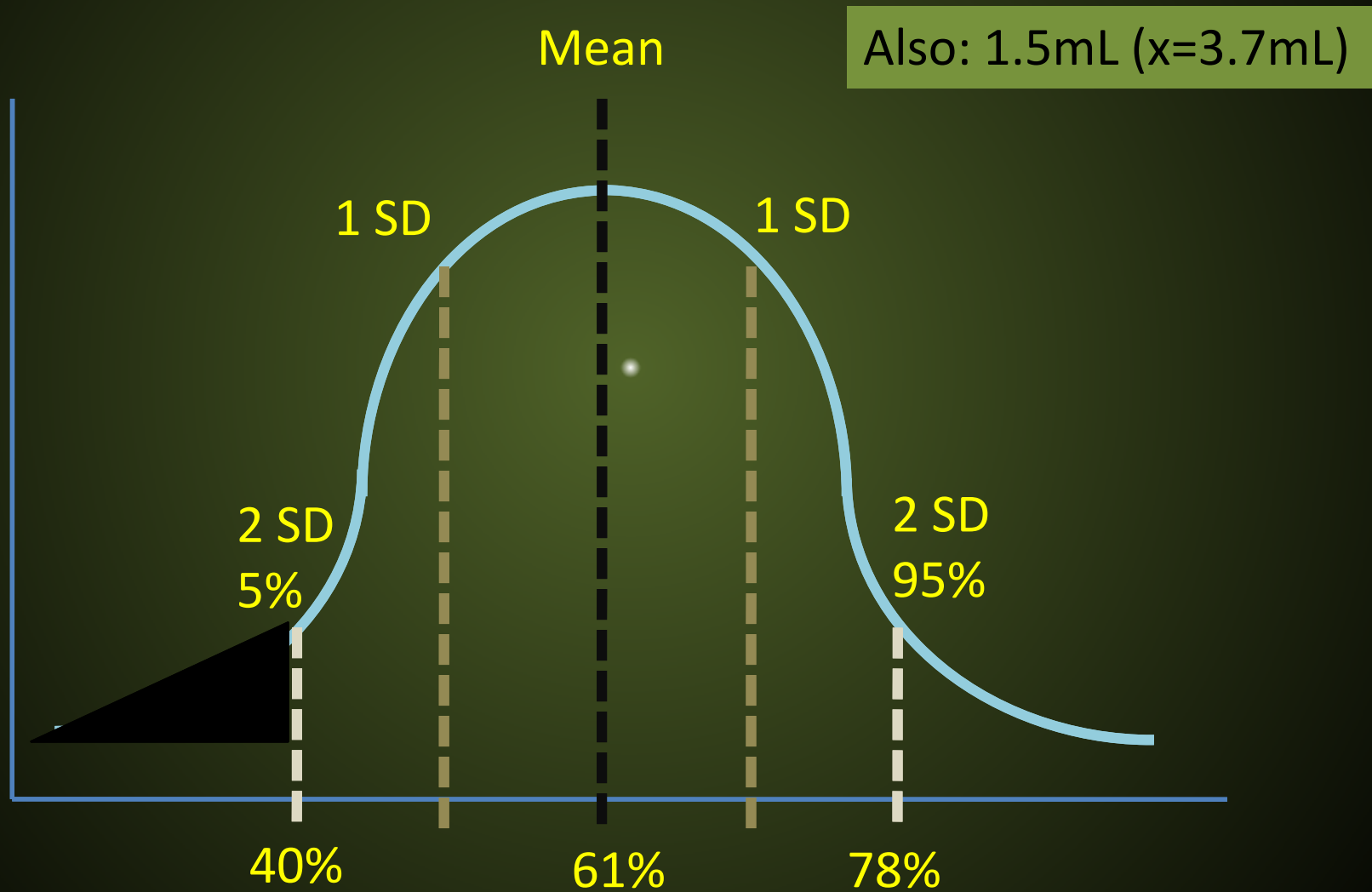


WHO 2010 Sperm Concentration

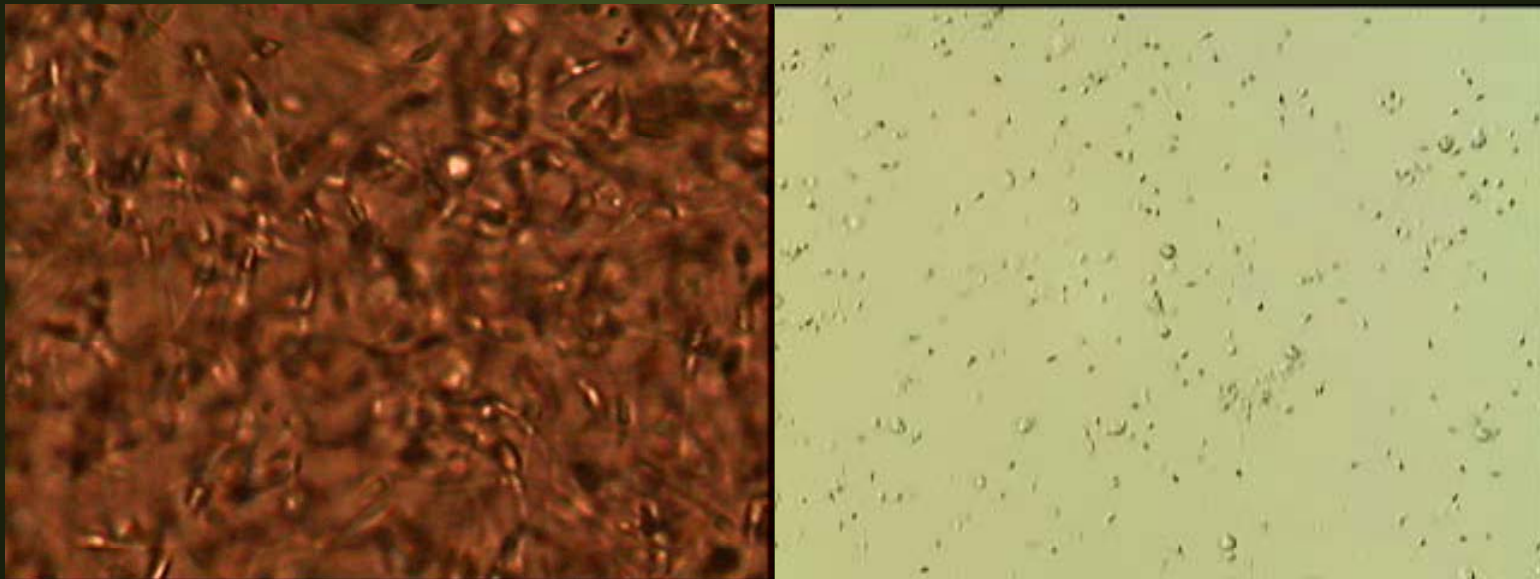
N=1800 new fathers
N=8 countries
N=3 continents



WHO 2010 Sperm Total Motility



Was Ejaculated Sperm Really Mean't to be Counted?



Which one is Human?
Which one is Dolphin?

Goals of the New WHO Reference Ranges

- *“to improve the quality of [the] semen analysis and comparability of results.”*
- *“reference values...allow decisions to be made about patient management and thresholds for clinical trials or investigations.”*

Intro, WHO 2010 Manual

What's the Published "Buzz" About the New WHO Reference Ranges?

- *The semen analysis provides valuable information about:*

Testicular sperm production

Sperm motility and viability

Reproductive tract patency

Accessory sex gland activity

Integrity of emission and ejaculation

What's the Published "Buzz" About the New WHO Reference Ranges?

- *Reference ranges are very valuable in clinical chemistry where homeostasis keeps things remarkably stable*

Examples: glucose, thyroid metabolism

- *Reference ranges are less valuable for biological parameters that are less tightly regulated due to temporal or geographical variation*

Who Can Forget this Figure?

