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Prenatal cell-free DNA test failure should not deter retesting

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Obstetricians and pregnant women should be reassured that prenatal cell-free DNA (cfDNA) test failure does not increase the chance of a positive finding of Down syndrome, nor should it deter an immediate retest from the same laboratory. A new review of 30 publicly available studies reported in this issue by Palomaki and Kloza provides context on test failure rates in real-world clinical testing. Of the 25 studies reporting primary results, there were 1020 Down syndrome pregnancies with 17 test failures and 9868 normal pregnancies with 288 test failures. The findings showed that for the small number of women who might be subject to a test failure, two-thirds would likely have a successful repeat sample test result. A follow-up that includes repeat cfDNA testing and targeted ultrasound is likely to identify the vast majority of common trisomies, the researchers conclude. Even the rare double failure was not associated with an increased risk of Down syndrome. Repeat testing includes using a duplicate sample from the same blood draw, or a subsequent sample from a new blood draw, or both. A number of factors were associated with test failure, including gestational age at testing, maternal body mass index, whether fetal fraction is available, and testing methodology. When evaluated by region of origin, eight studies from Asian countries collectively reported lower failure rates (0.6%) than Western countries (2.4%). The authors attribute this difference to the population of women in Asia having, in general, a lower body mass index. Higher body mass index is associated with lower quality sample draw. The findings demonstrate that repeat testing is effective and should provide peace of mind to obstetrical care providers, genetic counselors, and pregnant couples. — *Karyn Hede, News Editor*

Reanalyzing exome data increases yield, costs less than full genome

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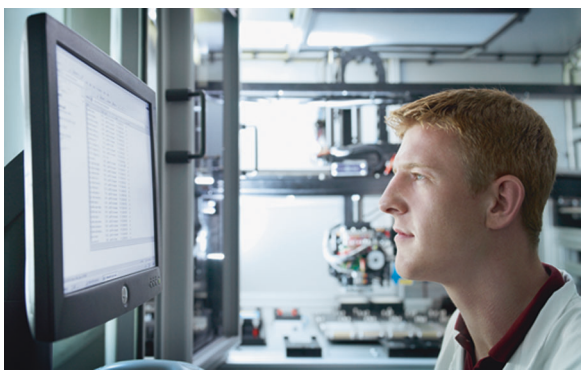
For health-care systems seeking cost-effective approaches to providing clinical genetic services, reanalyzing exome data, even a few months after a negative finding, may work just as well as escalating to genomic sequencing, according to a small study conducted in Saudi Arabia. In a small, focused study of 108 patient cases from King Abdulaziz Medical City, Riyadh, Saudi Arabia, Alfares et al. compared the diagnostic rate and cost of genomic sequencing with a hypothetical reexamination of an existing exome sample. For this small homogeneous population, the research team found that the cost of genomic sequencing was not justified by the additional diagnostic yield. Of the 108 patients with negative or inconclusive exome sequencing results, only 7 ultimately received a diagnosis through genomic sequencing. When these positive results were examined further, 4 of them could have been identified by reexamination of the exome. Only 3 could have been diagnosed solely by the full genomic sequencing and these cases were newly discovered genes or reported variants made public in the 5-month interval between the initial exome testing and the subsequent genomic testing. In the Saudi Arabian health-care setting, the cost of each exome sequence was US$1200, and the calculated exome reanalysis would have cost US$250, assuming accessible raw data versus approximately US$4200 for each genome sequenced. The researchers concluded that $529,200 spent on genomic sequencing to achieve a 7% higher detection rate could not be justified, and that in the future, reexamination of exome data should be considered before spending substantially more on genome sequencing. — *Karyn Hede, News Editor*



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