PRIMARY IMMUNODEFICIENCY DISEASES IN AMERICA: 2007

THE THIRD NATIONAL SURVEY OF PATIENTS

The National Patient Organization Dedicated to Advocacy, Education and Research for Primary Immunodeficiency Diseases

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Overview

The Immune Deficiency Foundation (IDF) conducted its Third National Survey of Patients with Primary immunodeficiency diseases (PIDD) in the fall of 2007. A total of more than 1,500 patients with diseases completed a two-page, self administered questionnaire as part of the survey. The survey was conducted by mail by the Immune Deficiency Foundation.

A national survey of the prevalence of primary immunodeficiency diseases was conducted in 2005 by the Immune Deficiency Foundation. A national sample of 10,000 households sampled by random digit dialing (RDD) with nearly 30,000 household members was screened to identify persons who had been diagnosed with primary immunodeficiency diseases. This national probability survey found the prevalence of diagnosed primary immunodeficiency diseases to be about 1 in 1200 persons in the United States. Although the prevalence of primary immunodeficiency diseases is higher than many "rare" diseases, it is too low to yield sample sizes large enough to permit generalizable estimates of the characteristics of patients and their treatment with probability samples.

At the time of the current survey, the only national estimates of the characteristics and experiences of patients with primary immunodeficiency diseases were from the previous two National Patient Surveys conducted by IDF in 1996/1997, and again in 2002. Nearly 3,000 persons with a diagnosis of a primary immunodeficiency disease participated in the first survey, while more than 1,500 participated in the second. These surveys provided estimates of the size and distribution of the population with primary immunodeficiency diseases in the United States at the time they were conducted. In an effort to obtain a more current picture of IDF patients and their experiences in the United States, the Immune Deficiency Foundation conducted a third National Survey of Patients with Primary Immunodeficiency Diseases in the fall of 2007.

The new patient sample was identified in much the same way as it was for the second survey. The IDF database was used as the sampling frame from the survey. The survey was limited to patients who had not participated in the two previous surveys. The questionnaire was designed to provide comparability to the 1996/1997 and 2002 surveys. A total of 2,704 likely patients from the IDF database were mailed the new questionnaire in the fall of 2007. More than 1,300 new patients with a diagnosis of primary immunodeficiency disease completed and returned the questionnaire by the end of January 2008.

The survey was funded by an unrestricted educational grant from Talecris.

Background: Immune Deficiency Diseases

Primary immunodeficiency diseases represent a class of disorders in which there is an intrinsic defect in the human immune systems (rather than immune disorders that are secondary to infection, chemotherapy, or some other external agent). In some cases, the body fails to produce any or enough antibodies to fight infection. In other cases, the cellular defenses against infection fail to work properly. There are more than 150 different primary immunodeficiency diseases currently recognized by the World Health Organization.

Medical recognition of primary immunodeficiency disease is a little more than fifty years old. Although these disorders may have existed in antiquity, it was not until the development of antibiotics that infections could be controlled long enough to recognize there was an underlying defect in the immune system. In addition, the parallel development of gamma-globulin in World War II provided a replacement therapy for the antibody deficiency forms of immune deficiency.

The major health surveys conducted by the government in the United States, the National Health Interview Survey and the National Health and Nutrition Examination Survey, do not collect information on primary immunodeficiency diseases. No comprehensive population survey has even been undertaken by the federal government to estimate the prevalence or the population characteristics of these diseases in the United States. The 2005 prevalence survey conducted by the Immune Deficiency Foundation provides the first reliable estimate of the prevalence of diagnosed primary immunodeficiency diseases in the United States. However, a probability sample of 10,000 households yielded only 23 cases of primary immunodeficiency diseases, which is too small to yield reliable estimates of the characteristics of patients and their treatment. Hence, although these diseases are clinically described in the medical literature, there is no comprehensive portrait available of the patient with primary immunodeficiency disease.

First National Survey of Patients with Primary Immune Deficiency Diseases

In 1995, the Immune Deficiency Foundation undertook the first national survey of the state of primary immunodeficiency diseases in the United States. This survey had a number of objectives. First, the survey sought to provide an estimate of the general magnitude of primary immunodeficiency in the American population, if not a precise estimate of population prevalence. Second, the survey sought to describe the general population characteristics of persons with these disorders. Third, the survey sought to describe the health of persons with primary immunodeficiency diseases. Fourth, the survey sought to identify problems in access to treatment in this population. All of these goals are related to the primary objective of the Immune Deficiency Foundation: improving the diagnosis and treatment of persons with primary immunodeficiency diseases. The survey was designed for IDF by Abt SRBI, Inc. (SRBI), a national public

opinion research organization. SRBI analyzed the survey data and prepared their report for IDF.

A national sample of 1,500 specialists who reported treating patients with primary immunodeficiency diseases had been identified in 1996. The physician sample was sent questionnaires for distribution to their patients with primary immunodeficiency disease. In addition, this questionnaire was sent to all self-identified patients in the IDF database. A total of nearly 3,000 questionnaires were completed and returned by unique patients in 1996 and 1997. This includes 1,289 adult patients, 1,190 parents or guardians of children with primary immunodeficiency diseases, and 335 where the respondents did not identify themselves as the patient or caregiver.

Second National Survey of Patients with Primary Immune Deficiency Diseases

In the fall of 2002, the Immune Deficiency Foundation undertook the second national survey of the state of primary immunodeficiency diseases in the United States. This survey was designed to supplement the 1996 survey. The IDF contact database provided the first stage in the construction of the sampling frame. Persons who were identified as being physicians, other health professionals, or other interested non-patients in the IDF database were eliminated from the sampling frame. Patients who had participated in the 1996 survey were also eliminated from the sampling frame for the second national survey. The approximately 6,000 cases remaining in the database after these two steps provided a sampling frame for the Second National Survey of Patients with Primary Immune Deficiency Diseases.

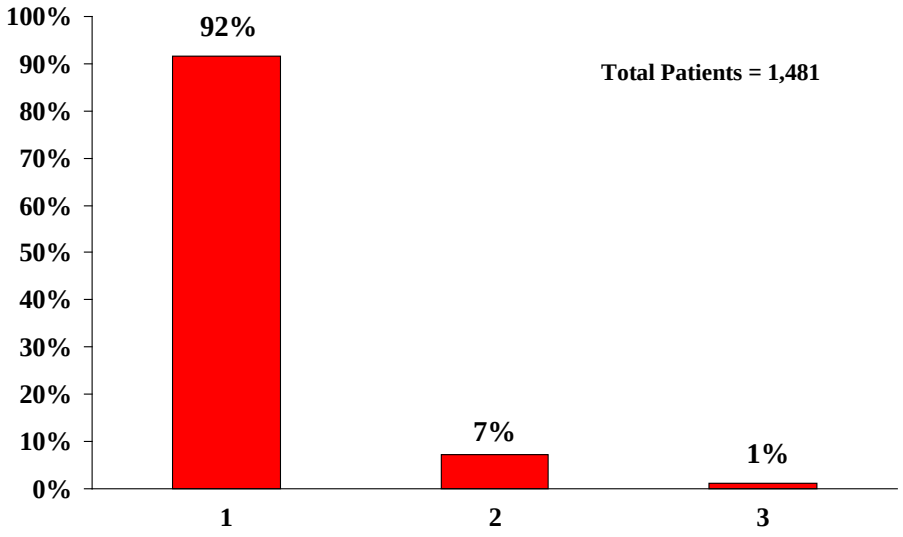
The first 1,000 cases from this frame were sent an advance letter in September 2002 inviting them to participate in the survey by Internet. They were provided a web address for the Internet survey and personal identification number to access the survey. However, less than ten percent of this sample contacted the survey website to begin the interview. Consequently, the remaining cases in the sample were mailed a two page (four sided) self-administered questionnaire, along with a cover letter explaining the purposes of the survey, and a postage paid return envelope. The first questionnaire mailing was conducted between 9/17/02 and 10/17/02. A second mailing to non-respondents was conducted on November 21, 2002.

A total of 1,587 completed short form questionnaires were returned by eligible respondents from the 5,922 cases in the sampling frame (26.8%). In addition, 49 cases were identified as deceased patients with primary immunodeficiency diseases. Another 18 cases had misdiagnosed, transient or treated immune deficiency diseases. Another 56 cases reported that they were patients, but their condition was not a primary immunodeficiency disease (e.g., autoimmune diseases).

Third National Survey of Patients with Primary Immunodeficiency Diseases

The Immune Deficiency Foundation undertook the third national survey of the state of primary immunodeficiency diseases in the United States in the fall of 2007. This survey was designed to build on the work done in the 1996 and 2002 surveys. The IDF contact database again provided the first stage in the construction of the sampling frame. Persons who were identified as non-patients in the IDF database, as well as those who participated in any of the previous Patient or Treatment surveys were eliminated from the sampling frame. The 2,704 remaining cases were mailed a two-page self-administered paper questionnaire, along with a cover letter explaining the purposes of the survey, and a postage paid return envelope. The first questionnaire mailing was conducted between 9/3/2007 and 10/4/07. A second mailing to non-respondents was conducted on October 8, 2007. A total of 1,351 completed short form questionnaires were returned by eligible respondents from the 2,704 cases (49.9%). The vast majority of these respondents reported only having one household member with PIDD (92%), but 7% reported having two household members with PIDD, and 1% reported having three or more PIDD patients in the household (Figure 1).

Figure 1
Number of Patients in the Household



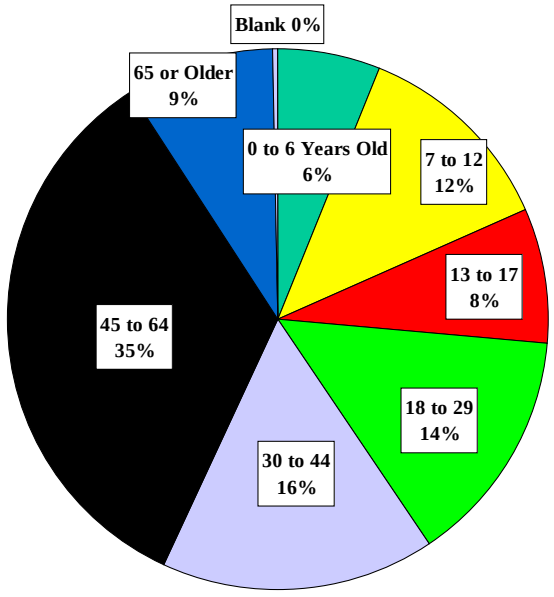
Q1. How many persons in your household have primary immune deficiency disease (PIDD)? (N=1,351)

Characteristics of the Patient Population

The Third National Patient Survey again confirms that primary immunodeficiency diseases are no longer a pediatric condition in the United States. Among the completed sample of patients with a primary immunodeficiency disease in the Third National Patient Survey, only 6% of the study subjects were six years of age or younger. Twelve percent were ages seven to twelve. Another 8% were adolescents, ages thirteen to seventeen. In total, about a quarter (26%) of the patient sample for the third national survey was under 18 years of age. Fourteen percent were young adults, ages 18 to 29. Sixteen percent of the patient population was 30 to 44 years old. Another 35% was middle aged, 45 to 64 years old. Nearly one in ten (9%) of immune deficient patients was age 65 or older (Figure 2).

The age distribution of persons in the household with primary immunodeficiency diseases in the 2007 survey is somewhat older than the age distributions for the first patient survey in 1996-1997 and the second patient survey conducted in 2002. The most recent patient survey found 26% of patients were under age 18, compared to 38% in the 2002 survey and 40% in the 1996/97 survey. Conversely, the proportion of patients aged 65 or older (9%) was slightly higher in the most recent survey, compared to 5% in 1996-97, compared to 4% in the survey conducted in 2002.

