SCID: Long Term Follow-Up: USIDNET and PI connect

Severe Combined Immunodeficiency (SCID)
National In-Person Meeting, August 8-9 2017

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USIDNET IMMUNODEFICIENCY NETWORK

"Resources to assist investigations in Primary Immunodeficiency Diseases"

USIDNET: cooperative agreement between
the
Immune Deficiency Foundation
and
National Institutes of Health

1. Education and mentoring
2. Repository for cells, DNA and other materials
3. Establish a Patient Registry

2003 -

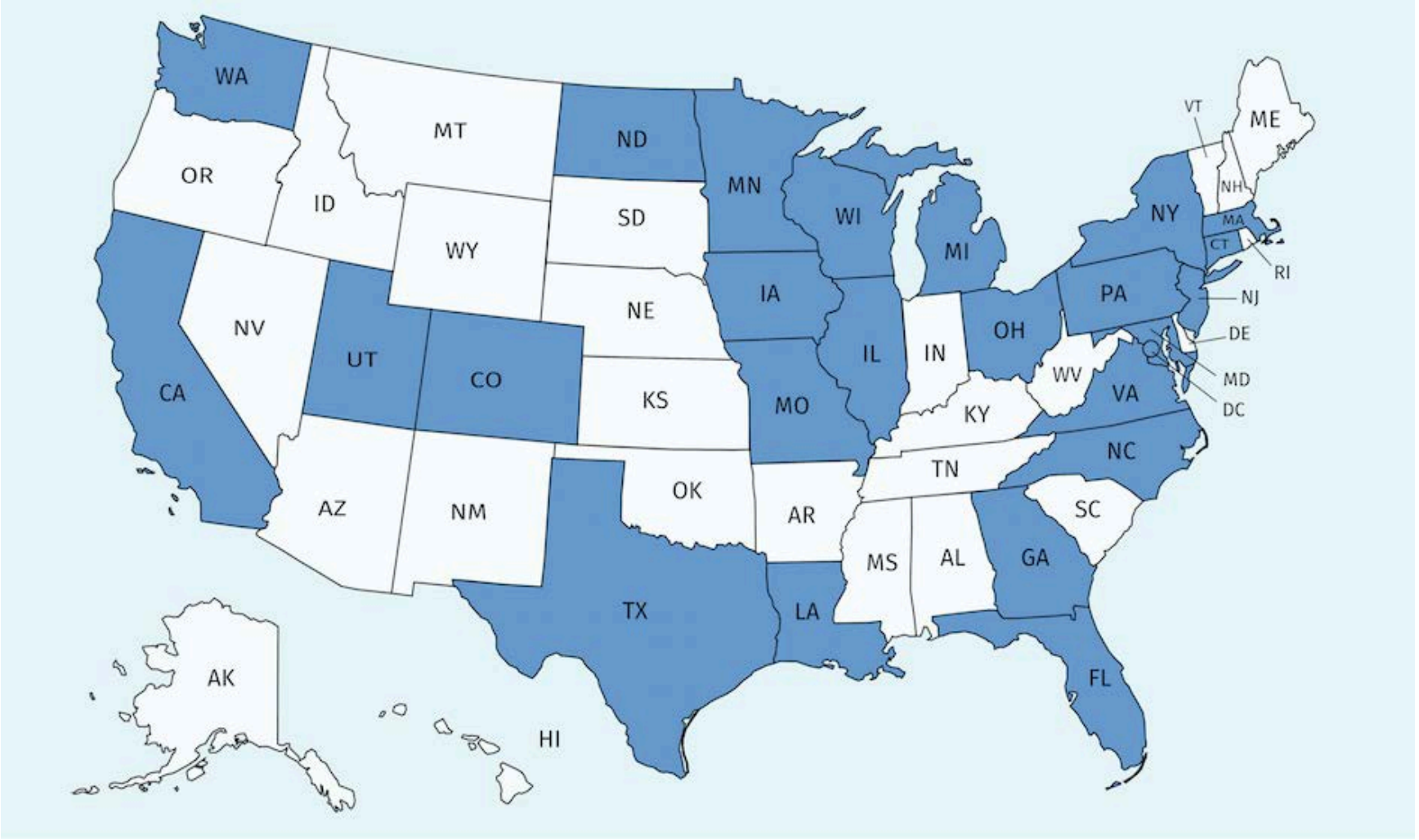
USIDNET
a program of IDF

Purpose of the Registry

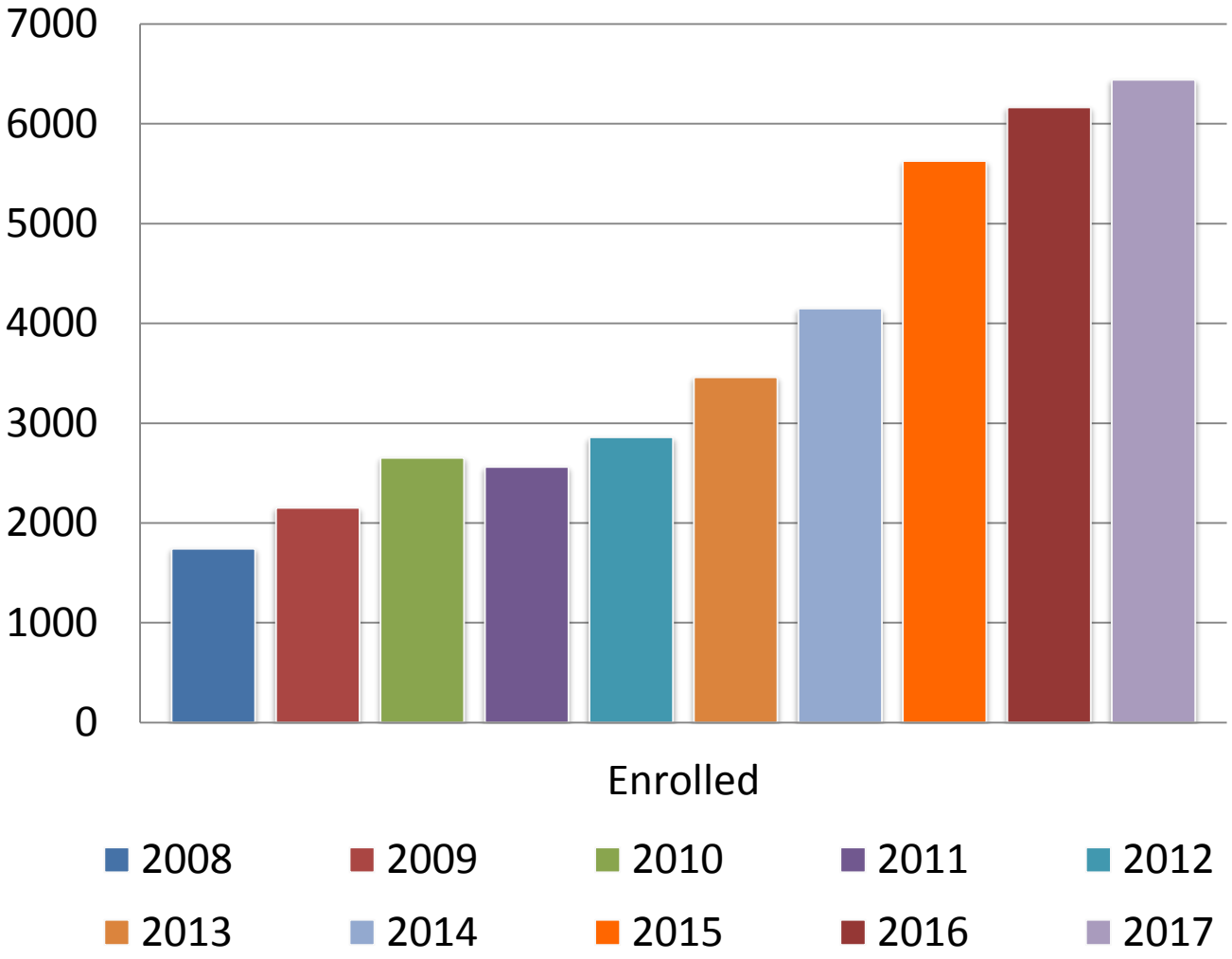
- Collect clinical and laboratory data on patients with these rare diseases.
- Define the natural history of these diseases
- Promote recognition of these defects
- Identify optimal therapies
- Improved research efforts
- Investigate what leads to better quality of life

