Undiagnosed Diseases Network

Quarterly Report

Summer 2026

Website: udnconnect.org
Contact email: UDN@hms.harvard.edu

Data through June 30, 2026

About the UDN

Mission: Our mission is to equitably provide diagnoses for patients with the most challenging conditions through multidisciplinary collaboration and exploration of new diagnostic approaches, advancing scientific discovery and sharing advances with the broader community.

Vision: We envision a world in which an evidence-based, collaborative approach ends the diagnostic odyssey for all with undiagnosed conditions, advances the science of disease identification, and delivers exceptional care for patients and families.

Values: Equity, Collaboration, Innovation, Partnership, Patient-centeredness, Discovery, Inclusive access, Community, Continuous improvement, Dedication, Integrity

Recent Publications

RNU4ATAC-opathy: Clinical, molecular and transcriptomic insights from a large cohort (Genetics in Medicine, PMID: 42322193)

Ensilication preserves high-molecular weight native DNA for clinical long-read sequencing (Genome Biology, PMID: 42298673)

MAJIQ-CLIN: A novel tool to help identify Mendelian disease-causing variants from RNA-Seq data (Genetics in Medicine, PMID: 42267532)

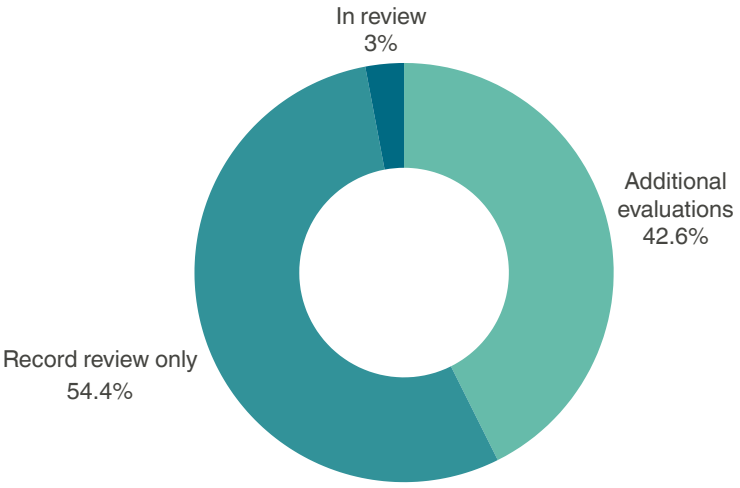
Bi-allelic loss-of-function variants in *TMEM63B* cause syndromic surfactant dysfunction disorder (American Journal of Human Genetics, PMID: 42259295)

Monoallelic *PSMB8* variants cause PRAAS with immunodeficiency through impaired immunoproteasome assembly (American Journal of Human Genetics, PMID: 42167218)