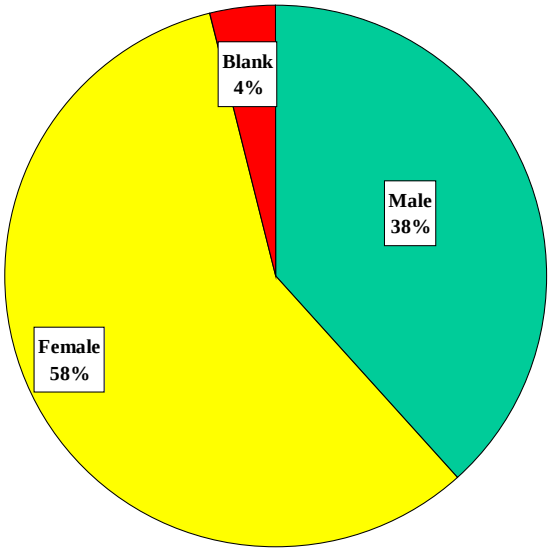
Figure 2
All Patients in Household by Age



Q2. What is the age and gender of these persons? (N=1,481)

The gender distribution of persons with primary immunodeficiency diseases in the third national survey is also shifting somewhat from previous surveys. Among the national sample of patients with primary immunodeficiency diseases, 38% were male and 58% were female. A small percentage (4%) did not indicate the gender of the patient (Figure 3). This proportion of males in the sample is somewhat lower than observed in the second survey in 2002 (42% male, 57% female), and significantly lower than the gender distribution of 48% male and 52% female in the first national survey.

Figure 3
All Patients in Household by Gender

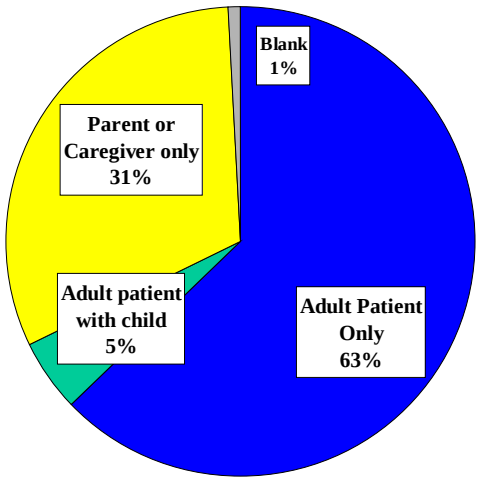


Q2. What is the age and gender of these persons? (N=1,481)

In the majority of households (63%) with any patients, there are one or more adult patients and no children with a primary immunodeficiency disease living in the household. In another 5% of households, there are both adults and children with primary immunodeficiency diseases living in the household. By contrast, there are children, but no adults, with primary immunodeficiency diseases living in 31% of households (Figure 4). It should be noted that parent and caregivers were likely to respond for college age children, aged 18-24, as well as legal minors.

In cases where there was more than one person with a primary immunodeficiency disease in a household, it was necessary to direct the survey recipient on how to select a single designated respondent for the survey. Although random assignment is preferable for unbiased population estimates, the average survey respondent does not know how to make a random or systematic selection. Hence, the questionnaire specified that if an adult patient had children with immune deficiency diseases the adult patient should answer the survey questions concerning their own health and treatment, rather than their affected children. If there were multiple children with primary immunodeficiency diseases, and no adult patients, the parent/caregiver was directed to answer the survey questions about the oldest child. This is an easily implemented selection procedure and tends to provide a sample with the longest diagnosis and treatment experience.

Figure 4
Parent or Patient

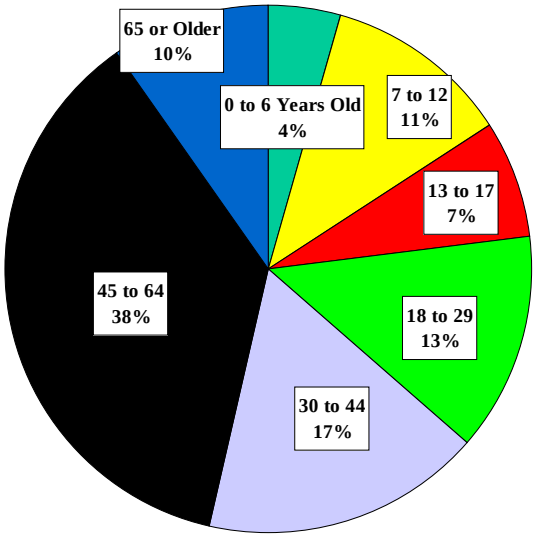


Q3. Are you a patient with a primary immunodeficiency disease (or a parent/caregiver of a child in the household with PIDD) ? (N=1,351)

These survey procedures do introduce some bias towards older respondents in households with multiple persons with immunodeficiency disease. In five percent of households with both adults and children with primary immunodeficiency diseases, the adults were selected with certainty. In another three percent of households with more than one affected child, but no adults with a primary immunodeficiency disease, the oldest affected child was selected with certainty. However, in almost nine out of ten households, there was only one eligible respondent, so the impact of the selection bias in the age of the sample is limited.

As a result, the age distribution of the selected patients mirrors the distribution of all patients quite closely. Among the selected patients 22% were below the age of 18 (<6 = 4%, 7 – 12 = 11%, 13 – 17 = 7%). Thirteen percent were young adults (ages 18 – 29), Seventeen percent were between the ages of 30 and 44, Thirty-eight percent were between 45 and 65, and Ten percent were 65 or older (Figure 5).

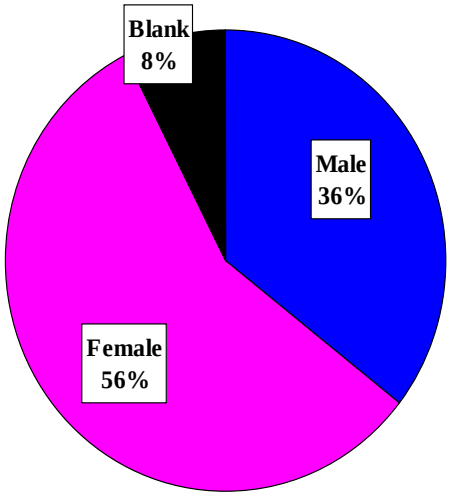
Figure 5
Selected Patient by Age



Q5. What is the date of birth of the (adult patient/oldest child) in the household with a primary immunodeficiency disease? (N=1,349 – excludes blanks)

The gender distribution of the selected patients was similar to that of all patients (36% male, 56% female) with the exception of slightly more (8%) missing data on respondent gender (Figure 6).

Figure 6
Gender of Selected Patient



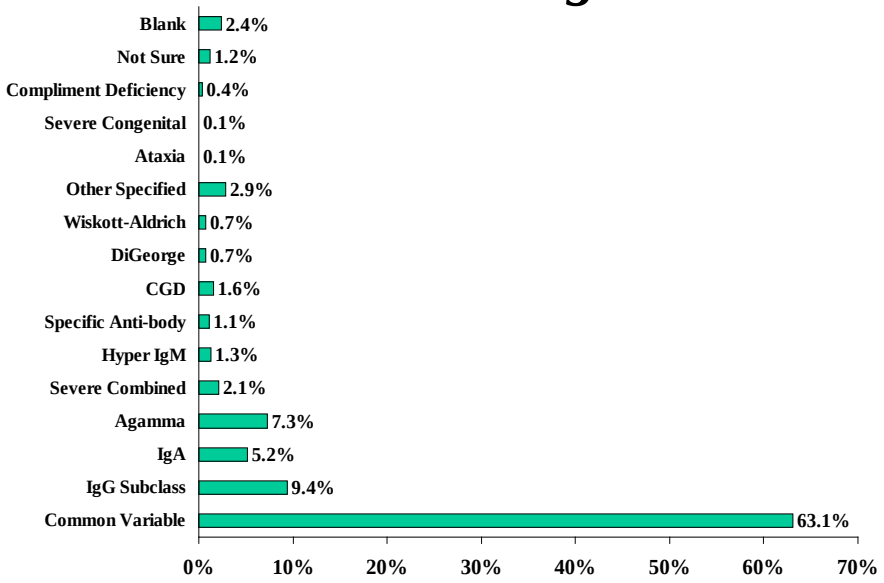
Q5. What is the date of birth of the (adult patient/oldest child) in the household with a primary immunodeficiency disease? Q2. What is the age and Gender of these persons? (N=1,351)

Diagnosis

The prevalence of specific diagnoses in the patient sample is similar to the distributions reported in the previous two patient surveys. The most common diagnosis is Common Variable Immune Deficiency (CVID), which accounts for a majority (63.1%) of the patient sample (Figure 7). In the 2002 Patient Survey, 52.4% of patients reported a diagnosis of common variable immunodeficiency. However, in the 1996/1997 survey, only 34% reported a diagnosis of CVID.

The increased rate of CVID in the patient survey between 2002 and 2007 probably reflects the increased age of the patient population between the two surveys. However, much of the difference in the rate of CVID between the first national survey and later surveys reflects better coding of conditions. In the first national survey, 17% of patients reported IgA deficiency and 24% reported IgG subclass deficiency, when all diagnoses were reported separately. In the second and third patient surveys when a patient reported both IgG and IgA deficiency, the diagnosis was treated as common variable immunodeficiency. As a result, in the current survey 9.4% of patients reported a diagnosis of IgG Subclass Deficiency (compared to 11.5% in 2002), and 5.2% reported Selective IgA Deficiency (compared to 10.0% in 2002).

Figure 7
Current Diagnosis



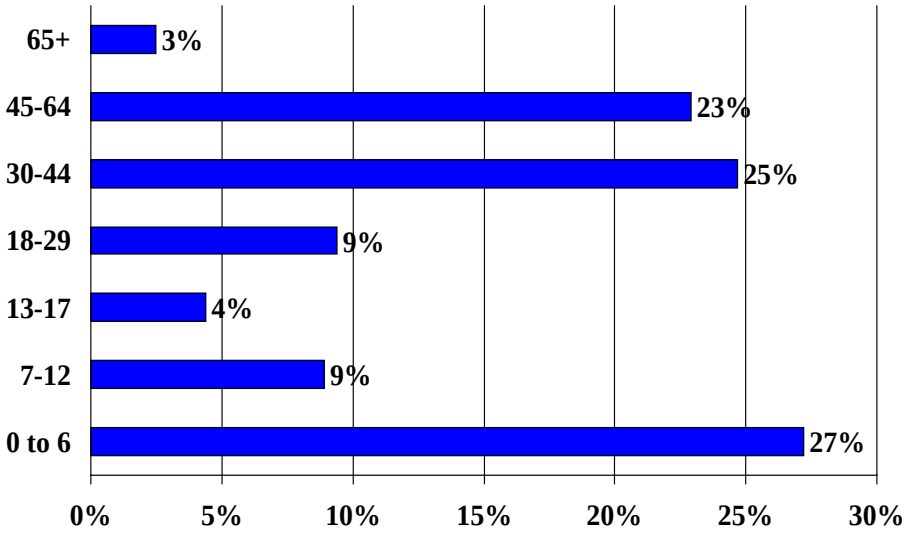
Q6. Mark the specific diagnosis of that person's immunodeficiency disease (current diagnosis if more than one)? (N=1,351)

By contrast, the proportion of patients with PIDD with x-linked agammaglobulinemia (XLA) has remained almost the same across the three surveys. In the 1996/97 survey we found 8% of patients with PIDD with XLA. In the 2002 survey, 8.2% of patients with PIDD reported a diagnosis of XLA. In the current survey, XLA is about the same proportion (7.3%) as in earlier surveys and the third most common diagnosis in the current patient sample.

Smaller proportions of patients in the third national survey report Severe Combined Immunodeficiency (2.1%), Chronic Granulomatous Disease (1.6%), Hyper IgM (2%), DiGeorge Anomaly (0.7%), and Wiskott-Aldrich Syndrome (0.7%). Nearly three percent reported other legitimate PIDD diagnoses. Only 3.6% of patients in the sample did not report a specific diagnosis. A small number of cases who reported a non-PIDD diagnosis (e.g., Alpha-1 antitrypsin deficiency were excluded from the survey findings.)