USIDNET.org

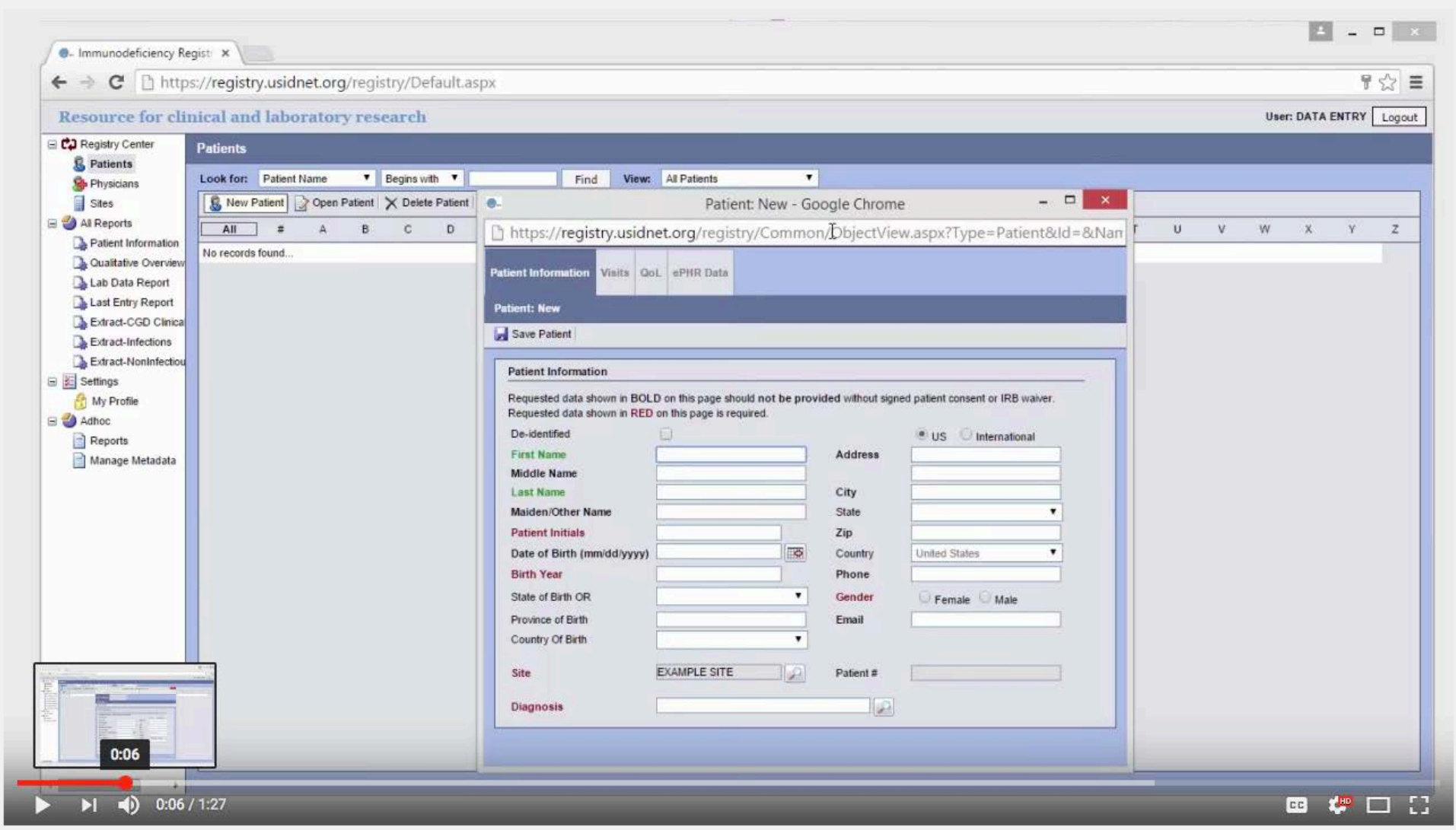
USIDNET enrolling sites - 2017



Overall Enrollment: 6,441 patients

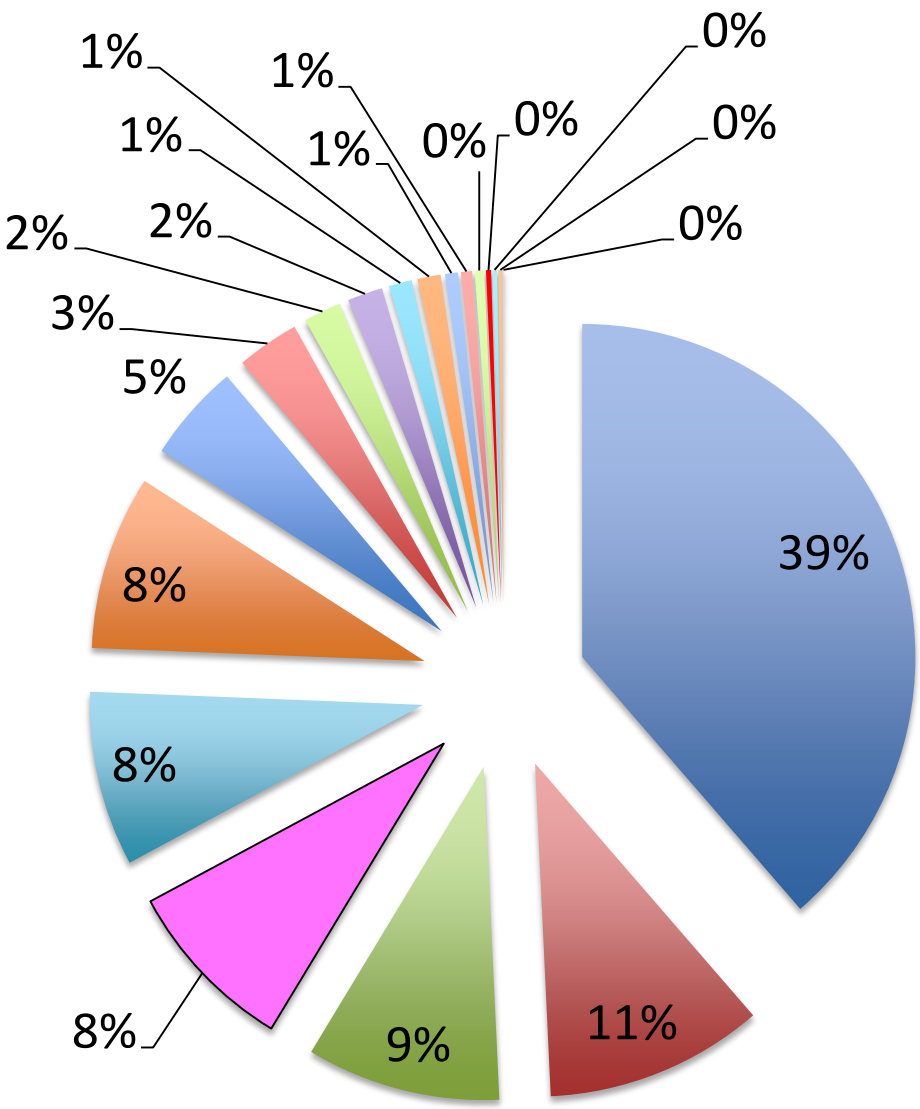


Video: instructions



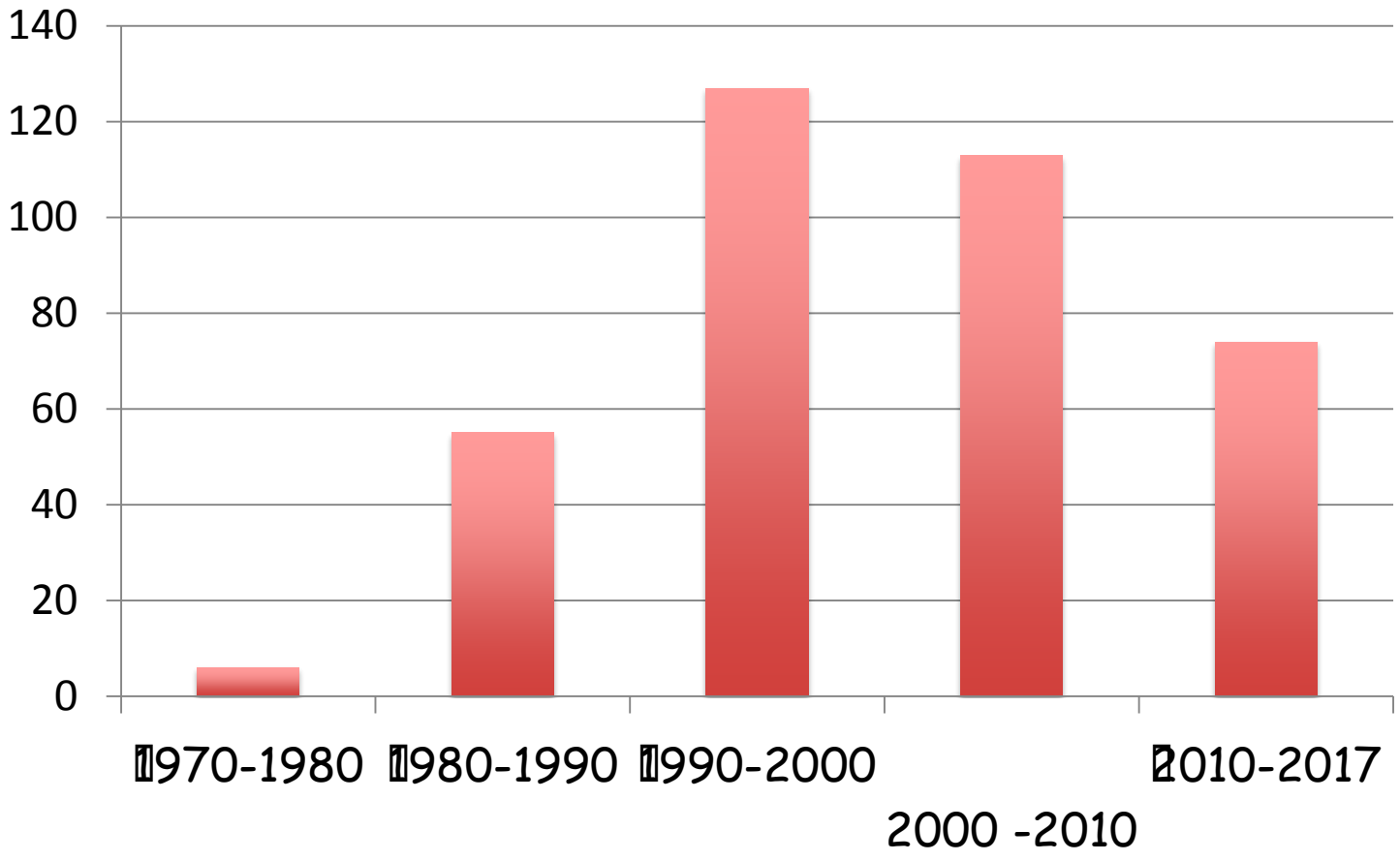