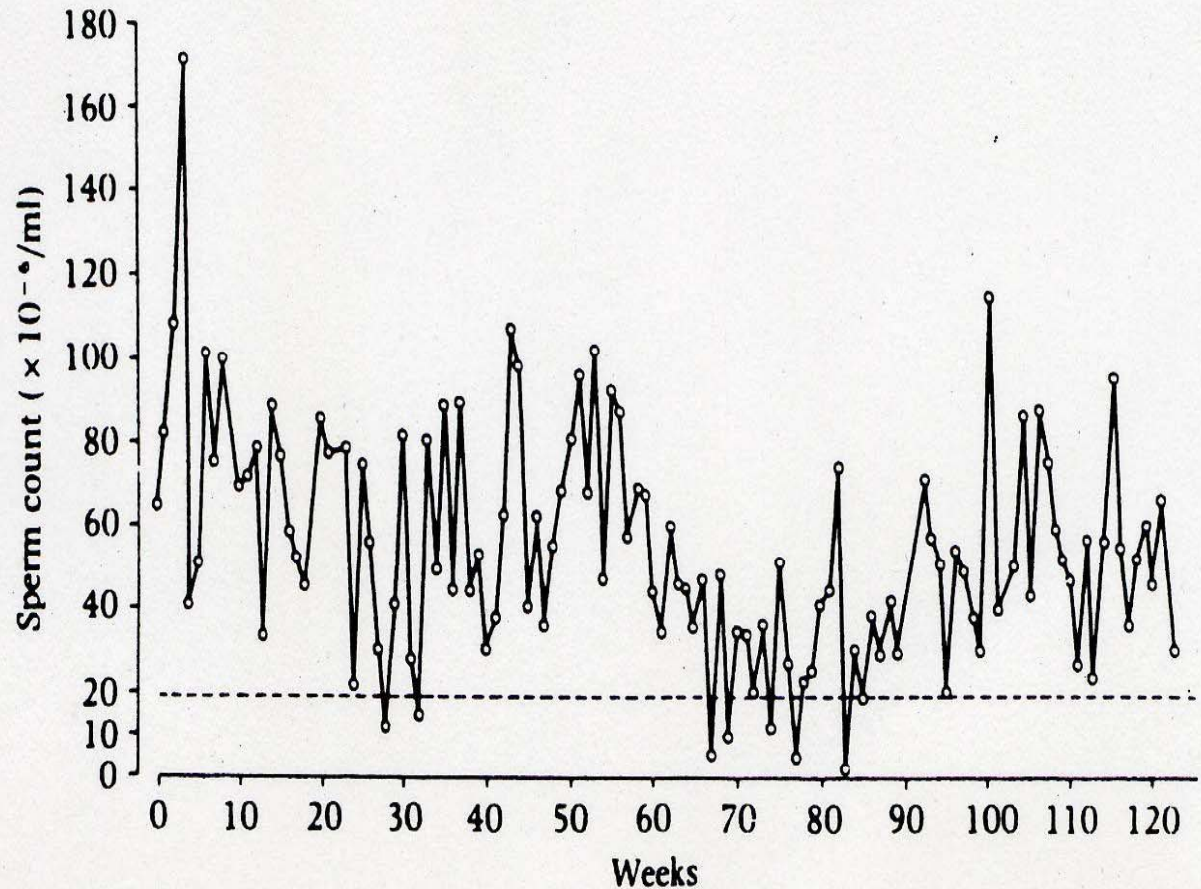
Fig. 2.1. Sperm concentrations in the semen of one man collected biweekly over 120 weeks. During this period the man received no medication and experienced no febrile illness. The dotted line indicates $20 \times 10^6/\text{ml}$ (see Appendix 1A). The data illustrate the marked variations in sperm concentration that can occur in the semen of some men. (Unpublished data from C.A. Paulsen.)

N=1

Biweekly SA

120 weeks

No Rx; No illness



WHO Manual, 4th edition, 1999, p.5.

Changes in Semen Quality with Time

- Cohort of n=7 men.
- Provided total of 673 semen specimens (61-205/subject).
- Provided semen over 72-324 weeks/subject (>1/year).
- “Noticeable sample to sample variability:”
 - Volume: 59%
 - Concentration: 54%
 - Motility: 96%

What's the Published "Buzz" About the New WHO Reference Ranges?