Only 27% of patients in the third patient survey were initially diagnosed with a primary immunodeficiency disease by age six. The proportion of patients with PIDD diagnosed before age 6 has declined from the previous surveys. In the 1996/97 survey, 38% of patients with PIDD reported being diagnosed before the age of 6. In the 2002 survey, 36% reported being diagnosed at age six or younger. In the current survey, forty percent of patients with PIDD were diagnosed before they were eighteen. The 2007 survey found over half (51%) of the persons with primary immunodeficiency diseases were not diagnosed until they were age 30 or older, while more than a quarter (26%) were not diagnosed until age 45 or older (Figure 8).

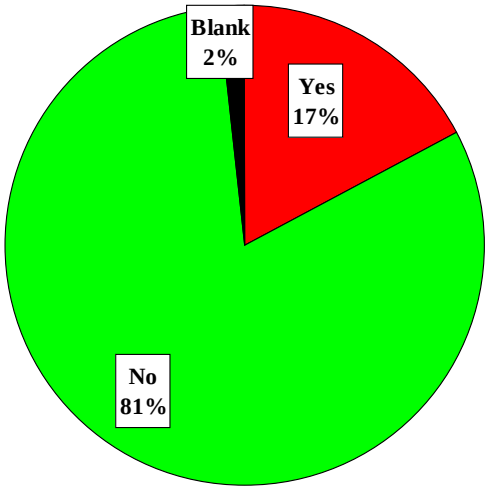
Figure 8
Patient Age at PIDD Diagnosis



Q9. At what age (in years) was that person first diagnosed with a primary immunodeficiency disease? (N=1,330 – excludes missing data)

One reason for late diagnosis is the absence of a family history of these disorders. Only 17% of persons with primary immunodeficiency disease in the 2007 survey report that any other family member has been diagnosed as having a primary immunodeficiency disease (Figure 9). This rate is similar to the 22% who reported a family history in the 2002 survey and the 24% who reported a family history in the 1996/97 survey.

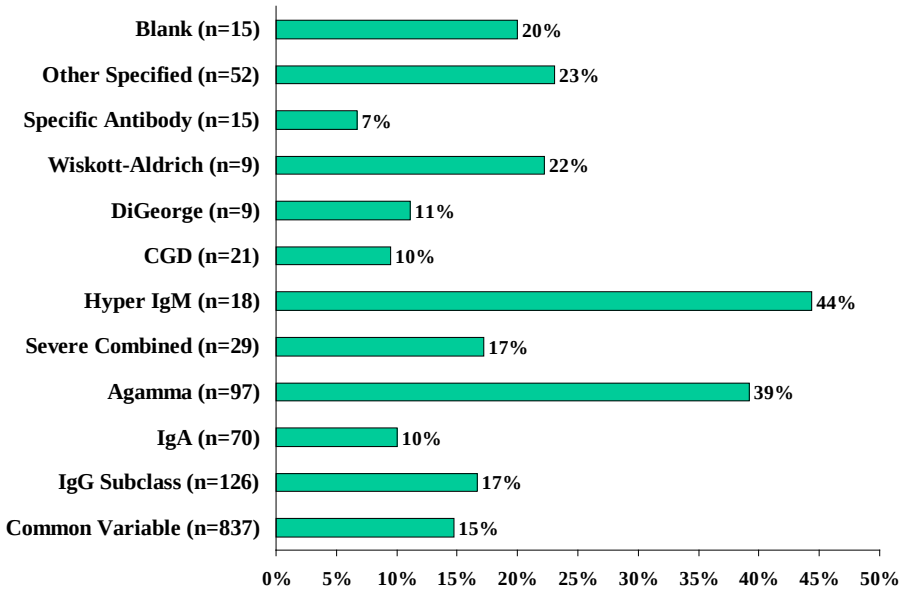
Figure 9
Family History of Immunodeficiency



Q4. Have any other family members (grandparents, cousins, etc.) been diagnosed as having a primary immunodeficiency disease? (N=1,351)

The likelihood of family history of primary immunodeficiency disease varies with the specific diagnosis. The proportion of patients with a family history in the 2007 survey is highest among those diagnosed with Hyper IgM Syndrome (44%), Agammaglobulinemia (39%), but even in these cases the majority of patients with these conditions had no family history of immune deficiency diseases. By contrast, some of the more common forms of primary immunodeficiency have lower than average rates of family history, including common variable (15%) and IgG subclass deficiency (17%). (Figure 10)

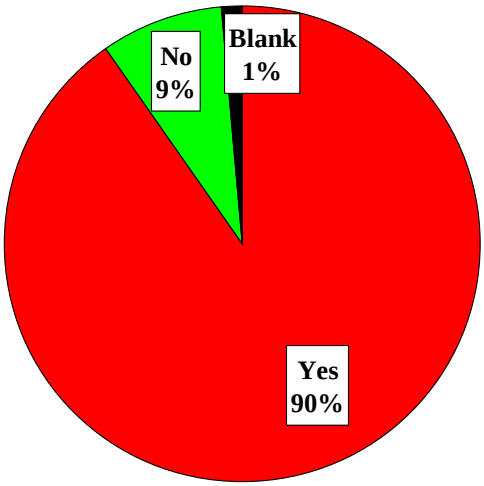
Figure 10
Family Member with PIDD by Diagnosis



Q4. Have any other family member (grandparents, cousins, etc.) been diagnosed as having an immunodeficiency disease? (N=1330 – excludes q4 missing)

While only a minority of patients has a family history of PIDD, almost all experienced repeated, serious or unusual infections prior to the diagnosis. Nine out of ten patients with primary immunodeficiency diseases in the 2007 survey (90%) reported that they experienced repeated, serious or unusual infections prior to initial diagnosis as immune deficient (Figure 11). The proportion of patients with repeat or unusual infections prior to diagnosis is effectively unchanged (89%) from the 2002 survey.

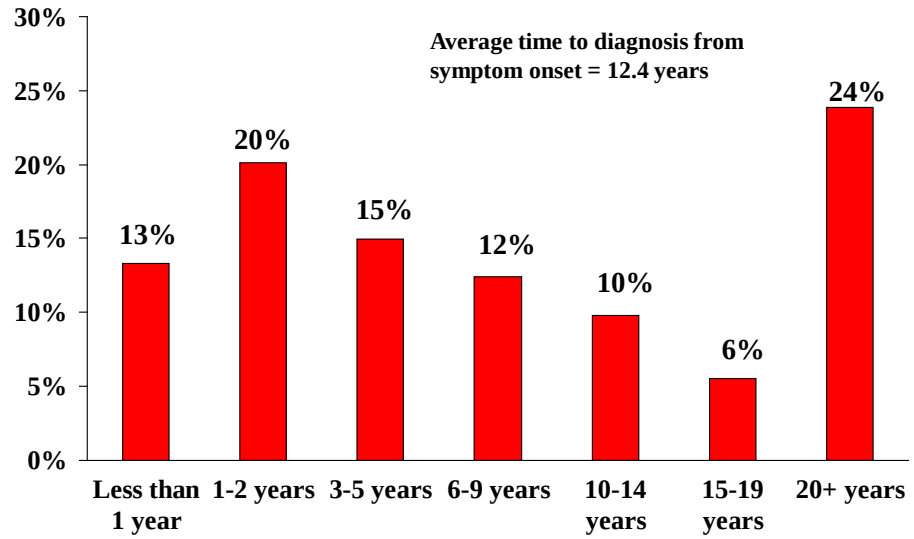
Figure 11
Repeated or Unusual Infections Prior to Diagnosis



Q7. Did the PIDD patient exhibit repeated, serious or unusual infections prior to initial diagnosis as immune deficient? (N=1,351)

Although repeated, unusual or serious infections are the hallmark for primary immunodeficiency diseases, among those who experience these types of infections prior to diagnosis; relatively few were diagnosed with PIDD quickly. Only a little more than one in ten patients (13%) were diagnosed within a year of onset of repeated, serious or unusual infections. Another 20% were diagnosed within one to two years of symptom onset. Nonetheless, the time between the onset of symptoms and diagnosis was 3-5 years for 15% of patients; 6-9 years for 12% of patients; 10-14 years for 10% of patients; and 15-19 years for 6% of patients. Nearly one in four patients (24%) with primary immunodeficiency diseases who experienced repeated, unusual or serious infections prior to diagnosis in this sample report 20 years or more between the onset of repeated, serious or unusual infections and their initial diagnosis as immune deficient. The average time between symptom onset and initial diagnosis was 12.4 years (Figure 12).

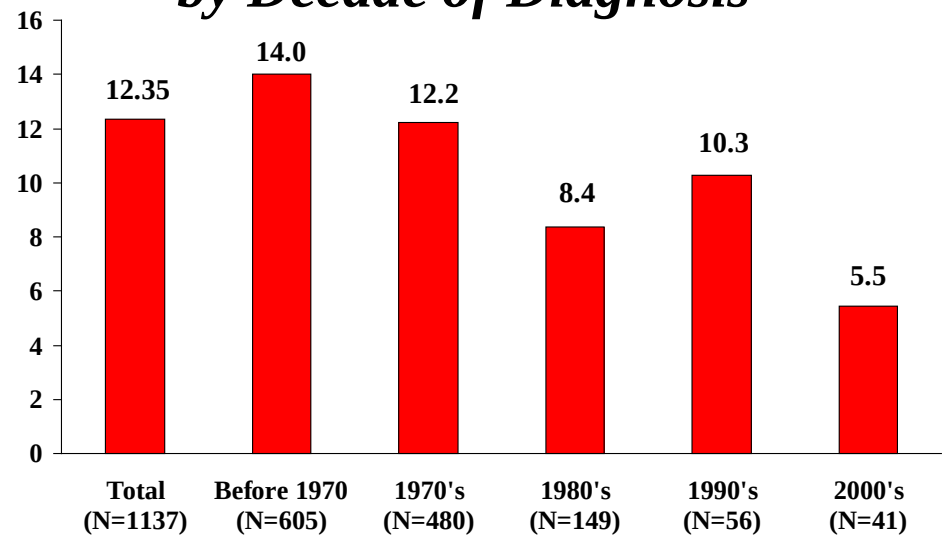
Figure 12
Time to Diagnosis After Symptom Onset



Q9. At what age was that person first diagnosed with a primary immunodeficiency disease? Q8. At what age (in years) did these repeated, serious or unusual infections begin?
(N=1,137 – excludes those with missing information)

The average time from symptom onset to diagnosis has increased from 9.3 years in 2002 to 12.4 years in 2007. Nonetheless, the results from the third national survey of primary immunodeficiency diseases suggests that the time to diagnosis for immune deficient patients may be showing signs of improvement. In the 2007 survey, the average number of years between symptom onset and diagnosis was 14.0 years for those initially diagnosed before 1970. It was 12.2 years for those initially diagnosed in the 1970's. It was 8.4 years for those initially diagnosed in the 1980's. The number of years between symptom onset and initial diagnosis was 10.3 years in the 1990's. Among those patients in the sample who were first diagnosed since 2000, the average number of years from symptom onset to diagnosis was 5.5 years (Figure 13).

Figure 13
Average Number of Years to Diagnosis by Decade of Diagnosis

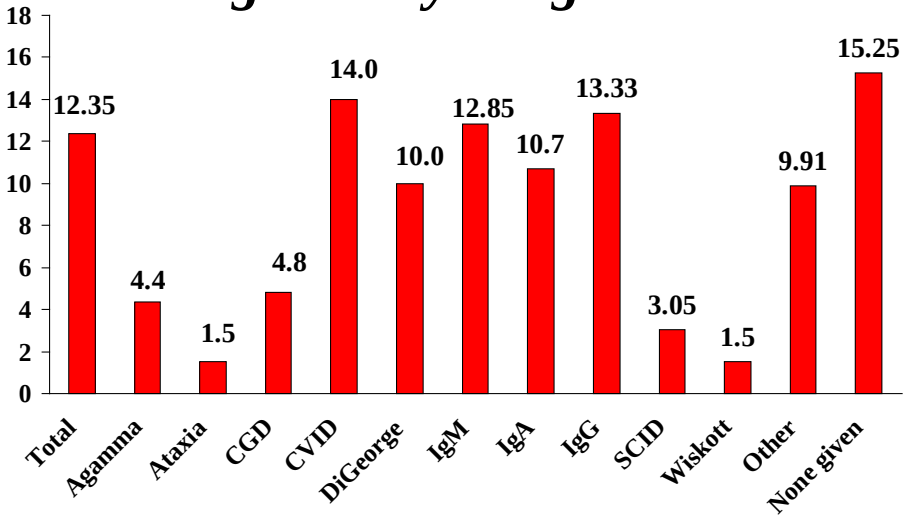


Q9. At what age was that person first diagnosed with a primary immunodeficiency disease? Q8. At what age (in years) did these repeated, serious or unusual infections begin? (Base: Infection prior to diagnosis- N = 1,218; 81 cases missing data to Q8 or Q9).