Creating a Patient Record

Diagnoses in USIDNET Registry

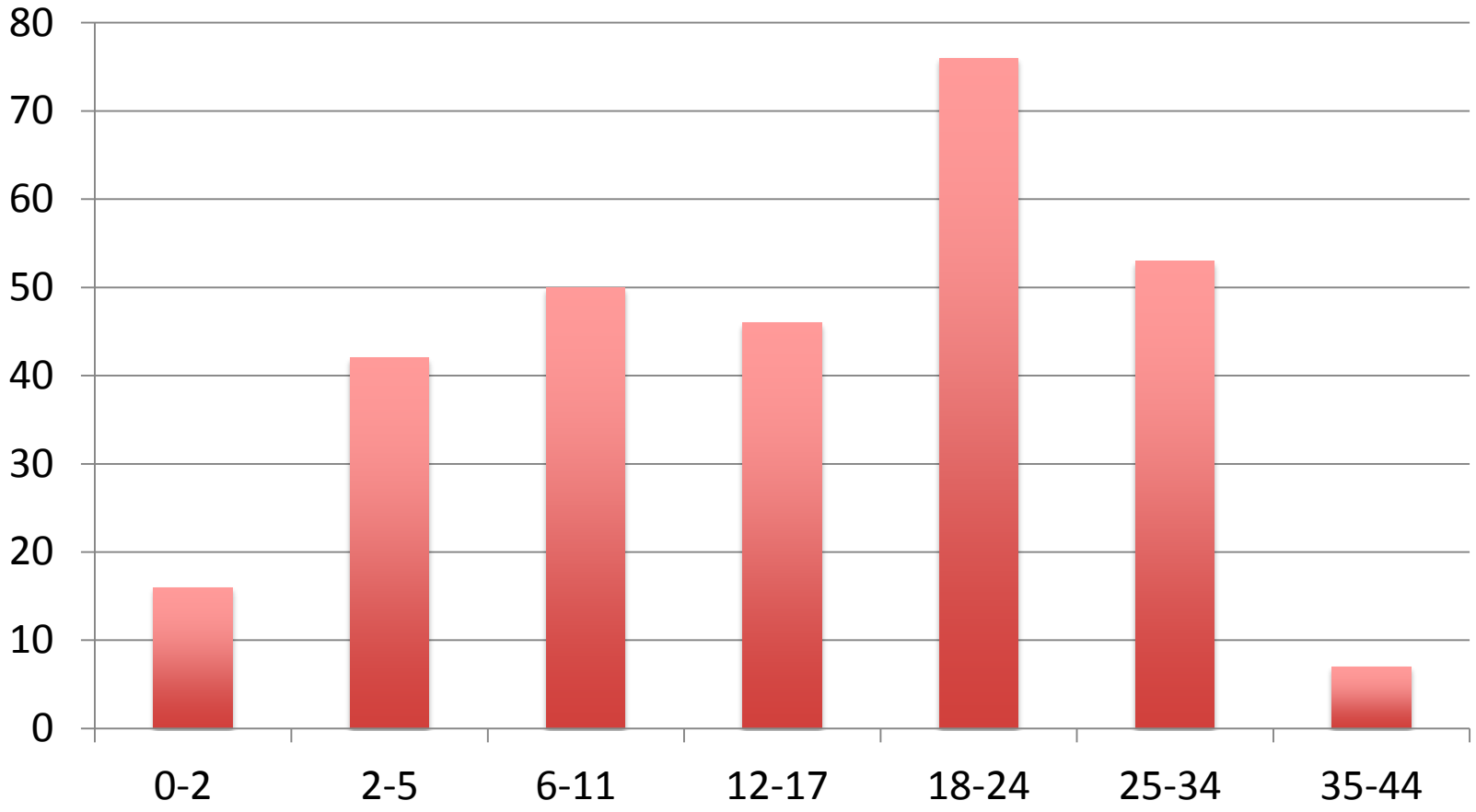


- Antibody defect
- CGD
- Unclassified
- SCID/CID
- Thymic defects
- Agammaglobulinemia
- Wiskott Alcrich
- Class switch
- Hyper IgE
- Innate
- HLH
- Mucocutaneous Candidiasis
- Immune dysregulation
- Complement
- DNA repair
- APLS
- Neutrophil defects
- Autoinflamatory
- Dyskeratosis

SCID Year of birth (n=377)