- *The WHO 2010 reference ranges are based on sound scientific principles*

For the first time are evidence-based

- *However, significant biological and technical variability still plague the accuracy of the intended measurement.*

Only 23% of AAB-PT reviewed labs use a hemocytometer for semen analysis

What's the Published "Buzz" About the New WHO Reference Ranges?

- *The WHO 2010 reference ranges are based on values derived from a fertile population.*

N=1800 men; 8 countries; 3 continents

- *The clinically relevant population to assess is infertile men.*
- *The semen analysis is not a measure of fertility.*
- *Fertility is a continuum; reference ranges impose an artificial dichotomy that limits prognostic value*

Lamb D. Asian J Androl. 2010, 12: 65

Haidl G. Asian J Androl. 2011, 13: 208

What's the Published "Buzz" About the New WHO Reference Ranges?

- *The WHO 2010 manual is essentially a laboratory tool, like others in clinical medicine.*

Likened to a clinical sign

- *It has been improved upon over past editions.*
- *The semen analysis is not a diagnosis. The root cause of an abnormal sample cannot be determined solely from the sample.*
- *Clinical interpretation remains a matter for care providers.*

What's the "Buzz" About the New WHO Reference Ranges Among SSMR Members?

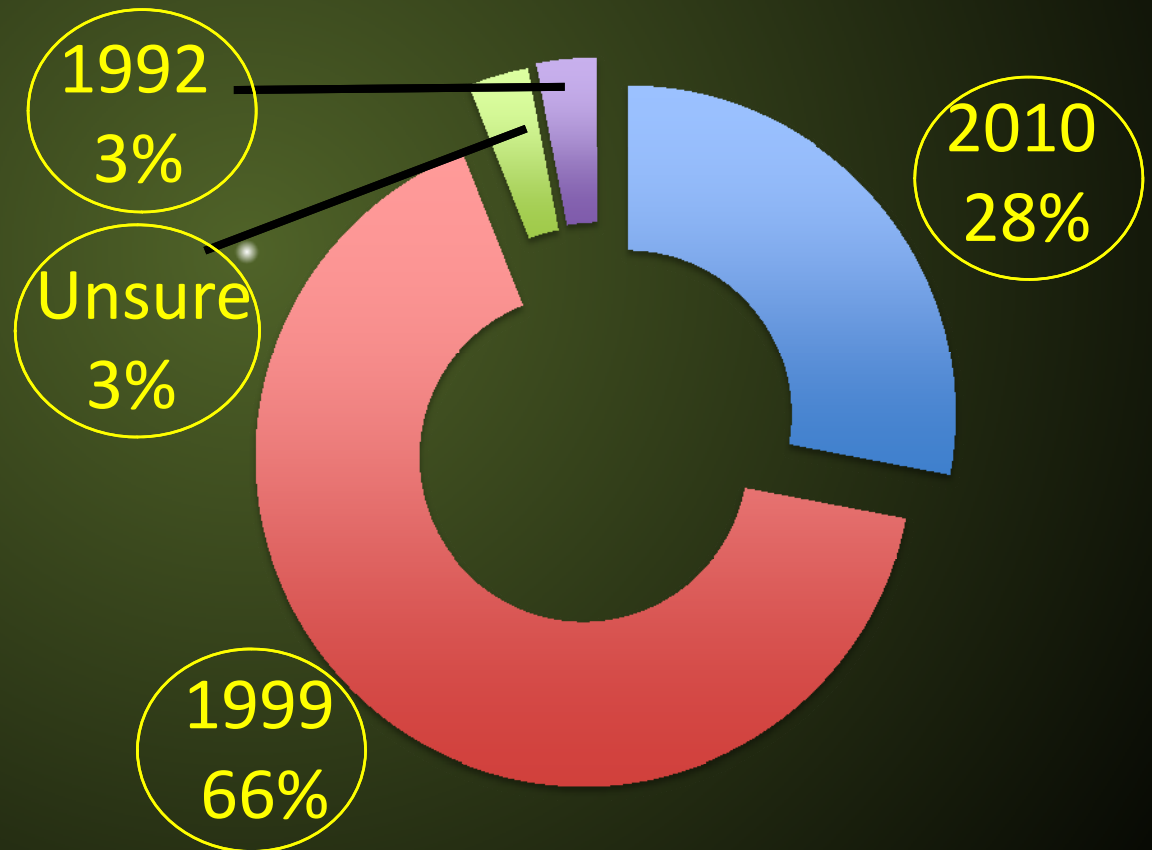
- SSRM membership surveyed online (SurveyMonkey.com)
- 10 questions; multiple choice format
- Focused on how the WHO references ranges are viewed and whether they were being adopted
- N=31 respondents over a 2 month period



