TITLE:

VARIABILITY IN THE INCIDENCE OF UNUSABLE RESULTS BY PREIMPLANTATION GENETIC TESTING: MULTI-LAB COMPARATIVE ANALYSIS

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Background
The enhancements to reproductive medicine conferred by Preimplantation Genetic Testing for Aneuploidy (PGT-A) hinge on the test delivering clinically relevant information, yet there is an inevitable percentage of samples that do not yield productive results. Reference laboratories employ diverse PGT-A platforms, each equipped with unique features. A next generation sequencing (NGS) platform capable of producing a superior average sequencing depth per sample has the potential to decrease the proportion of samples yielding clinically insignificant results.

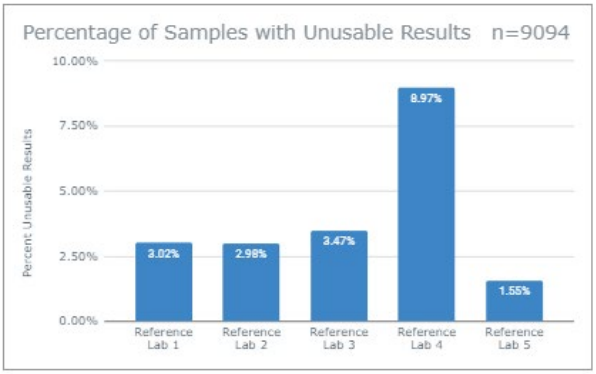
Objective
To assess the differences in rates of unusable results between PGT-A reference laboratories and correlate those rates with features of the sequencing platforms used.

Materials and Methods
The analyzed data originates from embryos produced at a network of IVF clinics spanning from 2021 to 2023. A total of 9,094 PGT results from five distinct genetic testing laboratories all using NGS, were selected for this comparative analysis and categorized by result: Euploid, Aneuploid, Mosaic, Inconclusive, and No Result. Inconclusive results (alternatively called noninformative) are those for which the sample produced a result that could not be confidently interpreted. This signifies a sample that failed to yield a result, typically due to the absence of DNA or an insufficient amount of DNA in the provided reaction tube. For the purposes of this study, a group with 'Unusable' results encompasses the combined set of 'Inconclusive' and 'No Results' samples. A Chi-squared test was performed to examine the relationship between testing laboratories and the rate of unusable results. A p-value of <0.05 was considered significant.

Results
The data sets for each reference laboratory were as follows: Lab 1 (n=597 samples tested, 3.2% unusable results), Lab 2 (n=504 samples tested, 2.75% unusable results), Lab 3 (n=3,199 samples tested, 3.46% unusable results), Lab 4 (n=847 samples tested, 8.97% unusable results), and Lab 5 (n=3,947 samples tested, 1.55% unusable results). Statistical comparisons between laboratories showed that Reference Lab 4 had a significantly higher incidence of unusable results than all other Reference Labs, while Reference Lab 5 had a significantly lower incidence of unusable results than all other Reference Labs. All other comparisons were not statistically significant.

Conclusions
Our data shows significant variation in the incidence of unusable results generated by different reference labs. Reference Laboratory 5, which yielded the fewest unusable results, employs a PGT-A platform generating, on average, eight times the quantity of sequencing data per sample compared to the platforms employed in Labs 1, 3, and 4. This suggests that samples at risk of producing an unusable result, for example biopsies of subpar quality, can gain advantages from a PGT-A platform capable of producing a superior average sequencing depth per sample. The implications of these findings extend to patients and clinicians seeking optimal

outcomes in assisted reproductive technologies, ultimately providing them with a more reliable and efficient PGT-A process and IVF treatment journey.