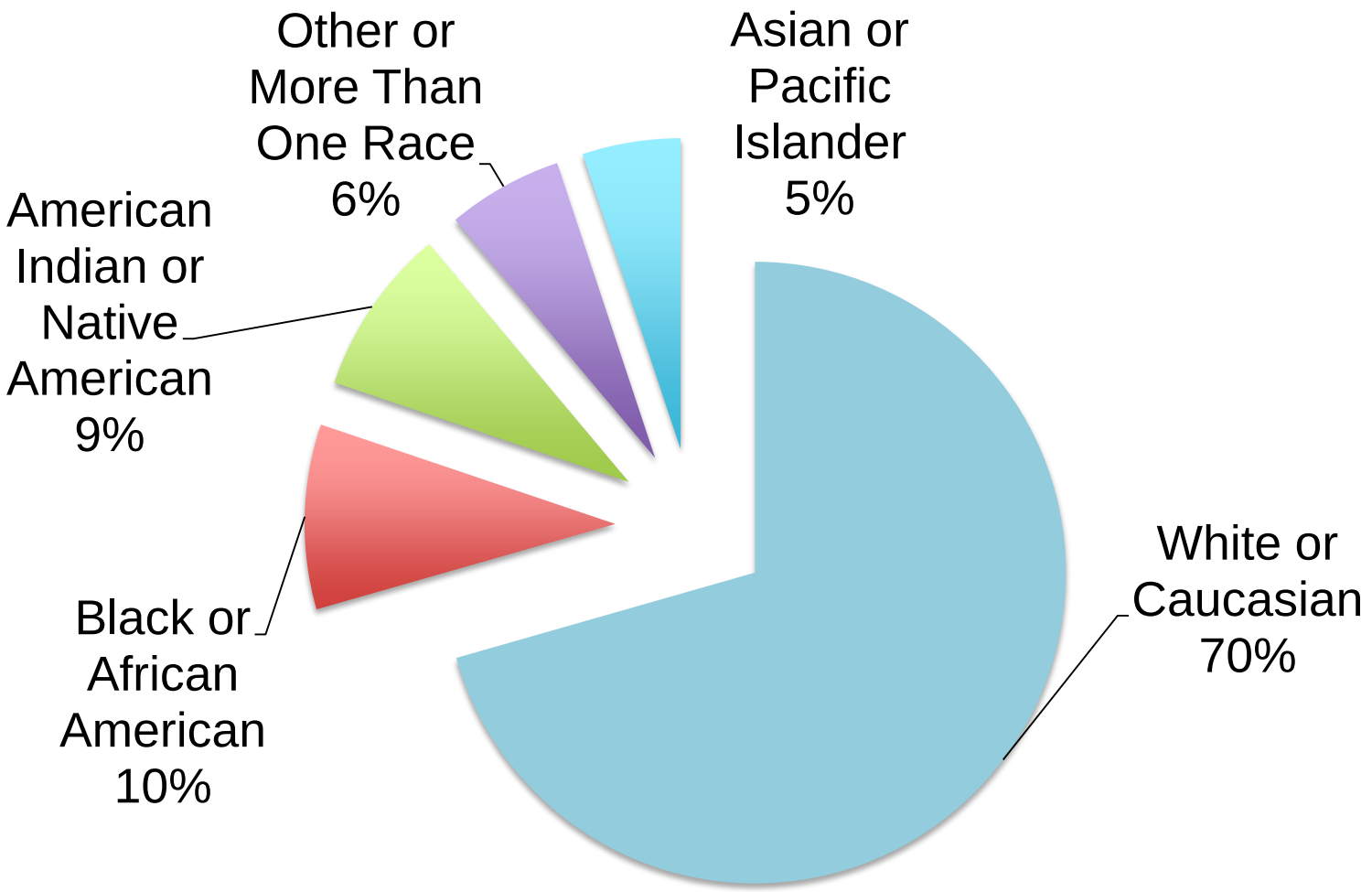


USIDNET: SCID: Age N = 280



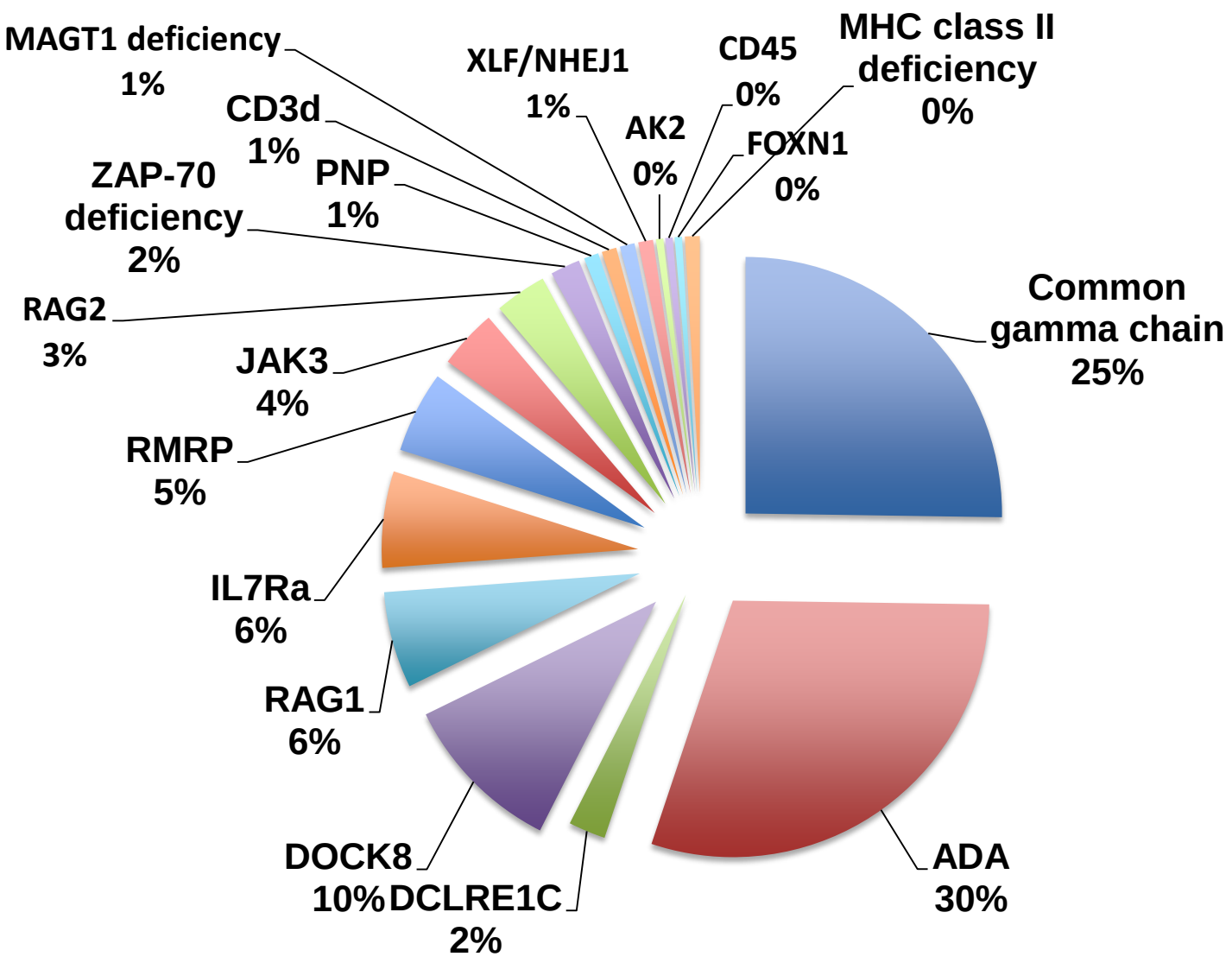
ALIVE	280
DECEASED	86
UNKNOWN	10

USIDNET: SCID Demographics (n=333)



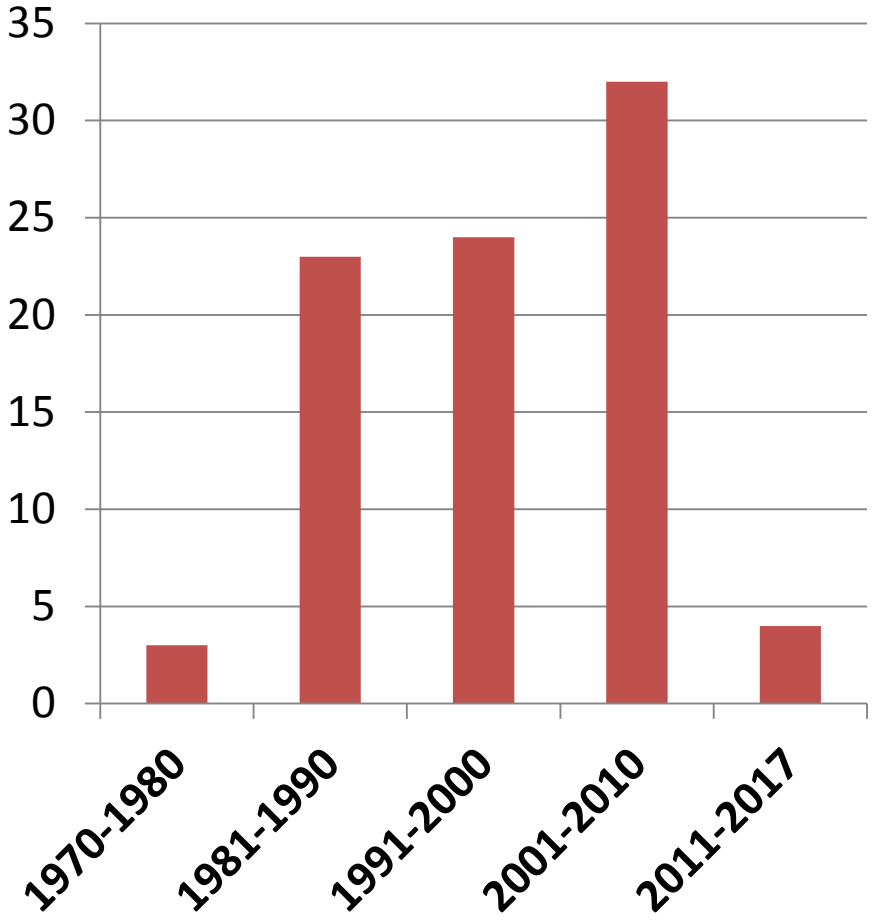
243 =Males; 134 Females

USIDNET: SCID: Genetics (n=282)



Deaths (86)

Years of Birth



Genetic types

ADA	11
Artemis	11
IL2 Common gamma	9
DOCK8	6
Unknown or other	4
RAG	3
JAK3	2
CHH	1
PNP	1
MAGT-1	1
IL-7Ra	1

Top 15 conditions at enrollment

Condition	Numbers
Diarrhea (Chronic)	88
Lymphopenia	66
Failure to thrive or weight loss	64
Anemia	59
Fever	56
Diarrhea (Intermittent)	51
Asthma	51
GE reflux	45
Neutropenia	44
Hypertension	41
Atopic dermatitis/eczema	41
Underweight	38
Developmental delay	35
Abdominal pain	32
Liver function abnormalities	31

An additional project

“Following Infants with Low Lymphocytes”

“FILL” Program

The FILL Program

Following Infants with Low Lymphocytes

- With support of a grant to the Clinical Immunology Society from the Jeffrey Modell Foundation, USIDNET is collecting data on infants with low lymphocytes identified by abnormal TRECs on NBS.
- Objective: Infants are identified by NBS, who have low lymphocytes for many medical reasons, not all of these understood.
- This study is collecting demographic, immunologic, treatment and outcome data on these infants.

jm Jeffrey Modell Foundation
Curing PI. Worldwide.