Latest Numbers

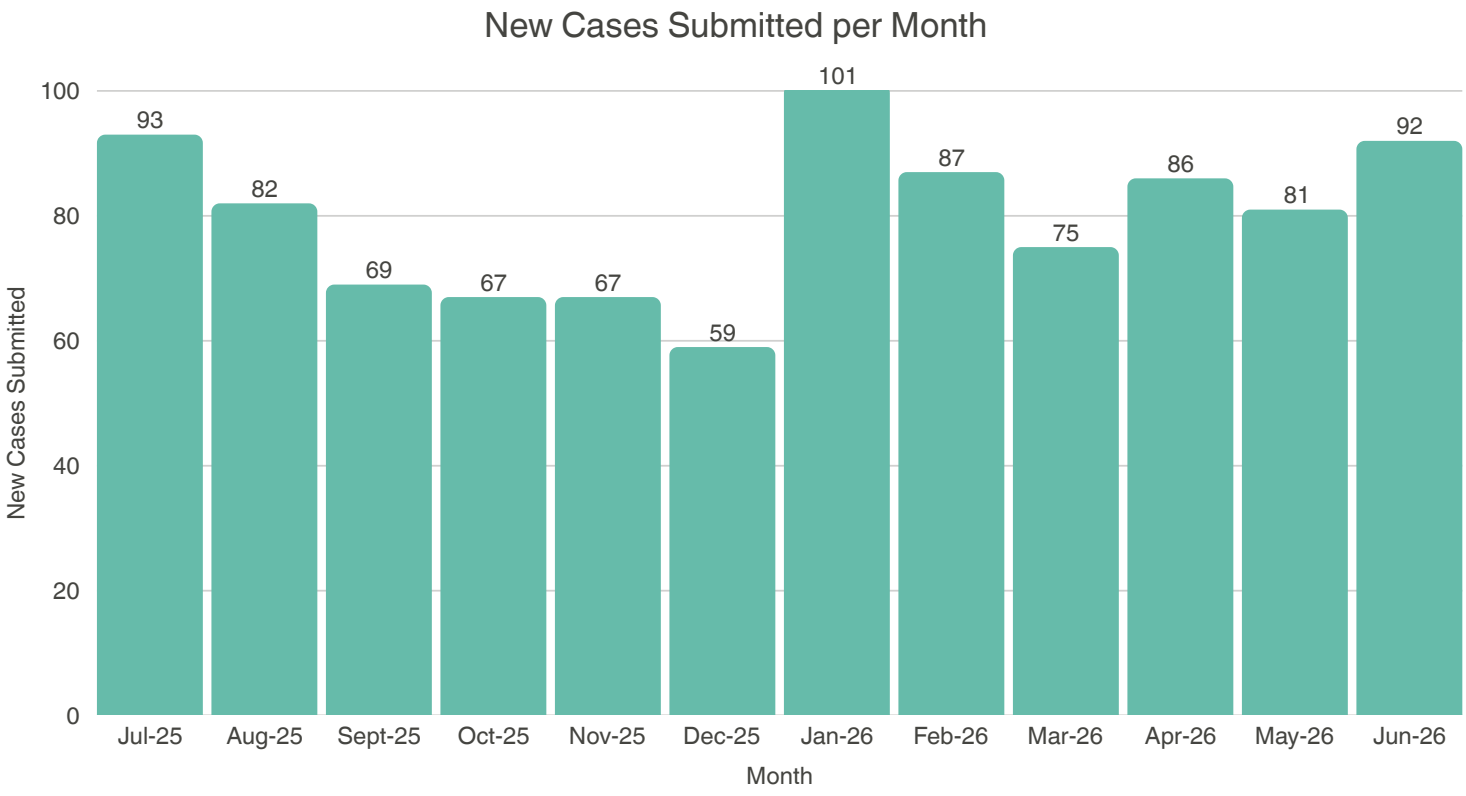
Of 8,967 cases submitted, 3,822 cases were assigned to additional telehealth, in-person, or research evaluations.

Participants come from every U.S. state, the District of Columbia, and 54 countries. Currently, there are 266 cases undergoing review. Not all participants are assigned for additional evaluations after medical record review. Participants assigned to receive medical record review only may receive useful feedback about their condition.



Participants present with a wide variety of symptoms, with neurologic symptoms being the most common clinical presentation (41%).

Of the participants assigned for additional evaluations, 50% are female, and 60% are under 18 years old. 66% of participants assigned for additional evaluations identify as non-Hispanic white.



Undiagnosed Diseases Network

Evaluation Process

As part of the UDN evaluation process, multiple specialists are consulted to provide input on each individual case. Often, participants are evaluated by these specialists at one of the UDN clinical sites. In cases where participants are not able to travel to a UDN site or additional in person evaluations are deemed unnecessary, telehealth visits may be performed.

To date, 3,334 participants have been evaluated in-person or via telehealth.

Diagnoses

Providing diagnoses to participants is a central goal of the UDN. Thus far, 1,093 certain or highly likely diagnoses (in 1,054 participants) have been identified.

The majority of diagnoses (78.5%) have been made through genome-scale sequencing. Other diagnoses were made primarily based on clinical grounds (7.8%) or directed clinical testing based on phenotype (8.7%). The remaining 5% of diagnoses were made through other testing methods, including genome-wide assays such as karyotype and chromosomal microarray.

97

Conditions have been newly described

180

Diagnoses have been made based on clinical grounds or through directed clinical testing

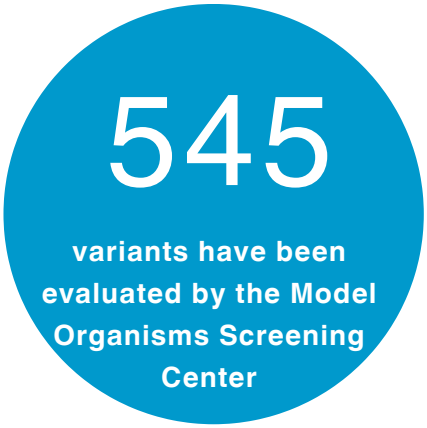
39

Participants have more than one diagnosis

Model Organisms

The UDN Model Organisms Screening Center (MOSC) is composed of three centers that use fruit fly (*Drosophila melanogaster*), nematode worm (*C. elegans*) and zebrafish (*Danio rerio*) genetics to evaluate the impact and function of genetic variants identified through the UDN.

Between May 24, 2017 and June 30, 2023, the MOSC received 179 gene submissions and 103 were accepted for modeling in fly, worm, and/or zebrafish. Positive functional data were obtained for 54 submissions (52.4%), contributing to 22 manuscripts that describe novel disease genes, phenotypic expansions, and pathogenic mechanisms of newly identified conditions.



