Diagnostic Exome Sequencing (DES) provides a diagnosis for 23% of adult patients

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Diagnostic exome sequencing (DES) is successful in solving the diagnostic odyssey for roughly 30% of undiagnosed patients with a broad range of underlying Mendelian disorders. Pediatric neurologic manifestations are the most common DES referral indication. However, DES has also been successful in diagnosing adult patients undergoing the diagnostic odyssey. Among the first 1000 reported DES families, 175 (17. 5%) adult patients (>18 years old) were referred for testing. Significant family history was more common among adult patients (81. 1%) than children (65. 3%) (p=1. 826e-5). Among adults tested, 79 (45. 1%) were between 18-29 years old, 50 (28. 6%) were between 30-49 years old, and 46 (26. 3%) were between 50-79 years old. The most common referral indication among adult patients was cancer susceptibility (25, 14. 3%), followed by multiple congenital anomalies (23, 13. 1%), neurodevelopmental anomalies (15, 8. 6%), skeletal anomalies (14, 8. 0%), and ataxia/spasticity (10, 5. 7%). Positive findings were uncovered in 23. 4% of these families (41 of 175), compared to 29. 3% of children (242 of 825). A novel genetic etiology was proposed for 9 families (5. 1%). The diagnostic rate among patients <30 years old (29. 5%) is significantly higher than among patients greater than 30 years old (16. 7%) (p=4. 125e-3). Among the 41 adults with positive results, over half of the gene findings (23, 56. 1%) were autosomal dominant, 12 (29. 3%) were autosomal recessive, and 6 (14. 6%) were X-linked. Overall, the rate of de novo and likely de novo findings among adult patients (17. 5%) was much lower than among children (44. 4%) (p=5. 278e-5). The highest diagnostic yields were observed among patients with ocular anomalies (3/3, 100%), integumentary anomalies (2/3, 66. 7%), muscular dystrophy (3/5, 60%), intellectual disability (4/7, 57. 1%), renal anomalies (1/2, 50%), and cardiovascular anomalies (6/15, 40%). These data, including the high DES diagnostic rate of 23% among adult patients, highlight the potential medical-economics savings to patients as well as payers given that achieving a diagnosis abrogates the expensive, time-consuming, and often invasive diagnostic odyssey.