WHO 2010: SSMR Member Survey

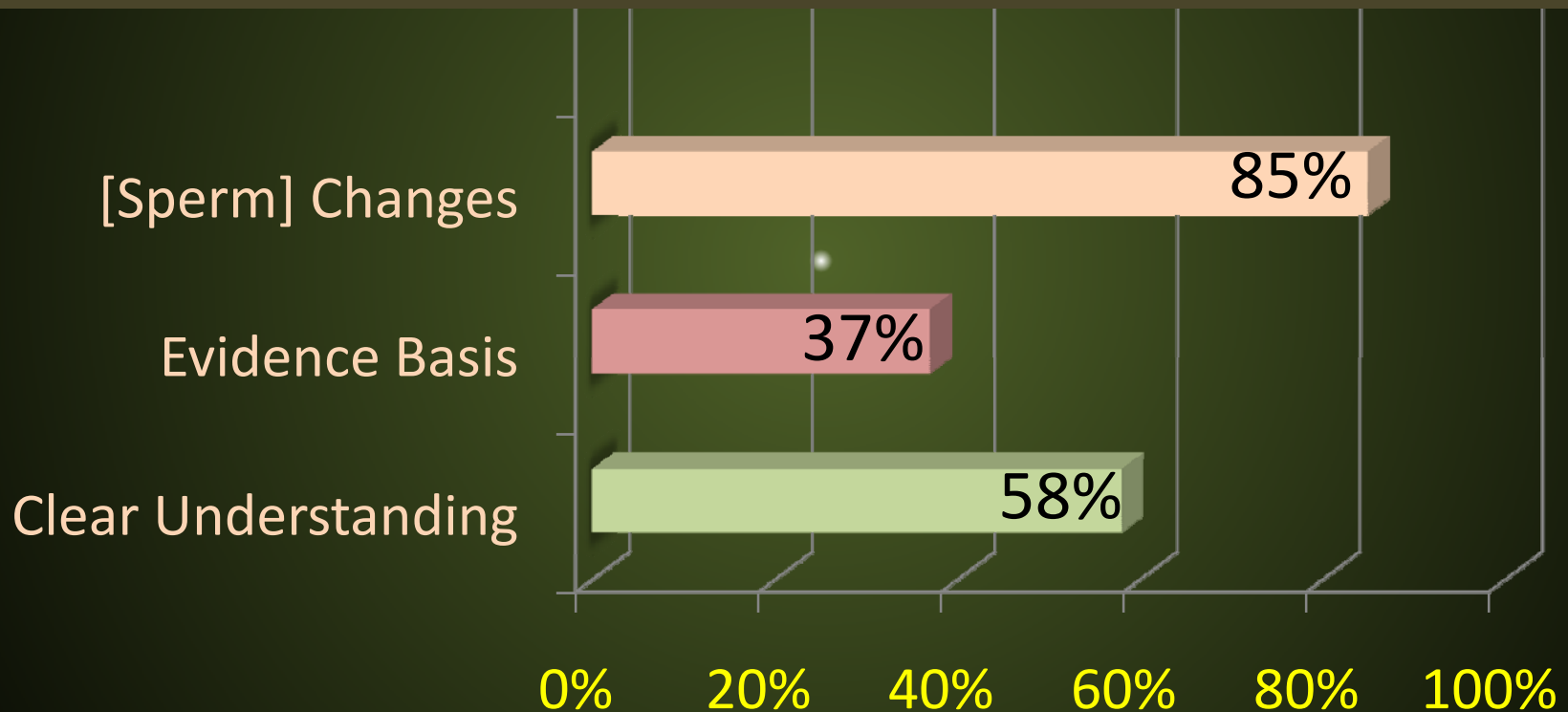
Which WHO Edition?