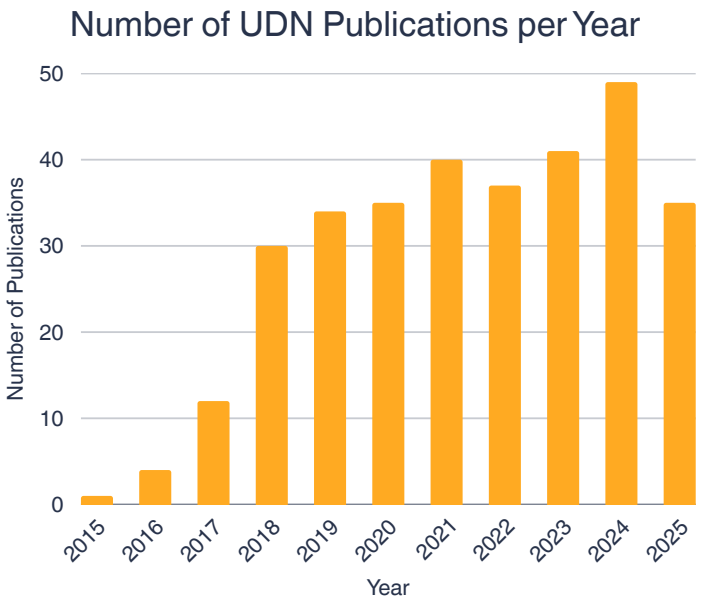
Exome and Genome Sequencing

2,594 participants have undergone exome and/or genome sequencing through the UDN. This figure includes both exome and genome sequencing, but is most often genome sequencing. Many participants had non-diagnostic exome sequencing prior to enrollment in the UDN.

RNA Sequencing

The UDN uses next-generation RNA sequencing methods to analyze the transcriptome of select UDN participants. RNA sequencing has the capability to quantify gene expression and can also facilitate the discovery of novel transcripts, identification of alternatively spliced genes, and detection of allele-specific expression.

Data Sharing



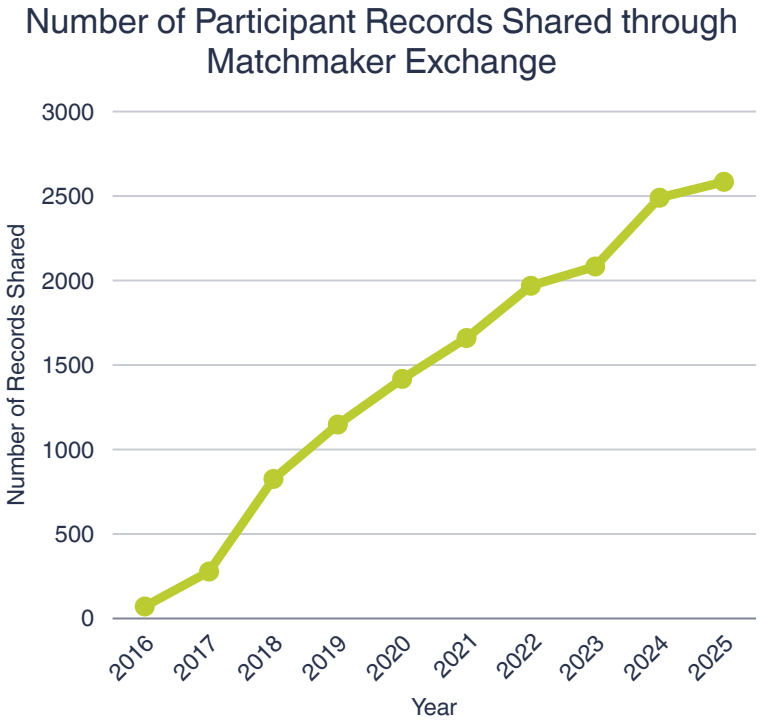
The UDN is committed to collecting and sharing data in useful, sustainable, and responsible ways. In addition to sharing data in relevant research repositories as described below, for those participants who would like to do so, the UDN shares their information via participant pages on the UDN website to identify other similar patients. Investigators also disseminate UDN research by publishing in the scientific literature. The graph on the left shows the number of UDN publications per year since the launch of the UDN in 2015.

Genomic Data

Genomic data are shared in the database of Genotypes and Phenotypes (dbGaP) under accession phs001232.

Variant-level Data

Variant-level data are submitted to ClinVar, shared across the Matchmaker Exchange, and posted on the UDN website to facilitate collaborations and connections among researchers and families. The graph on the right shows the number of participant records shared across the Matchmaker Exchange over time.



1074

Variant interpretations submitted to ClinVar

2584

Records shared across Matchmaker Exchange

233

Participant pages published on UDN website