USIDNET
a program of IDF

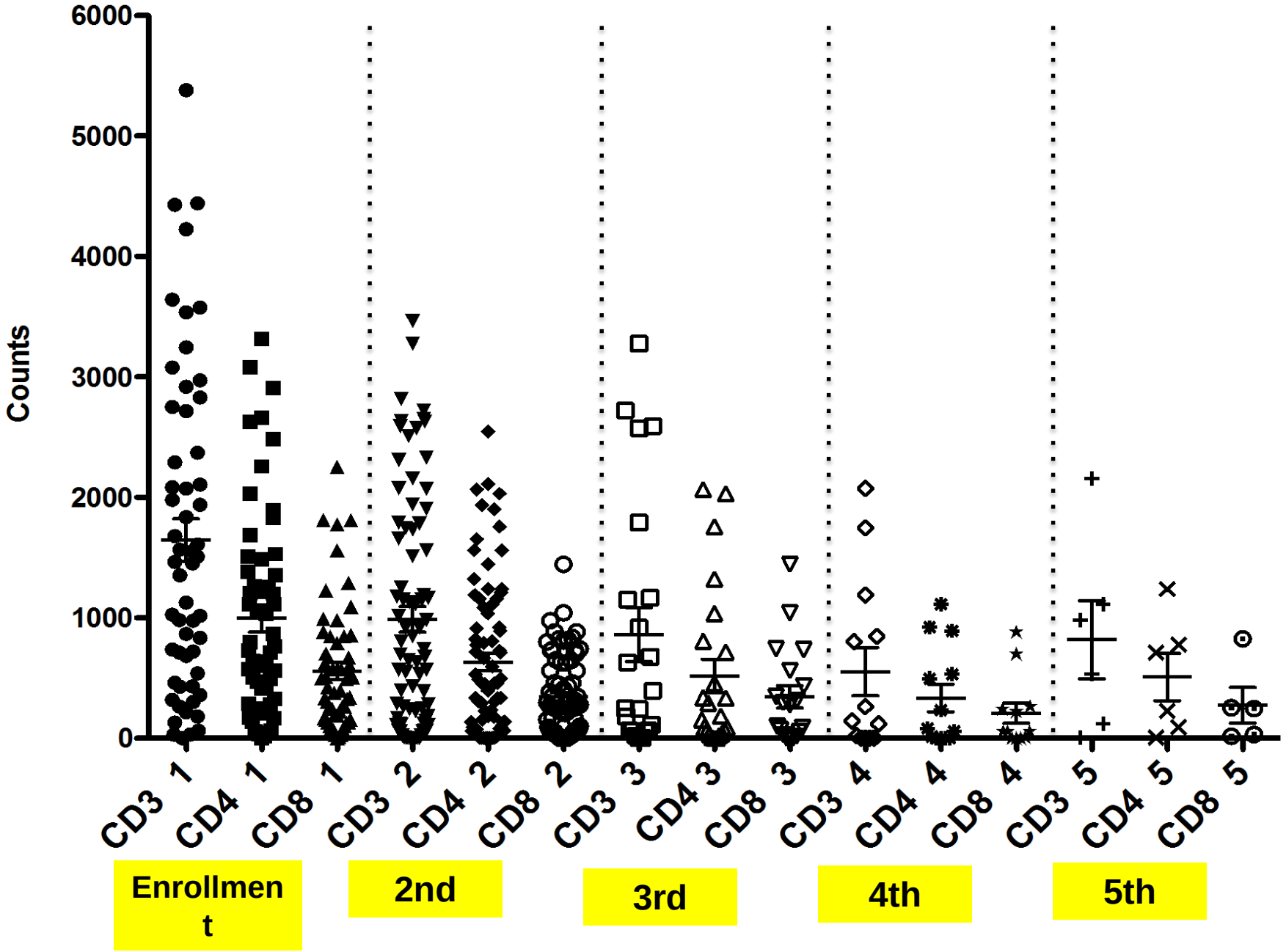
CIS Clinical Immunology Society

71 infants*

Best Diagnosis	Initial Evaluation
Idiopathic T lymphopenia / or unknown at this time	28
No significant T lymphopenia or normal	1
Preterm birth alone	4
SCID/leaky SCID/Omenn syndrome*	26
Secondary T lymphopenia	5
Syndrome with variable T cell impairment (CHARGE syndrome)	1
Syndrome with variable T cell impairment (DiGeorge/22q deletion (or TBX1 mutation))	1
Syndrome with variable T cell impairment (Jacobsen syndrome)	1
Syndrome with variable T cell impairment (XLP- type 2)	1

- **ADA, balanced translocation 3/14, BCL11B, BRIP1, CHD7, Common gamma chain, IL7R, JAK3, RAG1, RAG2, TBX1**