The time to diagnosis varies considerably by the specific primary immunodeficiency disease. The average time from onset to diagnosis was one and a half years for Ataxia Telangiectasia and Wiskott-Aldrich Syndrome, and less than five years for Severe Combined Immunodeficiency (3.1 years), Agammaglobulinemia (4.4 years) and Chronic Granulomatous Disease (4.8 years). By contrast, the average time to diagnosis for the three most common diagnoses was 14.0 years for Common Variable Immunodeficiency, 13.3 years for IgG subclass deficiency and 10.7 years IgA deficiency. Despite a relatively high proportion of cases with family histories of immune deficiency, the average time to diagnosis for Hyper IgM disease was 12.9 years (Figure 14). The average number of years to diagnosis was also relatively high for DiGeorge syndrome (10.0 years).

It is important to note that the overall increase in the average time to diagnosis between the 2002 survey (9.2 years) and the 2007 survey (12.4 years) may reflect an increase in patient age between the two surveys, but is not necessarily a result of a difference in the mix of diagnoses between the two surveys. The average time to diagnosis was shorter in the 2002 survey for relatively early diagnosed conditions like XLA (3.0 vs 4.4 years) and relatively late diagnosed conditions, like Selective IgA deficiency (9.3 vs.10.7), IgM (8.7 vs. 12.9). IgG subclass deficiency (11.6 vs. 13.3) and Common Variable Immunodeficiency (11.4 vs. 14.0).

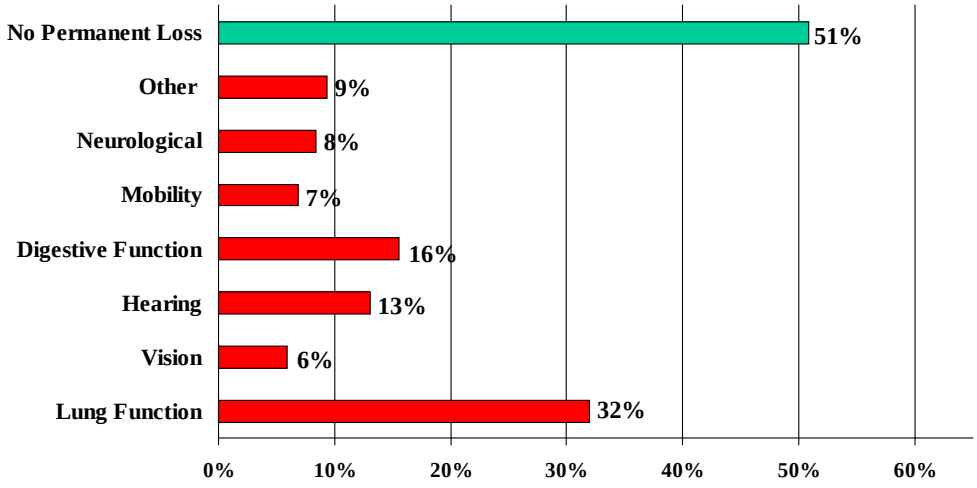
Figure 14
Average Number of Years to Diagnosis by Diagnosis



Q9. At what age was that person first diagnosed with a primary immunodeficiency disease? Q8. At what age (in years) did these repeated, serious or unusual infections begin?

As a result of the relatively long period between onset of repeated, severe or unusual infections and diagnosis, many patients report permanent functional impairment prior to initial diagnosis as immune deficient. Nearly a third of patients with PIDD in the third national survey (32%) reported that they suffered permanent loss of lung function prior to initial diagnosis as immune deficient. Sixteen percent reported a permanent impairment of digestive function, while 13% reported a permanent hearing impairment prior to initial diagnosis as immune deficient. Smaller proportions report permanent loss of mobility (7%), vision (6%), neurological (8%) or other (9%) functions by the time of initial diagnosis. In total, almost half (49%) of patients with primary immunodeficiency disease in the 2007 survey report some type of permanent functional impairment prior to diagnosis (Figure 15).

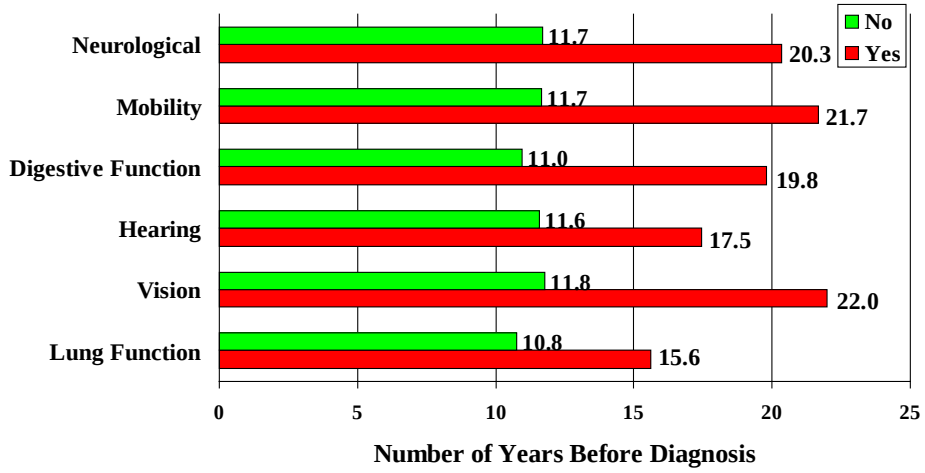
Figure 15
Type of Permanent Functional Impairment Prior to Diagnosis



Q10. By the time of initial diagnosis as immune deficient, had the patient suffered any permanent loss of…? (N=1,327 – excludes missing data)

The length of time between symptom onset and diagnosis as immune deficient affects the likelihood of permanent impairment before diagnosis. The average time to diagnosis is roughly twice as long for those who suffered permanent loss of digestive function (19.8 years to 11.0 years), vision (22.0 to 11.8 years), mobility (21.7 to 11.7 years) and neurological function (20.3 to 11.7 years) prior to diagnosis. The time to diagnosis is about fifty percent longer for persons with permanent hearing loss before diagnosis (17.5 years to 11.6 years) and loss of lung function (15.6 to 10.8 years). (Figure 16) Hence, shorter delays in diagnosis after symptom onset may produce permanent loss of lung function and hearing compared to other functional disabilities.

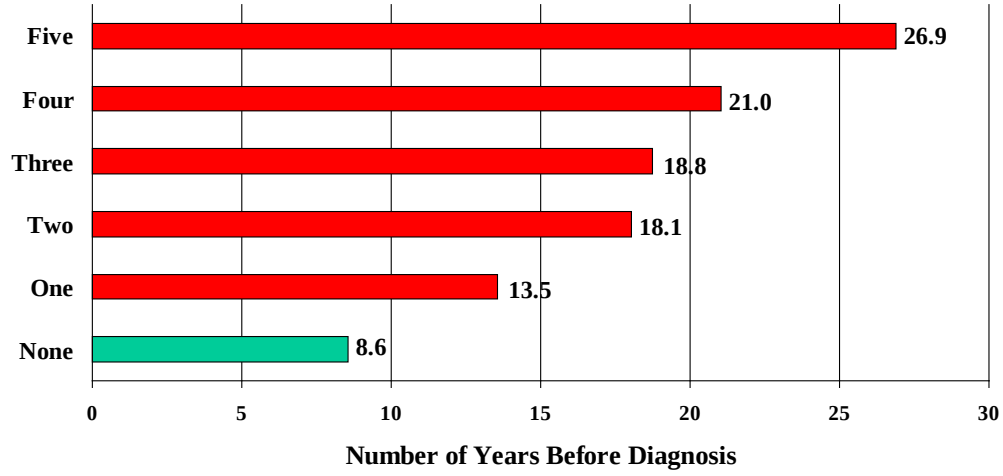
Figure 16
Permanent Functional Impairment Prior to Diagnosis by Time to Diagnosis



Q10. By the time of initial diagnosis as immune deficient, had the patient suffered any permanent loss of…? (N=1,327 – excludes missing data)

The longer the time to diagnosis from symptom onset, the greater the number of permanent functional impairments in patients with PIDD. Those who reported no permanent functional impairments before initial diagnosis as immune deficient reported an average of 8.6 years between symptom onset and diagnosis. The time to diagnosis increases to 13.5 years for those with one area of functional impairment, to 18.1 years for those with two areas of functional impairment, and 18.8 years for those with three areas of functional impairment prior to diagnosis. The average length of time to diagnosis increases to 21.0 years for those with four areas of permanent impairment and 26.9 years for those with five areas of permanent impairment prior to diagnosis as immune deficient (Figure 17).

Figure 17
Number of Permanent Functional Impairments by Time to Diagnosis



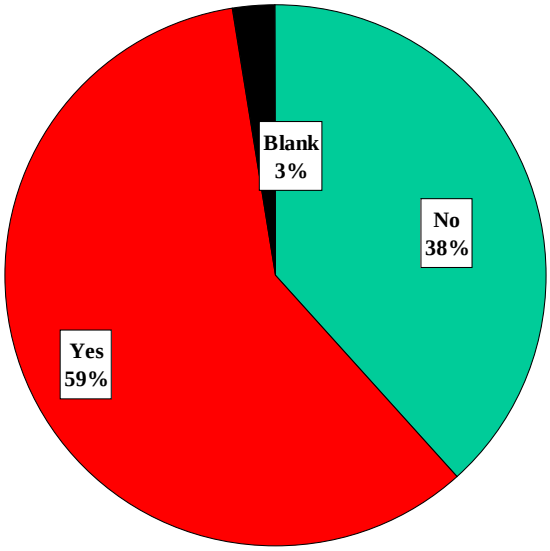
Q10. By the time of initial diagnosis as immune deficient, had the patient suffered any permanent loss of…? (N=1,327 – excludes cases with missing information)

Co-Morbidities

Since the current health and quality of life of patients with primary immunodeficiency diseases may be affected by medical conditions other the primary immunodeficiency disease, the national sample of patients in 2007 was asked about other serious or chronic health conditions. These conditions may or may not be related to the immune deficiency disease. However, at minimum, they represent important co-morbidities with the immune deficient condition.

Over half of the patients with primary immunodeficiency disease (59%) reported other serious, chronic diseases (Figure 18). The most frequently reported other chronic disease among PIDD patients was asthma.