94% use WHO
semen analysis
standards to
guide care



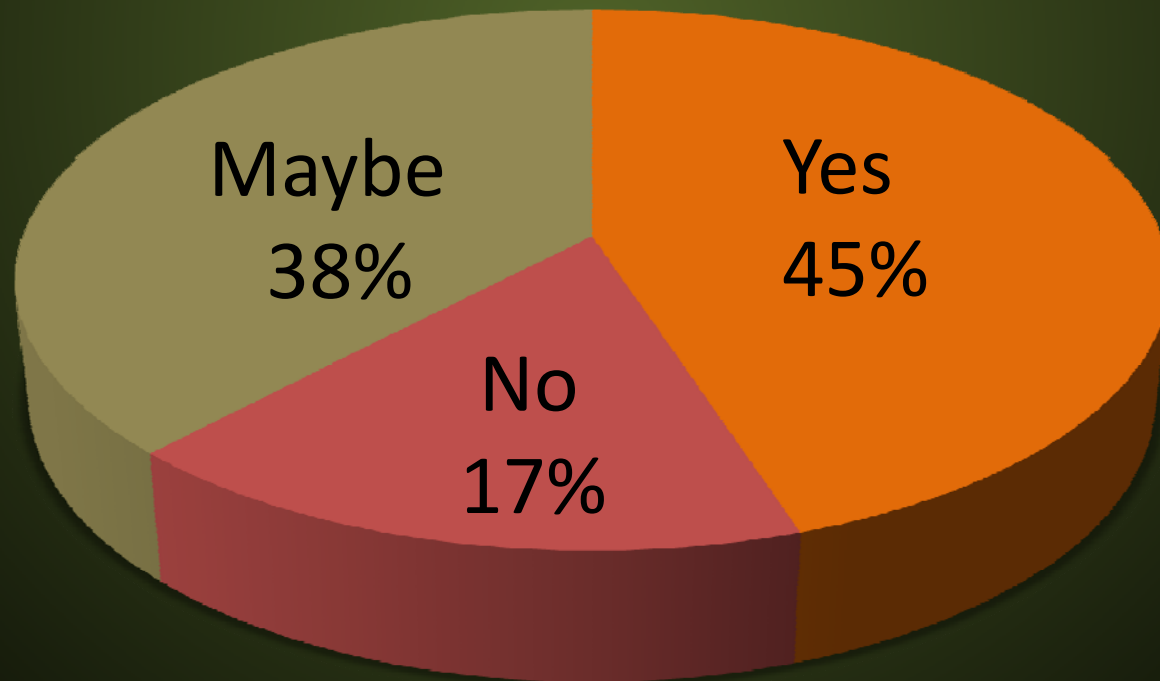
WHO 2010: SSMR Member Survey

Clear understanding of the new reference ranges?