Lymphocyte phenotypes of enrolled infants over time

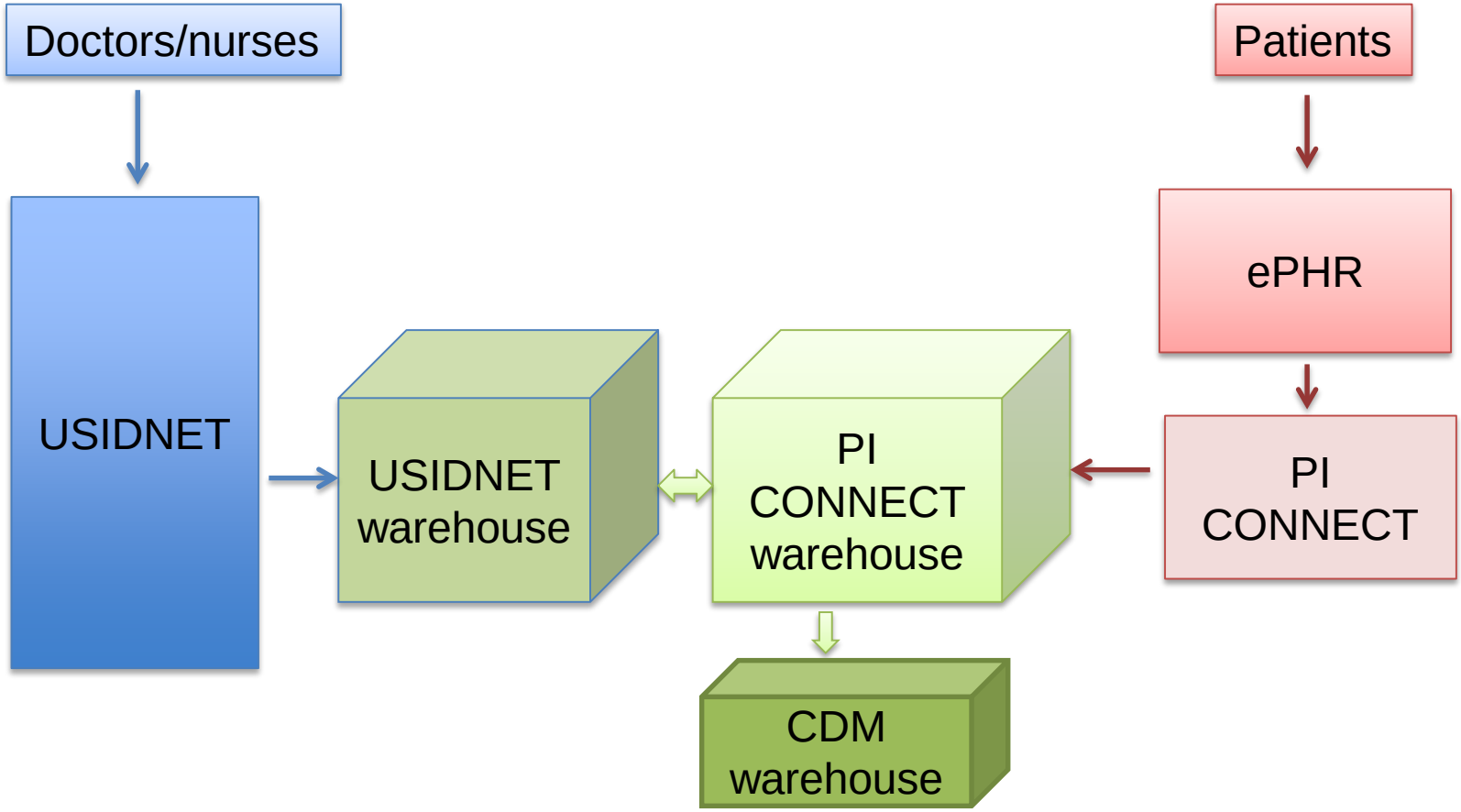


How can patients and families get involved in USIDNET research?

- Patients create an IDF ePHR account,
- With one click one can consent into **PI CONNECT**
- This allows data to become a part of the USIDNET Registry.
- Consent can done on any computer, Ipad or smart phone.
- Then sign consent to have records released
- Improves longitudinal and quality of life data

USIDNET **PI CONNECT**

The concept



Goals of PI CONNECT

- Develop an integrated community of people with an interest in research in primary immune deficiencies
  - Engage patients in developing the research portfolio
  - Engage clinicians in results
  - Engage researchers to pursue patient-oriented research

Synergies

- **Strong lab data**
- **Weak on longitudinal (20%)**
- **6441 discrete patients**
- **Validated diagnoses**
- **No patient entries**
- **May miss interim diagnoses**

- **Better personal data**
- **More longitudinal data**
- **2109 discrete “patients”**
- **Diagnoses not validated**
- **Lab data weak**
- **Participation spotty**

Goals of PCORnet

- PI CONNECT is one of 18 patient groups
- There are 11 large health consortia

- PCORnet is a large network of data that is meant to support research
  - Agreeing on consistent nomenclature
  - Agreeing on consistent data collection
  - Prioritizing research questions

pcori®

Patient-Centered Outcomes Research Institute

PI CONNECT
IDF Patient-Powered Research

- Bonus to joining PI CONNECT is exclusive access to the PI CONNECT Research Forum. On the forum one can:
- See research questions as they're posed and offer opinions about them.
- Propose research questions that matter.
- Track personal data and see how this compares to others with the same disease.
- Have ideas heard and translate them into action

Recent Publications

- Sanchez LA, Maggadottir SM, Pantell MS, Lugar P, Rundles CC, Sullivan KE; USIDNET Consortium. Two Sides of the Same Coin: Pediatric-Onset and Adult-Onset CVID. J Clin Immunol. 2017 Jul 28.
- Mayor PC, Eng KH, Singel KL, Abrams SI, Odunsi K, Moysich KB, Fuleihan R, Garabedian E, Lugar P, Ochs HD, Bonilla FA, Buckley RH, Sullivan KE, Ballas ZK, Cunningham-Rundles C, Segal BH. Cancer in primary immunodeficiency diseases: Cancer incidence in USIDNET. J Allergy Clin Immunol. 2017
- Hajjar J, Guffey D, Minard CG, Orange JS. Increased Incidence of Fatigue in Patients with Primary Immunodeficiency Disorders: Prevalence and Associations Within the USIDNET. J Clin Immunol. 2017;37(2):153-165.
- Hartman H, Schneider K, Hintermeyer M, Bausch-Jurken M, Fuleihan R, Sullivan KE, Cunningham-Rundles C, Bonilla FA; USIDNET Consortium, Verbsky J, Routes J. Lack of Clinical Hypersensitivity to Penicillin Antibiotics in Common Variable Immunodeficiency. J Clin Immunol. 2017;37(1):22-24.
- Leven EA, Maffucci P, Ochs HD, Scholl PR, Buckley RH, Fuleihan RL, Geha RS, Cunningham CK, Bonilla FA, Conley ME, Ferdman RM, Hernande Trujillo V, Puck JM, Sullivan K, Secord EA, Ramesh M, Cunningham-Rundles C. Hyper IgM Syndrome: a Report from the USIDNET Registry. J Clin Immunol. 2016;36(5):490-501.
- Al-Herz W, Notarangelo LD, Sadek A, Buckley R; USIDNET Consortium. Combined immunodeficiency in the United States and Kuwait: Comparison of patients' characteristics and molecular diagnosis. Clin Immunol. 2015;161(2):170-3.

USIDNET Partners

American Academy of Allergy Asthma & Immunology

Clinical Immunology Society

European Society for Immunodeficiencies

National Institute of Allergy and Infectious Diseases

Leading research to understand, treat, and prevent infectious, immunologic, and allergic diseases.