Resources on Whole Genome Sequencing

The Genomic Answers for Children's Health (GACH) Alliance has put together several compilations of studies and resources on whole genome sequencing (WGS). This document focuses on studies that illustrate what rare diseases currently cost the health care system.

About the GACH Alliance

The GACH Alliance is a diverse group of health care stakeholders committed to expanding access to WGS and helping to end the diagnostic odyssey. Our mission is to ensure that any child with a rare disease or suspected genetic disorder who is enrolled in Medicaid has timely access to genomic sequencing, especially whole genome sequencing. We also seek to ensure that patients and their families have the opportunity to share the sequencing results with medical researchers, to help aid in the discovery and development of new treatments for rare diseases.

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Cost-Burden of Rare Disease

1.Gonzaludo, N., Belmont, J.W., Gainullin, V.G. et al. Estimating the burden and economic impact of pediatric genetic disease. Genet Med 21, 1781–1789 (2019). https://doi.org/10.1038/s41436-018-0398-5

- **Abstract:** “Purpose: To identify the economic impact of pediatric patients with clinical indications of genetic disease (GD) on the US health-care system.
- **Methods**: Using the 2012 Kids' Inpatient Database, we identified pediatric inpatient discharges with International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) codes linked to genetic disease, including well-established genetic disorders, neurological diseases, birth defects, and other physiological or functional abnormalities with a genetic basis. Cohort characteristics and health-care utilization measures were analyzed. Discharges with a GD-associated primary diagnosis were used to estimate the minimum burden; discharges with GD-associated primary or secondary codes established the maximum burden.
- **Results**: Of 5.85 million weighted discharges, 2.6-14% included GD-associated ICD-9-CM codes. For these discharges, mean total costs were $16,000-77,000 higher (P < 0.0001) in neonates and $12,000-17,000 higher (P < 0.0001) in pediatric patients compared with background, corresponding to significantly higher total charges and lengths of stay. Aggregate total charges for suspected GD accounted for $14 to $57 billion (11-46%) of the "national bill" for pediatric patients in 2012.
- **Conclusion**: Pediatric inpatients with diagnostic codes linked to genetic disease have a significant and disproportionate impact on resources and costs in the US health-care system.” https://pubmed.ncbi.nlm.nih.gov/30568310/

2.Schroeder BE, Gonzaludo N, Everson K, et al. The diagnostic trajectory of infants and children with clinical features of genetic disease. NPJ Genom Med. 2021;6(1):98. Published 2021 Nov 22. doi:10.1038/s41525-021-00260-2

- **Abstract:** “We characterized US pediatric patients with clinical indicators of genetic diseases, focusing on the burden of disease, utilization of genetic testing, and cost of care. Curated lists of diagnosis, procedure, and billing codes were used to identify patients with clinical indicators of genetic disease in healthcare claims from Optum's de-identified Clinformatics® Database (13,076,038 unique patients). Distinct cohorts were defined to represent permissive and conservative estimates of the number of patients. Clinical phenotypes suggestive of genetic diseases were observed in up to 9.4% of pediatric patients and up to 44.7% of critically-ill infants. Compared with controls, patients with indicators of genetic diseases had higher utilization of services (e.g., mean NICU length of stay of 31.6d in a cohort defined by multiple congenital anomalies or neurological presentations compared with 10.1d for patients in the control population (P < 0.001)) and higher overall costs. Very few patients received any genetic testing (4.2-8.4% depending on cohort criteria). These results highlight the substantial proportion of the population with clinical features associated with genetic disorders and

underutilization of genetic testing in these populations." https://pubmed.ncbi.nlm.nih.gov/34811359/

3.Yang, G., Cintina, I., Pariser, A. et al. The national economic burden of rare disease in the United States in 2019. Orphanet J Rare Dis 17, 163 (2022). https://doi.org/10.1186/s13023-022-02299-5

- **Abstract:** "Background: To provide a comprehensive assessment of the total economic burden of rare diseases (RD) in the United States (U.S.) in 2019. We followed a prevalence-based approach that combined the prevalence of 379 RDs with the per-person direct medical and indirect costs, to derive the national economic burden by patient age and type of RD. To estimate the prevalence and the direct medical cost of RD, we used claims data from three sources: Medicare 5% Standard Analytical File, Transformed Medicaid Statistical Information System, and Optum claims data for the privately insured. To estimate indirect and non-medical cost components, we worked with the rare disease community to design and implement a primary survey.
- **Results**: There were an estimated 15.5 million U.S. children (N = 1,322,886) and adults (N = 14,222,299) with any of the 379 RDs in 2019 with a total economic burden of $997 billion, including a direct medical cost of $449 billion (45%), $437 billion (44%) in indirect costs, $73 billion in non-medical costs (7%), and $38 billion (4%) in healthcare costs not covered by insurance. The top drivers for excess medical costs associated with RD are hospital inpatient care and prescription medication; the top indirect cost categories are labor market productivity losses due to absenteeism, presenteeism, and early retirement.
- **Conclusions**: Our findings highlight the scale of the RD economic burden and call for immediate attention from the scientific communities, policy leaders, and other key stakeholders such as health care providers and employers, to think innovatively and collectively, to identify new ways to help improve the care, management, and treatment of these often-devastating diseases." https://pubmed.ncbi.nlm.nih.gov/35414039/

4.EveryLife Foundation. The Cost of Delayed Diagnosis in Rare Disease: A Health Economic Study. 2023 Sept. https://everylifefoundation.org/wp-content/uploads/2023/09/EveryLife-Cost-of-Delayed-Diagnosis-in-Rare-Disease_Final-Full-Study-Report_0914223.pdf

- **Abstract:** "The economic impact of a delayed diagnosis is up to $517,000 in avoidable costs per patient. Shortening the more than six-year average diagnostic odyssey saves money for individuals, caregivers, and the healthcare system, while improving health outcomes by:
  - Providing earlier access to supportive therapies and treatment
  - Delaying or preventing disease complications and physical disabilities
  - Reducing or eliminating costly and unnecessary services or procedures"

https://everylifefoundation.org/delayed-diagnosis-study/#about-study