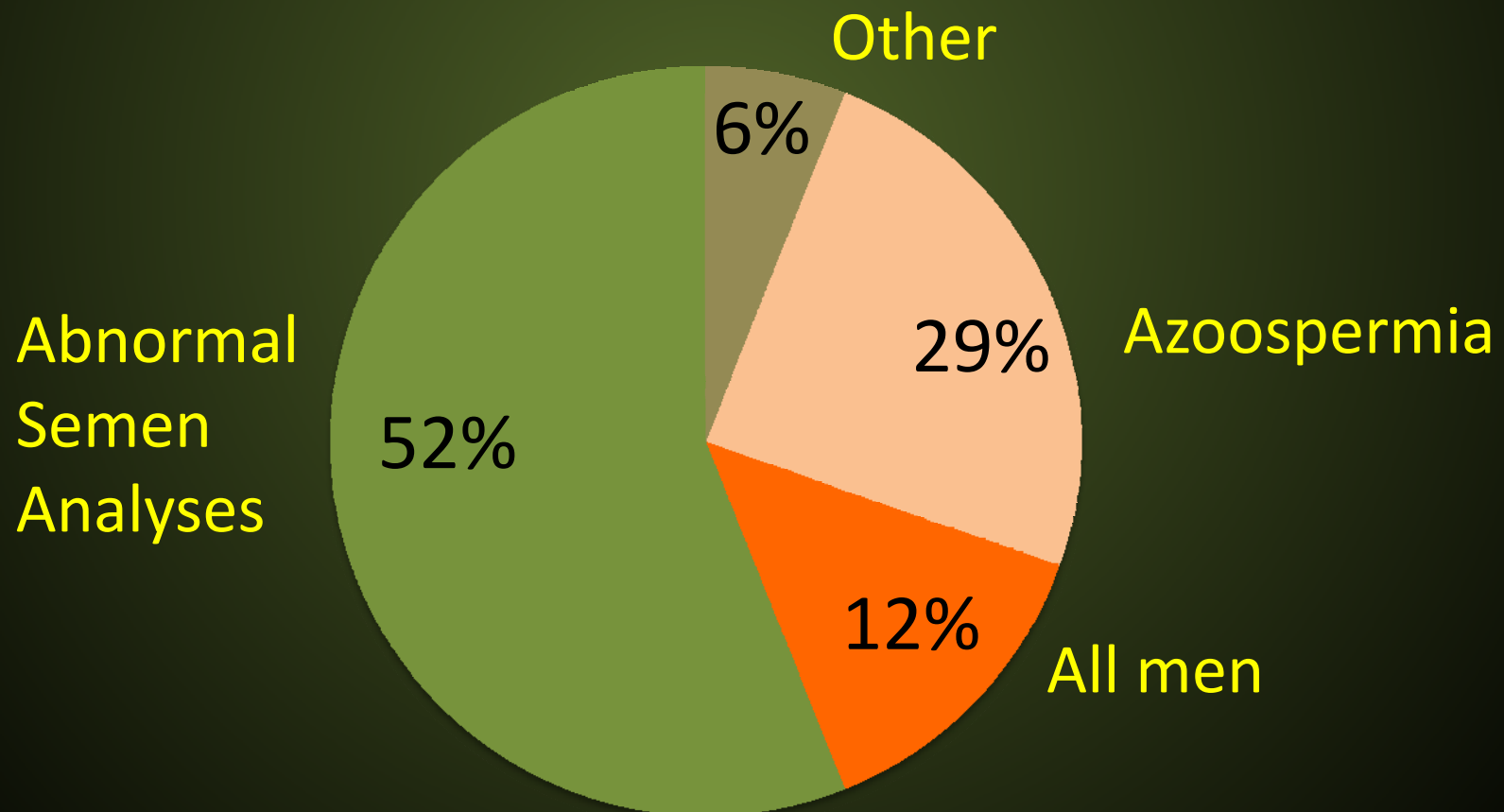
WHO 2010: SSMR Member Survey

If the reference range for sperm concentration is lowered...do you feel that many currently “infertile” men will be considered “fertile?”



WHO 2010: SSMR Member Survey

What criteria are used by your IVF centers to send male infertility patients for evaluation?



WHO 2010: SSMR Member Survey

- 87% believe all infertile men, regardless of semen analysis, should undergo male factor evaluation.

10%: men with abnormal semen analysis

- The most valuable semen analysis information:

46% Reference ranges from fertile men

32% Reference ranges from infertile men

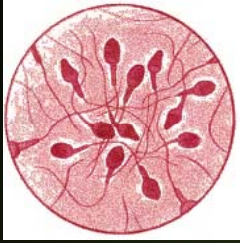
22% Other/skipped question

- Would a reference range that accurately defined fertility be helpful?

87% Yes

6% Maybe

6% No



2010 WHO Reference Values: *Summary*

- There is **evidence** and there is **confusion**.
- Are these changes simply a “**tempest in a tea pot?**”
- Incidence of “**idiopathic**” infertility cases will likely **increase** (as will ART treatments).
- Proportion of cases referred from IVF programs for male factor evaluation will likely **decrease** in U.S.
- New reference ranges will likely affect **third party payments**.
- New reference ranges will likely affect **interpretation of outcomes** from research studies.