Figure 18
Other Serious Chronic Disease

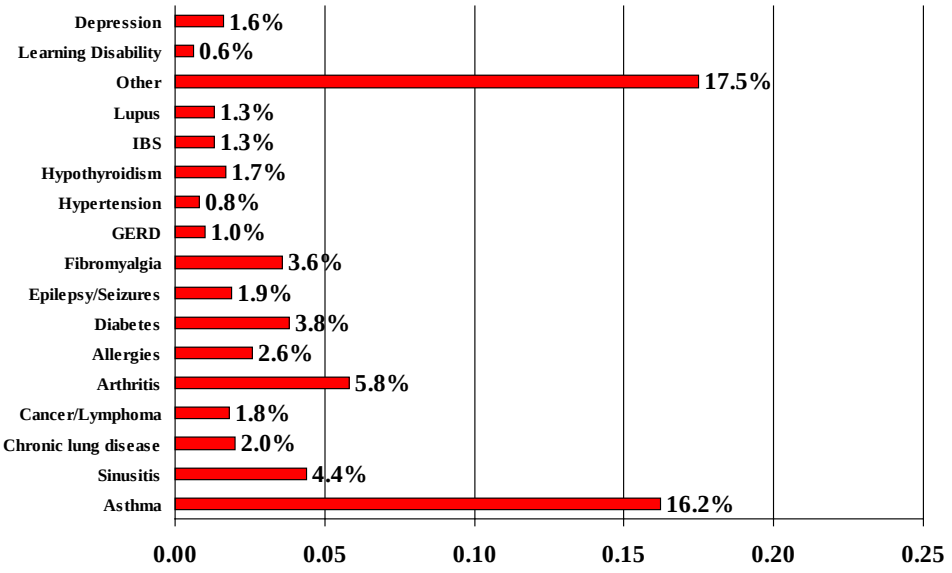


Q13. Does the PIDD patient suffer from any other serious, chronic disease (not counting immune deficiency)? (N=1,351)

Approximately one in seven patients with PIDD in the 2007 survey (16.2%) reported suffering from asthma (Figure 19). This is similar to the rate of asthma among patients with PIDD (17.8%) reported in the 2002 patient survey.

Other conditions reported by patients with PIDD in the 2007 survey as serious, chronic conditions which they suffered included Arthritis (5.8%), Sinusitis (4.4%), Diabetes (3.8%) and Fibromyalgia (3.9%). A somewhat smaller proportion reported Allergies (2.6%), Chronic Lung Disease (2.0%), Epilepsy/Seizures (1.9%) and Cancer/Lymphoma (1.8%) as a serious chronic condition that they suffered from. Other chronic diseases reported by patients with PIDD were Hypothyroidism (1.7%), Depression (1.6%), Irritable Bowel Syndrome (1.3%), Lupus (1.3%), GERD (1.0%), Hypertension (0.8%) and Learning Disabilities (0.6%).

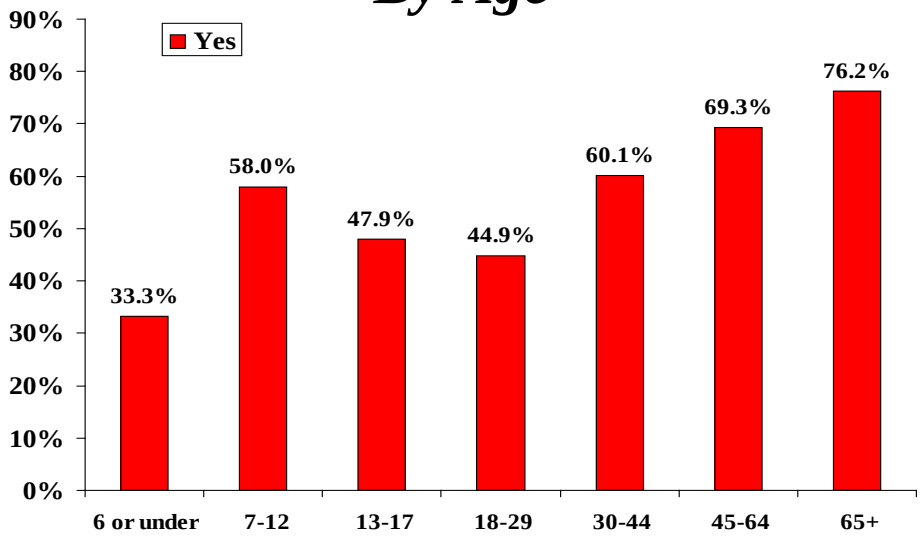
Figure 19
Rates of Specific Chronic Conditions



Q13. Does the PIDD patient suffer from any other serious, chronic disease (not counting immune deficiency)? Please describe. (Base: All Patients - N=1,351)

The presence of other serious, chronic diseases among patients with PIDD varies with age. As one might expect, the prevalence of other diseases generally increases with age from about one-third (33.3%) at ages 6 years and under, to over one-half (58.0%) at ages 7 to 12 years (Figure 20). The prevalence of other chronic diseases then drops to just fewer than one-half (47.9%) at ages 13 to 17, and again to 45% at ages 18 to 29 years. The rates of other chronic diseases then steadily increases at ages 30 to 44 years (60.1%), 45 to 64 years (69.3%), and 65 years or older (76.2%). Although the progressive increase in chronic conditions by age is found in the general populations, the rates of reported serious chronic disease is strikingly high in children and young adults with PIDD.

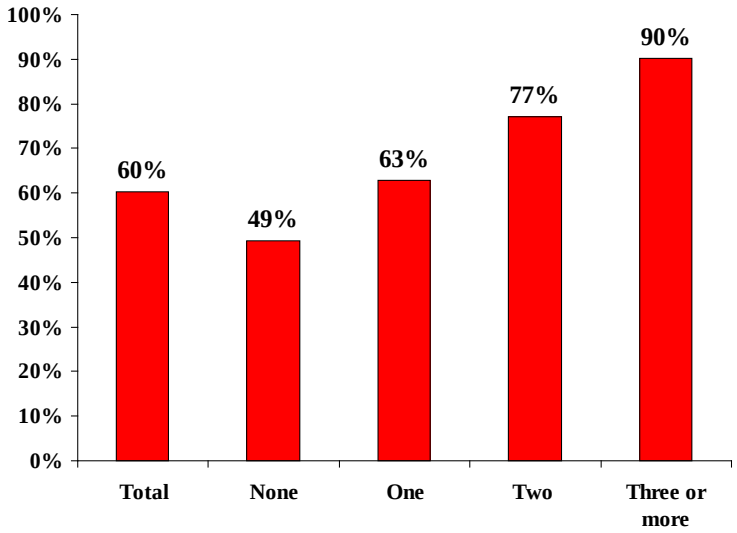
Figure 20
Other Serious Chronic Condition By Age



Q13. Does the PIDD patient suffer from any other serious, chronic disease (not counting immune deficiency)? (N=1,314 – excludes missing data)

The presence of other serious, chronic conditions also tends to increase with the number of permanent impairments prior to diagnosis of the primary immunodeficiency disorder (Figure 21). The rate of other chronic conditions is just under half (49%) among those with no impairments prior to diagnosis, 63% for those with one impairment, 77% for patients with two impairments, and 90% for those with three or more permanent impairments prior to diagnosis. This is comparable to the rates of other chronic conditions by the number of permanent impairments seen in the 2002 patient survey (0 impairments = 46%, 1 impairment = 61%, 2 impairments 65%, 3+ impairments = 87%).

Figure 21
Other Serious Chronic Condition by Number of Impairments before Diagnosis

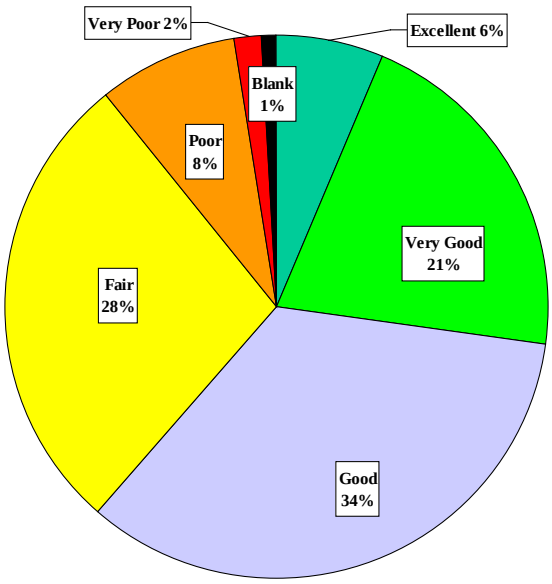


Q13. Does the PIDD patient suffer from any other serious, chronic disease (not counting immune deficiency)? (N=1,293 – excludes missing data)

Current Health

More than three out of five patients with primary immunodeficiency diseases (61%), describe their current health status as good or better. Specifically, 6% describe their current health status as excellent, 21% as very good, and 34% as good. Twenty-eight percent describe their current health as only fair. Only 8% of patients report their current health status as poor or very poor (Figure 22). This is consistent with the current health status ratings observed in the 2002 patient survey in which 59% of patients reported their current health status as good or better.

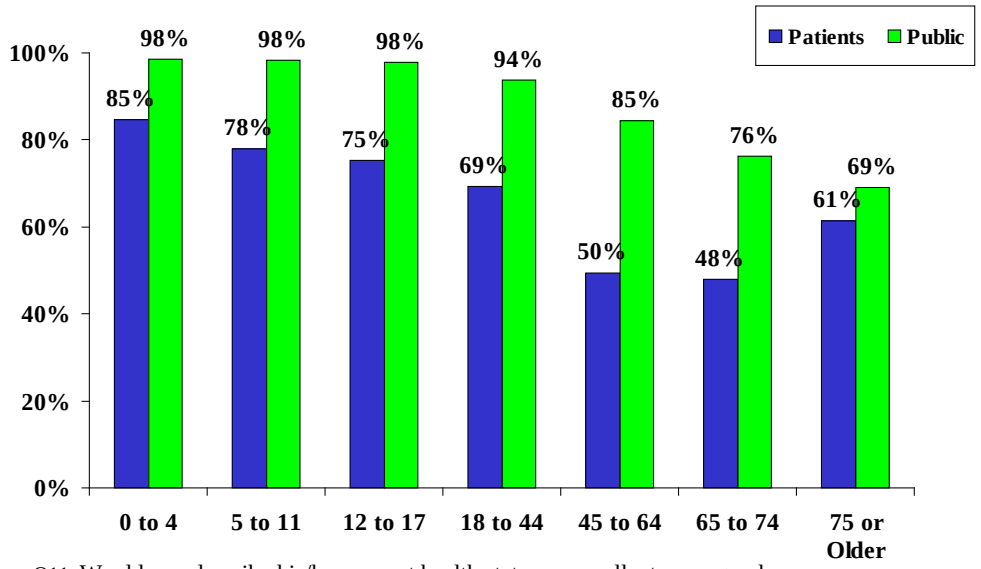
Figure 22
Current Health Status



Q11. Would you describe his/her current health status as: (N=1,351)

Although most immune deficiency patients describe themselves as being in good health, if the current health rating of immune deficient patients is compared to the general public, using an equivalent measure from the National Health Interview Survey, it is clear that patients do not feel as healthy as the general public of the same age. For example, 98% of the general public under the age of 18 rates their health as excellent, very good or good, compared to 75%-85% of persons with primary immunodeficiency disease less than 18 years of age. Among persons aged 45 to 64 in the general public, 85% rate their health as good or better, compared to only 50% of immune deficient patients in that age range. Among persons aged 65 to 74 in the general public, 76% rate their health as good or better, compared to only 48% of immune deficient patients in that age range. Only among persons aged 75 or older does the proportion who their current health status as being good or better among patients with primary immunodeficiency disease (61%) approach the proportion who rate their health as good or better (69%) in the general public (Figure 23).

