IN THIS ISSUE

Prenatal exome sequencing yields clinical impact, aids parental decision-making

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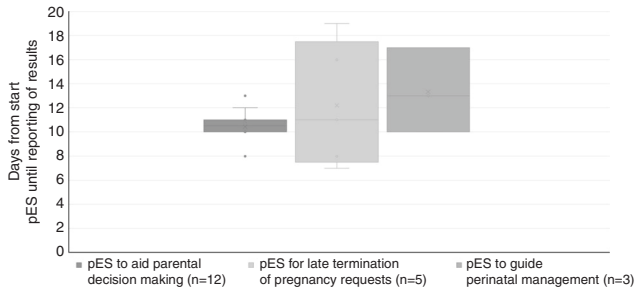

Congenital anomalies are a prime cause of perinatal mortality, but knowing whether an anomaly is isolated or part of a genetic syndrome may influence prognosis. Yet, so far very few studies have investigated the impact of prenatal exome sequencing (pES) during pregnancy. These earlier studies evaluated diagnostic yield but not the clinical impact of pES. In this issue, de Koning et al. report the clinical impact of implementing pES for ongoing pregnancies in routine care. The team defined clinical impact as pES results that (1) significantly influenced parents' decision to continue or terminate pregnancy, (2) supported the request for late termination, or (3) changed pre- or perinatal management in cases with severe anomalies. The researchers carried out a retrospective analysis in a small cohort of 20 pregnancies referred for pES counseling based on prenatal ultrasounds showing structural anomalies. Fetal samples were collected via amniocentesis or chorionic villi sampling. The scientists then used what's described as a comprehensive gene panel focused on developmental disorders in the postnatal setting in the initial analysis. If the panel did not identify a clear answer, exome analysis directly followed. Turnaround time from pES request to final diagnostic report was less than 17 days in most cases. In cases where pES might aid parental decision-making, researchers obtained a genetic diagnosis in 4 of 12 pregnancies (33.3%). pES results facilitated parents' decision to terminate in three of the four diagnosed cases. In five pregnancies, pES results did not lead to a diagnosis and parents said pES results were key to their decision to continue the pregnancies. Altogether, pES had an impact on parental decision-making in 75% of cases (9/12). In two pregnancies where parents were considering requesting late termination, pES revealed diagnoses associated with extremely poor neonatal prognosis. Results supported parents' request for late termination. Finally, in cases where sequencing could facilitate pre- or perinatal management, pES identified a genetic cause for structural anomalies in two of three pregnancies. Overall, de Koning and team found pES has a high overall clinical impact of 70%, though they acknowledge that challenges remain, such as the need to provide appropriate genetic counseling to couples. The authors recommend continued investigation of pES in a study setting. —*V. L. Dengler, News Editor*

Researchers suggest how to facilitate pharmacogenetic testing in the clinic

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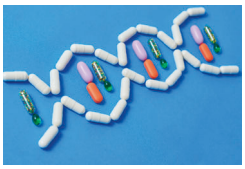
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One way precision medicine can improve patient care is by including a patient's genotype in the clinical decision-making process. Pharmacogenetics individualizes patient care by using genotyping results to inform medication decisions. However, implementation challenges likely hinder routine use of pharmacogenetic testing results in the clinic. In the article by Cicali et al., researchers from the University of Florida (UF) Health Precision Medicine Program outline challenges and lessons learned from clinical implementation of three gene–drug pairs—*CYP2D6*-opioids, *CYP2D6/CYP2C19*-selective serotonin reuptake inhibitors (SSRIs), and *CYP2C19*-proton pump inhibitors (PPIs)—during pharmacogenetic clinical trials carried out at UF Health and its partner sites. The researchers solicited anecdotal feedback from stakeholders, including prescribers and research coordinators, via email and in-person discourse. They also discussed potential solutions via teleconference and compared outcome measures with stakeholder responses to identify challenges, successes, and lessons learned. Cicali and team highlight five challenges and recommendations. First, a primary outcome for all the trials was patient-reported improvement documented via questionnaires. The researchers found that completion rate ranged from 44% to 98%. Trials that limited questionnaire frequency showed higher completion rates. Second, children do not like to be poked. When blood samples were necessary, only 73% of children consented to enrollment. However, 100% of children agreed when buccal samples were used. Adults did not show such preferences. The researchers recommend noninvasive sample collection with children when possible to achieve enrollment goals. Third, the team anticipated knowledge gaps for prescribers. They found that formal grand rounds presentations were the most effective educational strategy, followed by in-person discussions over lunch. On-demand web-based educational strategies were the least effective. Relatedly, prescribers highly valued pharmacist consultations and best practice advisories for how to interpret and integrate pharmacogenetic results. Clear, concise guidance via consults and action alerts assisted prescriber workflow. Finally, scheduling a patient's next appointment when genotyping results are ready improves adherence to genotyping-guided recommendations. Face-to-face follow-ups soon after results are available help prescribers act on suggested advice and may facilitate patient medication changes. Cicali and colleagues advocate continued discussions relating to lessons learned from challenges in the clinical implementation of gene–drug pairs as these are representative of challenges likely to be encountered when kicking off a new pharmacogenetic trial or clinical service. They say ongoing discourse will benefit future integration of pharmacogenetic testing into clinical care. —*V. L. Dengler, News Editor*

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