Graph 1. Percent of unusable results from reference labs 1-5

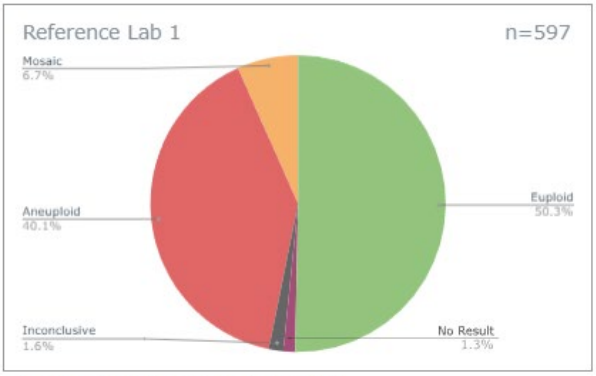


Chart 1 : Lab 1 Result Category Percentages

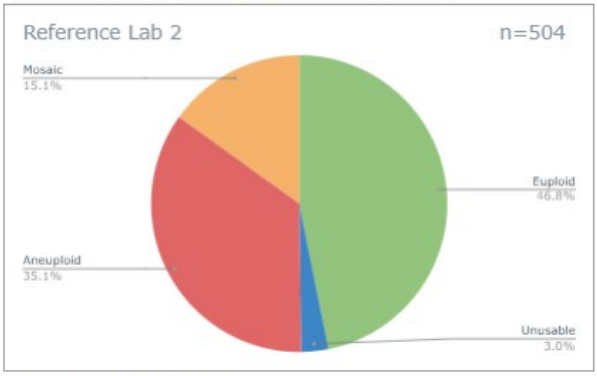


Chart 2 : Lab 2 Result Category Percentages

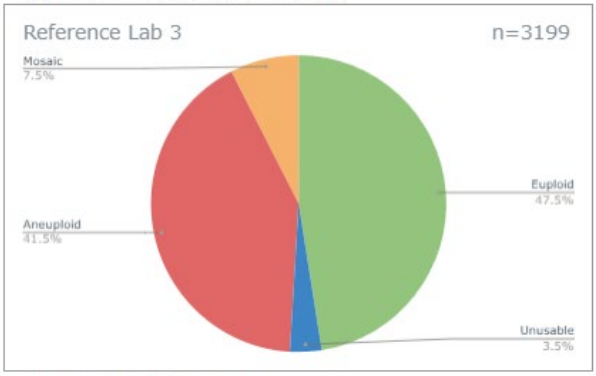


Chart 3 : Lab 3 Result Category Percentages

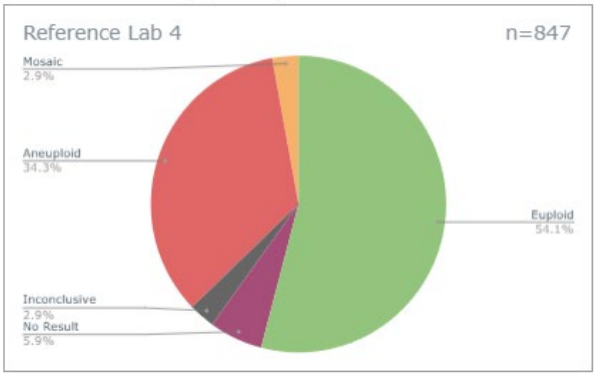


Chart 4 : Lab 4 Result Category Percentages

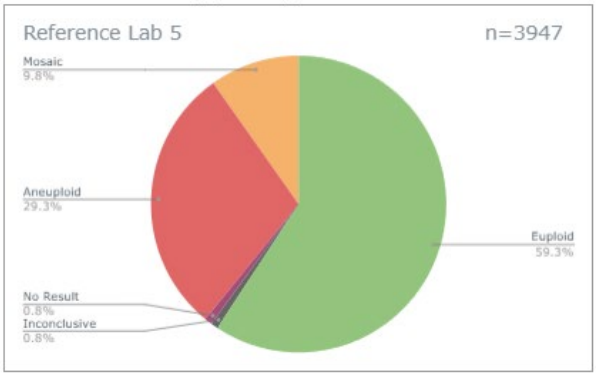


Chart 5 : Lab 5 Result Category Percentages

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References
N/A