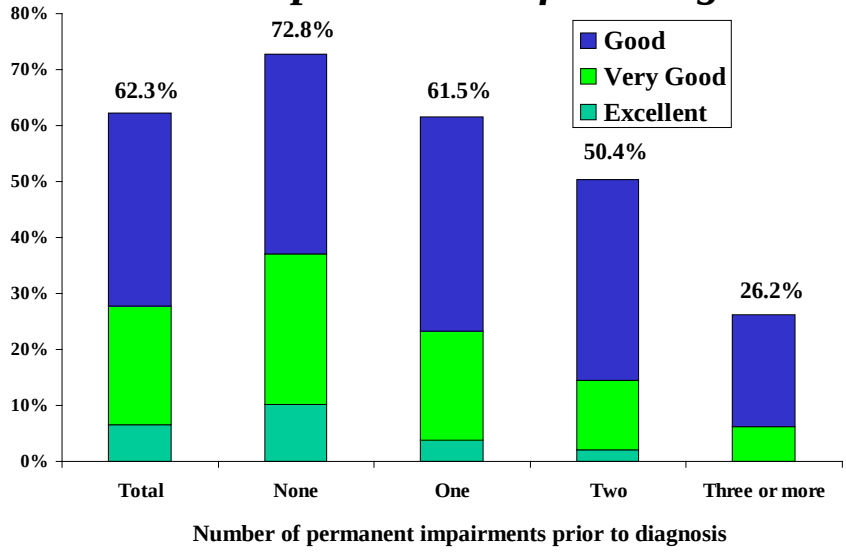
Figure 23
Health Status Good or Better



Q11. Would you describe his/her current health status as excellent, very good, good, fair, poor, or very poor? (N = 1,317 – excludes missing data)

The comparatively low rating of their current health by immune deficient patients is strongly affected by the development of permanent functional impairments prior to diagnosis. Nearly three out of four patients with PIDD with no permanent impairments prior to diagnosis (73%) rate their health as good or better. The proportion of patients who rate their current health as good or better declines to 62% of those with one permanent impairment, to 50% of those with two permanent impairments, and 26% of those with three or more permanent impairments (Figure 24). Consequently, it is the functional impairments developed as a result of repeated, serious or unusual infections prior to diagnosis and treatment that is responsible for much of the disparity in health status found in patients with primary immunodeficiency disease.

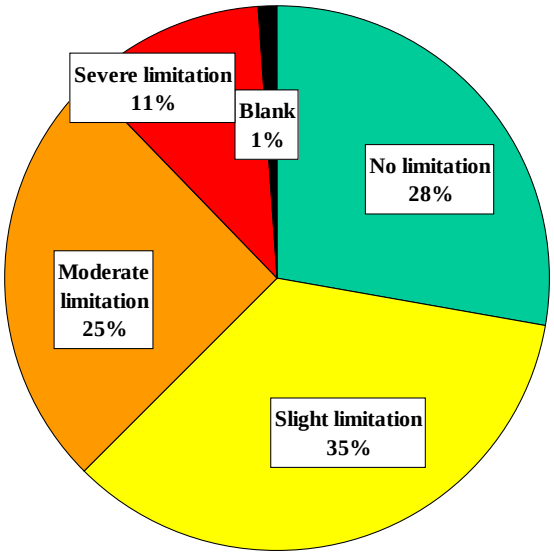
Figure 24
Current Health Status by Number of Permanent Functional Impairments before Diagnosis



Q11. Would you describe the patient's current health status as: (N=1,317 – excludes missing data)

Only 28% of patients with PIDD report no limitations in work, play or normal physical activity as a result of their health. However, most patients with primary immunodeficiency diseases report only slight (35%) or no physical limitations (28%) as a result of health. One-quarter (25%) of PIDD patients report moderate activity limitations, while 11% report severe physical limitations as a result of their health (Figure 25).

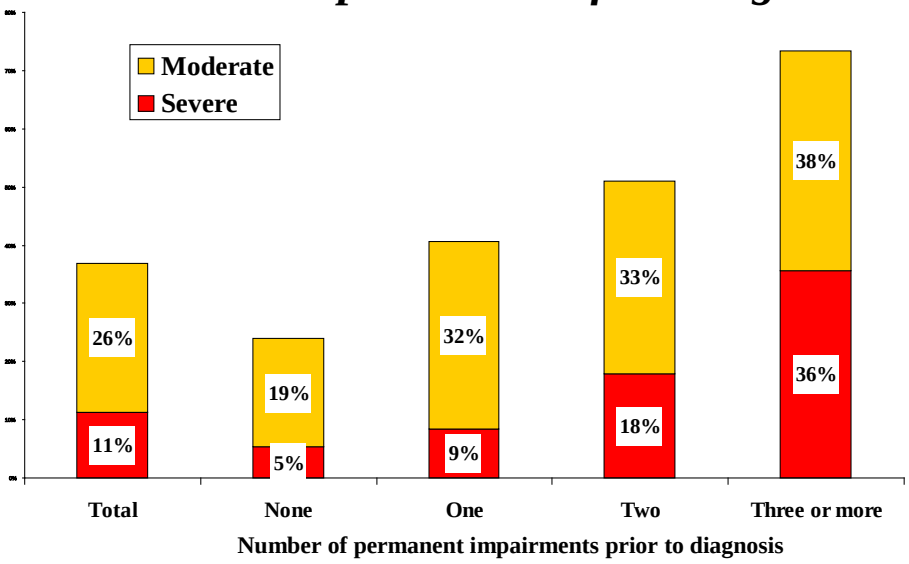
Figure 25
Current Activity Limitation



Q12. How much is the patient limited in work, play or normal physical activity as a result of his/her health? (N=1,351)

Current activity limitation, like current health rating, is strongly affected by the development of permanent functional impairments prior to diagnosis. Only about a quarter of patients with PIDD with no permanent impairments prior to diagnosis (26%) say their activities are severely or moderately limited as a result of their health. The proportion of patients who say their activities are severely or moderately limited by their health increases to 41% of those with one permanent impairment, to 51% of those with two permanent impairments, to 74% of those with three or more permanent impairments (Figure 26). Like current health status, the degree of health-related activity limitation in patients with PIDD is primarily a result of functional impairments suffered as a result of infections prior to diagnosis and treatment.

Figure 26
Current Activity Limitation by Number of Permanent Impairments before Diagnosis

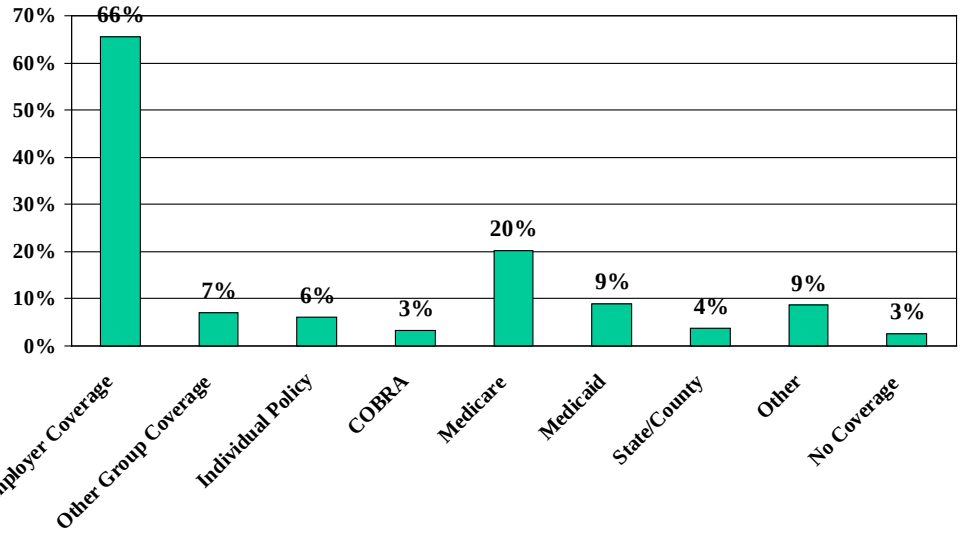


Q12. How much is the patient limited in work, play or normal physical activity as a result of his/her health? (N=1,336 – excludes missing data)

Health Care Access and Utilization

Almost all persons with primary immunodeficiency diseases have some form of health insurance or health care coverage. The majority (67%) have insurance through an employer group policy. Another 7% have their health insurance from a non-employer group policy, while 6% report having an individual policy. About one in five (21%) have Medicare coverage, while 9% report Medicaid coverage, and 4% are covered by a state or county health program. A small proportion has their health care coverage through COBRA (3%), or other health insurance programs (9%). Only three percent of patients with PIDD report no health care coverage from any of these sources (Figure 27).

Figure 27
Source of Current Health Insurance

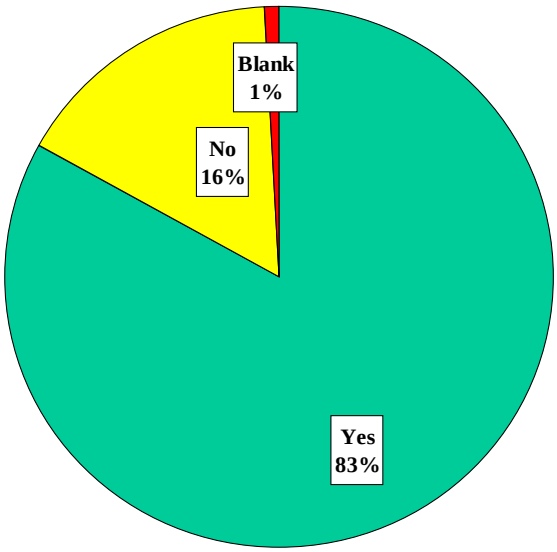


Q21. What is the current source(s) of the patient's health care coverage (including through other family members)? (Base: All Patients – N=1,351)

Treatment

More than four out of five patients with primary immunodeficiency disease (83%) in the Third National Patient Survey report that they have been treated with immunoglobulin therapy (IG therapy). Patients can receive either intravenous immunoglobulin (IVIG) or subcutaneous immune globulin (SCIG) for their disorder (Figure 28).

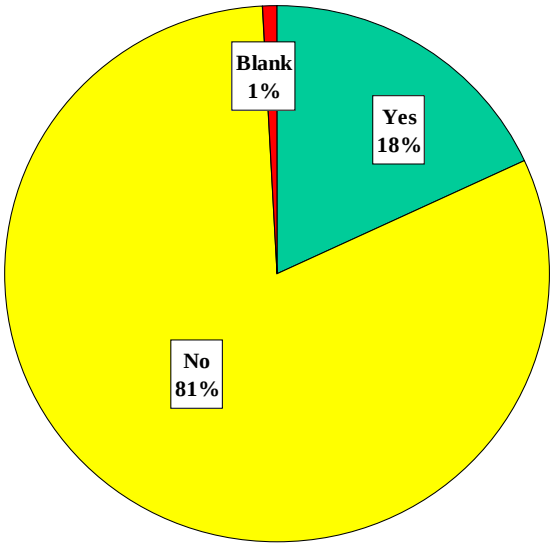
Figure 28
Ever Use IG Therapy



Q14. Has the patient ever been treated with intravenous immune globulin (IVIG) or subcutaneous immune globulin (SCIG) a regular basis? (N=1,351)

Nearly one in five (18%) patients with PIDD in the 2007 survey report that they have been treated with Subcutaneous Immune Globulin (SCIG) for their disorder (Figure 29). However, this should not be treated as an estimate of national market share for SCIG since the patients with PIDD most likely to be exposed to SCIG through clinical trials and academic medical centers are more likely to be in the IDF database.

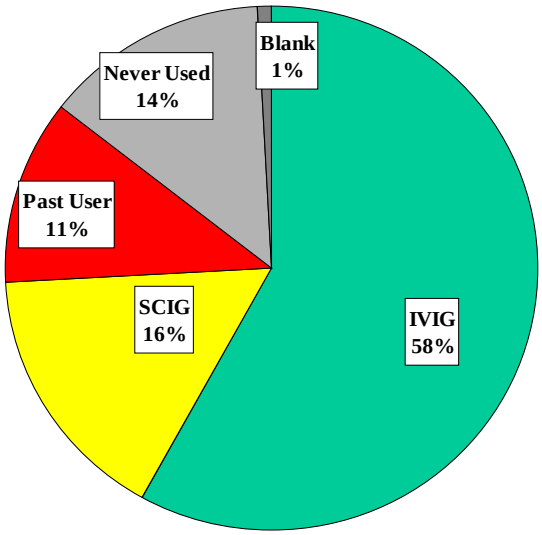
Figure 29
Ever Use SCIG



Q14. Has the patient ever been treated with intravenous immune globulin (IVIG) or subcutaneous immune globulin (SCIG) a regular basis? (N=1,351)

Nearly three quarters of patients with PIDD (74%) in the Third National Patient Survey report that they are currently being treated with some form of immunoglobulin therapy. Over half (58%) are currently being treated with IVIG, while 16% are currently being treated with SCIG, 11% are no longer being treated with an IG therapy, and 15% have never been treated with either product (Figure 30).

Figure 30
Current IG Use



Q15. Is the patient currently being treated with IVIG or SCIG? (N=1,351)

Those who have used IVIG or SCIG in the past, but are not using either of these products now, were asked why they were no longer being treated. Some discontinuing users reported that better health (12%) and/or normal to near normal immunoglobulin levels (5%) were the reasons that stopped the therapy (Figure 31). Others did so because their doctors did not think it was necessary (4%), they felt that there were no real benefits (7%) or they wanted to see if the body produced antibodies without IgG (5%). A small proportion had been cured by bone marrow transplantation (7%). Nonetheless, a not inconsequential proportion of patients with PIDD who had discontinued immunoglobulin therapy said that they had done so because of insurance problems (12%), side effects or reactions to IG (19%), fear of contracting disease through the product (2%), could not afford it (3%), or lack of product availability (1%). Hence, cost, coverage, side effects and concerns about product safety appear to be causing some patients with PIDD from discontinuing otherwise effective treatment for their condition.

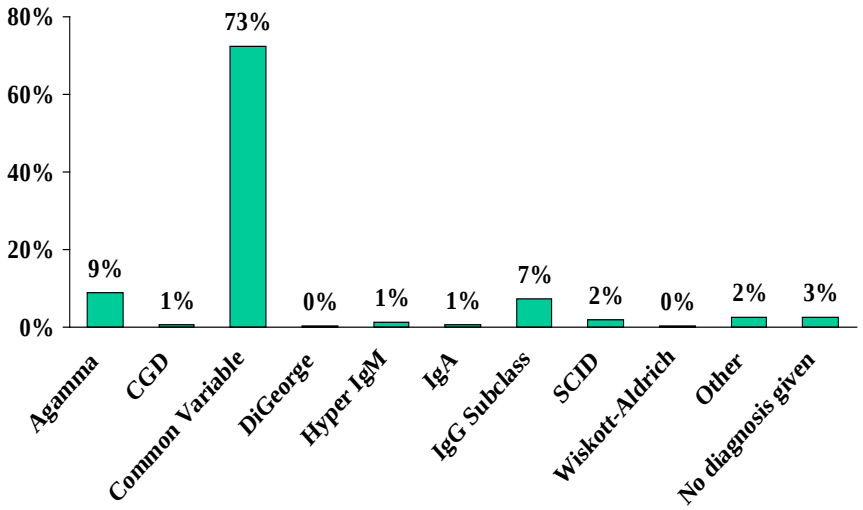
Figure 31
Reason No Longer Using IG Product

• Insurance Problems	11.6%
• Side effects/reaction	19.4%
• Health improved/symptoms gone	11.6%
• Normal/near normal levels	4.7%
• Doctor doesn't think it is necessary	3.9%
• No real benefits	7.0%
• To see if body will produce antibodies	4.7%
• Can't afford/too expensive	3.1%
• Cured/Bone marrow transplantation	7.0%
• Fear of contracting diseases	1.6%
• Lack of product	.8%
• Transient disease	.8%
• Other reasons	18.6%

Q15a. Why is the patient no longer being treated?
(Base: Past users - N=154)

The vast majority of current immunoglobulin users among patients with PIDD have Common Variable Immunodeficiency (73%). Patients with X-linked Agammaglobulinemia (9%) and IgG Subclass Deficiency (7%) comprise most of the other PIDD users of immunoglobulin therapy. Most other diagnoses of primary immunodeficiency diseases comprised only a small proportion of current IG therapy users. Severe Combined Immunodeficiency represents 2% of current IG therapy users, while Hyper IgM Syndrome, Selective IgA Deficiency, and Chronic Granulomatous each comprised 1% of the current IG therapy users in the PIDD patient population (Figure 32).

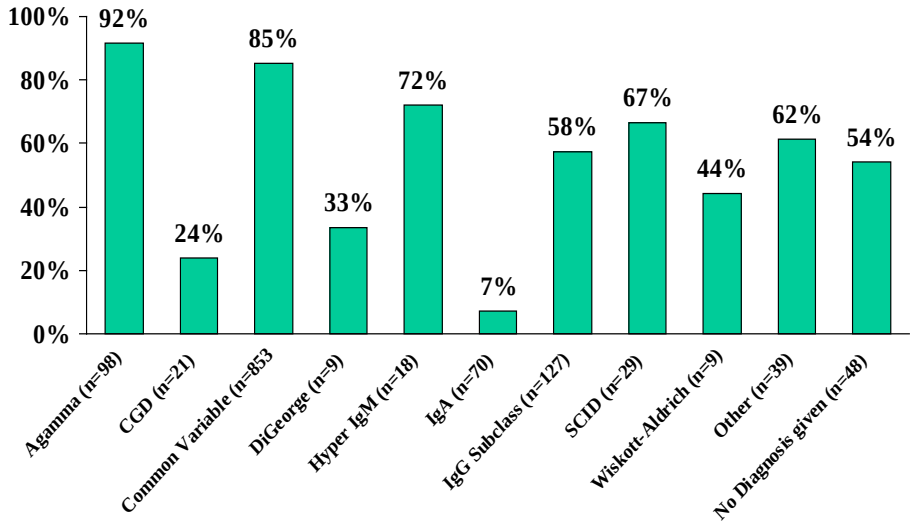
Figure 32
Diagnosis By Current IG Use



Q15. Is the patient currently being treated with IVIG or SCIG? Q6. Mark the specific diagnosis of that person's immunodeficiency disease (current diagnosis if more than one. (Base: Current IG users - N=1,001)

Current IG therapy use varies by diagnosis among primary immunodeficiency diseases. It is most common for patients with Agammaglobulinemia (92%). It is also commonly reported by six out of seven patients (85%) with Common Variable Immunodeficiency seven out of ten patients with Hyper IgM (72%) and two-thirds of patients with severe combined immunodeficiency (67%). Current IG therapy use is also reported by a majority of patients with IgG Subclass Deficiency (58%). It is least commonly used for IgA deficiency (7%). (Figure 33)

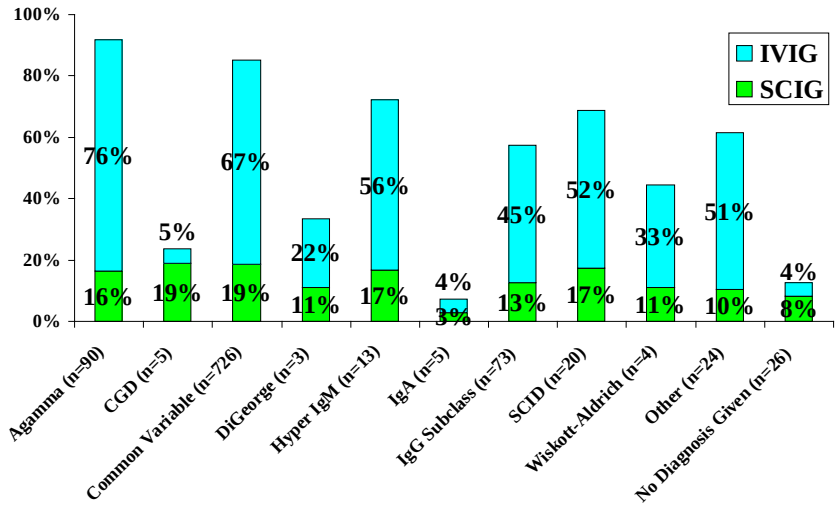
Figure 33
Current IG Use By Diagnosis



Q15. Is the patient currently being treated with IVIG or SCIG? Q6. Mark the specific diagnosis of that person's immunodeficiency disease (current diagnosis if more than one. (Base: All Patients - N=1,351)

IVIG is the dominant mode of IG therapy for specific PIDD diagnoses as well as primary immunodeficiency diseases in general (Figure 34).

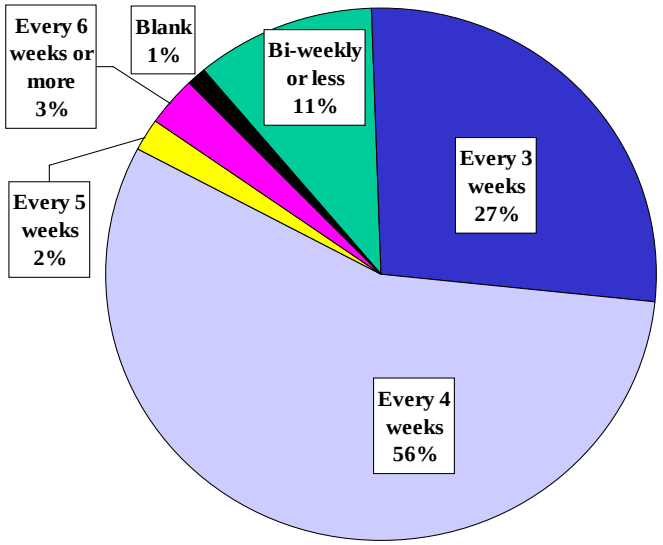
Figure 34
IG Product By Diagnosis



Q15. Is the patient currently being treated with IVIG or SCIG? Q6. Mark the specific diagnosis of that person's immunodeficiency disease (current diagnosis if more than one.
Base: All Patients (N=1,351)

The frequency of infusions varies considerably among persons with primary immunodeficiency diseases currently being treated with IVIG. A majority (56%) reports that, on average, they get an infusion every four weeks. Nearly three in ten (27%) reports they get an infusion every three weeks. One in ten (11%) say they get their infusion every two weeks or more often. A small proportion of current IVIG users say that they get their infusion every five weeks or less often (5%). (Figure 35)

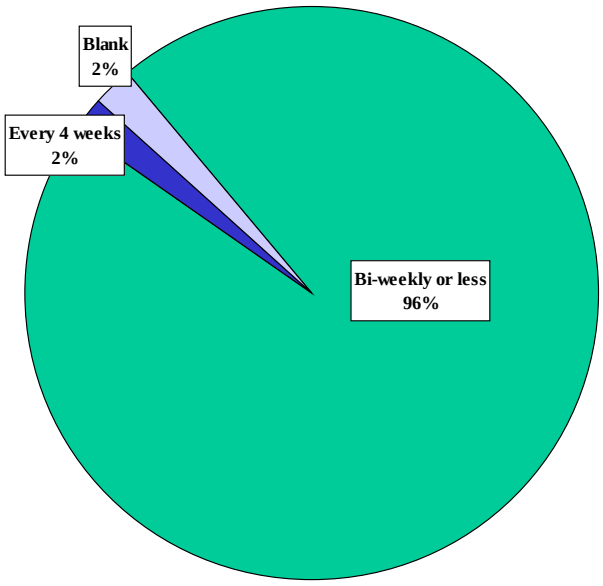
Figure 35
Frequency of IVIG Infusions



Q17. On average, how often does the patient get an infusion of immune globulin (IVIG or SCIG)? (N=775 – current IVIG users)

By contrast, nearly all SCIG treatments occur bi-weekly or less (96%), with a small number (2%), who reported getting their subcutaneous immunoglobulin every 4 weeks (Figure 36).

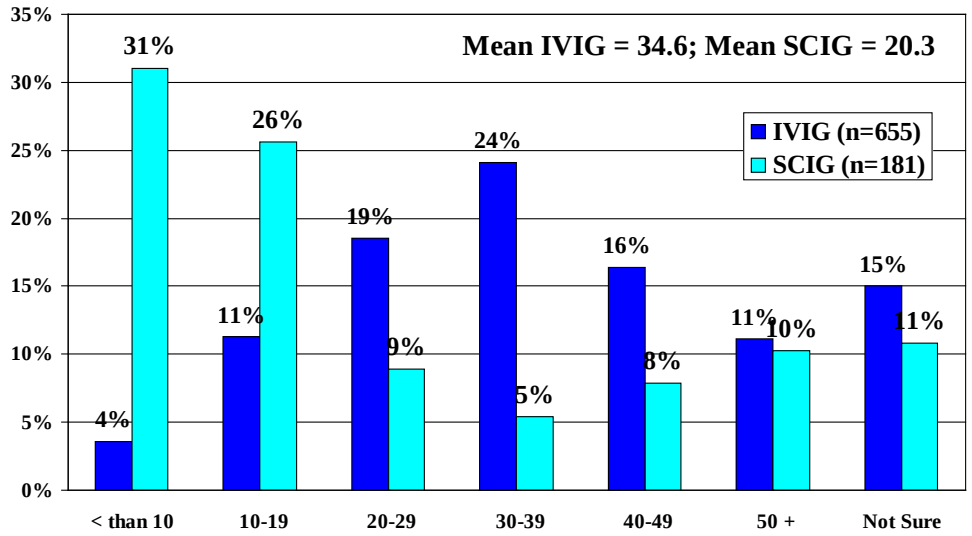
Figure 36
Frequency of SCIG Infusions



Q17. On average, how often does the patient get an infusion of immune globulin (IVIG or SCIG)? (N=218 – current SCIG users)

As expected, the average dosage for IVIG and SCIG among immune deficiency patients is quite different. Most commonly, patients being treated with SCIG report that the average number of grams per infusion as being less than 10 grams (31%) or 10-19 grams (26%). Relatively few SCIG users report their usual dosage as 20-29 grams (9%), 30-39 grams (5%), 40-49 grams (8%) or 50 grams or more (10%). There is a broader range of dosage among IVIG users with 11% reporting 10-19 grams per infusion, 19% reporting 20-29 grams, 24% reporting 30-39 grams, 16% reporting 40-49 grams, and 11% reporting 50 or more grams per infusion (Figure 37). The mean number of grams per infusion for patients with PIDD using IVIG was 34.6 grams in 2007, compared to 31.3 grams in 2002. This difference could be associated with greater body mass among the somewhat older patient population in the current survey rather than treatment differences.

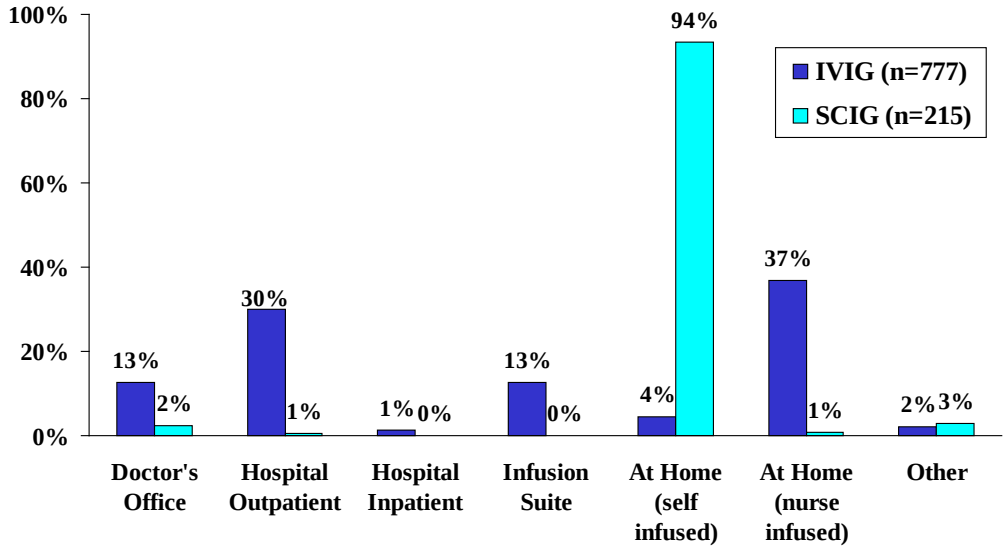
Figure 37
Grams of IG per Infusion



Q18. About how many grams of immune globulin per infusion does the patient normally receive? (Base: current IG users, excluding missing data)

More than two out of five IVIG users in the Third National Patient Survey report that they usually receive their infusion at home, either self-infused (4%) or nurse-infused (37%). This is somewhat higher than the 35% of IVIG users reporting home infusion in 2002. Nearly one-third (30%) IVIG users in 2007 usually get their infusion in a hospital outpatient setting, which is similar to the rate (32%) getting their infusions in hospital outpatient settings in 2002. A very small proportion of IVIG users reported usually getting their infusion in a hospital in-patient setting in 2007 (1%) like 2002 (3%). Thirteen percent of the patients using IVIG say that they usually get their infusion in a doctor's private office in 2007, effectively unchanged from 14% in 2002. In 2007, 13% of IVIG users said that they usually got their treatment in an infusion suite, compared to 18% in 2002 (Figure 38). By contrast, nearly all of the patients receiving SCIG (95%), report that their usual place of infusions was at home (self infused = 94%). A small number of SCIG users reported getting treatments in a doctor's office (2%), or some other place (3%).

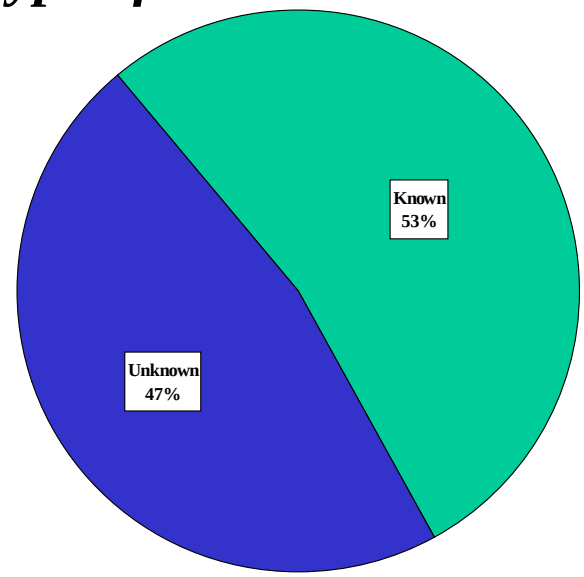
Figure 38
Usual Place of Infusion by IG Type



Q19. Where does the patient usually receive his/her infusions? (Base: Current IG users, excluding missing data)

The sample of current IG therapy users in the Third National Patient Survey was asked which of seven currently licensed IG therapy preparations they usually receive. Only a little more than half (53%) of patients currently being treated with immunoglobulin therapy were able to correctly identify the IG therapy product that they usually receive (Figure 39).

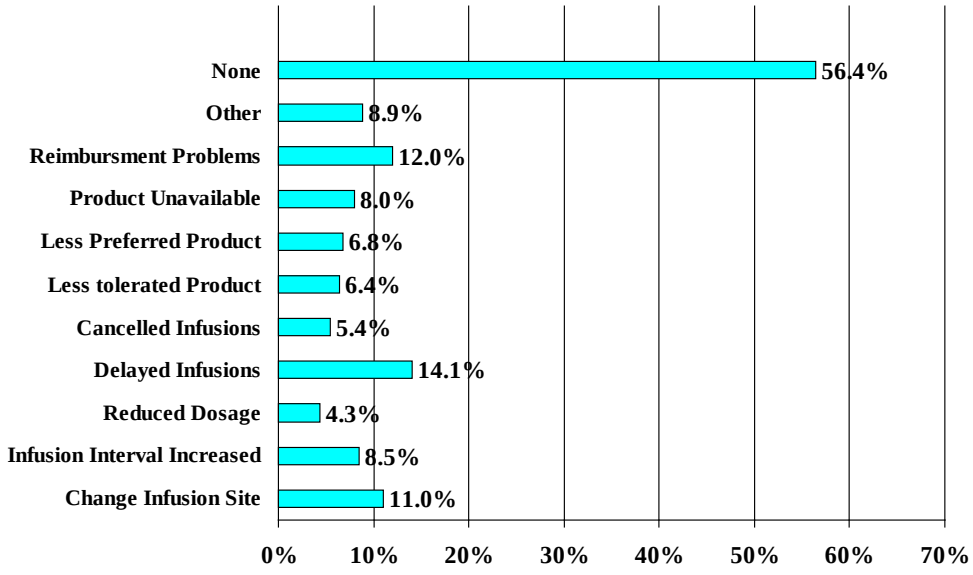
Figure 39
Type of IG Product Known



Q16. What is the Usual immune globulin product the patient receives?
Base: Current users (N=1,001)

More than half of the patients that responded to the question (56%) reported that they had no problems with product availability or reimbursement in the past 12 months (Figure 40). Nonetheless, a not insignificant proportion of patients with PIDD reported that in the past 12 months as a result of product availability or reimbursement they had experienced delayed infusions (14%), reimbursement problems (12%), changes in infusion site (11%), increased infusion intervals (9%) or product unavailability (8%). Other patients with PIDD reported switching to a less preferred (7%), or less tolerated product (6%), cancelled infusions (5%) and reduced dosage (4%) in the past 12 months as a result of product availability or reimbursement.

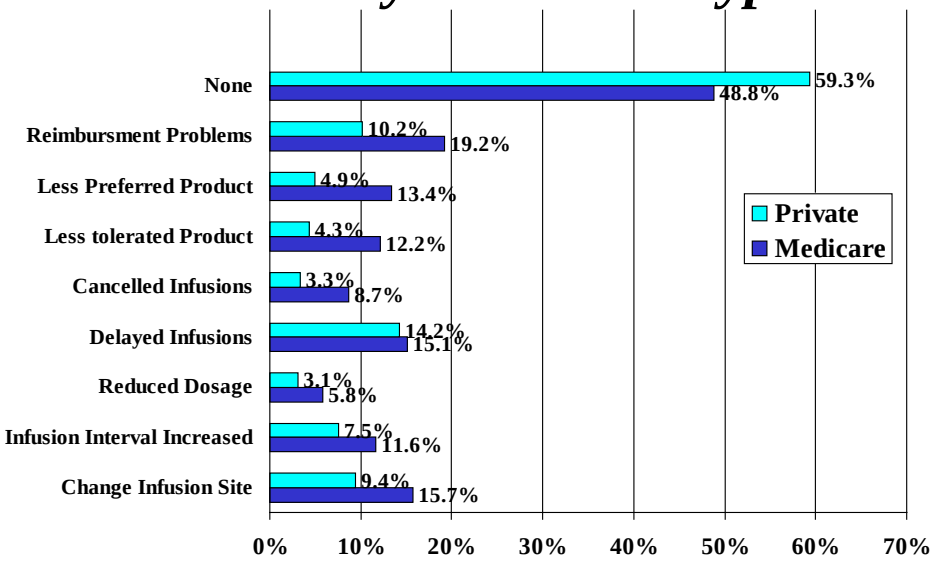
Figure 40
Availability / Reimbursement Problems



Q20. In the past twelve months, has the patient experienced any of the following as a result of product availability or reimbursement? (Base: current IG users - N=828, excluding missing data)

Patients with private insurance were more likely to report having no problems (59%), than patients with Medicare (49%). (Figure 41) Patients with Medicare were much more likely to report problems with reimbursement (19% vs. 10%), switching to a less preferred product (13% vs. 5%), and/or switching to a less tolerated products (12% vs. 4%), cancelled infusions (9% vs. 3%), change in infusions site (16% vs. 9%), increased intervals between infusions (12% vs. 8%), and. reduced dosage (6% vs. 3%).

Figure 41
Problems by Insurance Type



Q20. In the past twelve months, has the patient experienced any of the following as a result of product availability or reimbursement? Q21. What is the current source(s) of the patient's health care coverage (including through other family members)? (Base: current IG users - N=680, excluding missing data)

Conclusions

Primary immunodeficiency diseases are a set of comparatively rare genetic disorders. However, the IDF 2005 Prevalence Survey of 10,000 households indicates that approximately 1 in 1,200 persons in the United States have a diagnosed primary immunodeficiency disease, which would project to an estimated 250,000 cases in this country. Hence, primary immunodeficiency diseases are more common in the United States than some better known genetic disorders, including hemophilia (less than 15,000), cystic fibrosis (30,000) and Huntington's Disease (30,000), among others.

Half of all persons with primary immunodeficiency diseases are not diagnosed until they are aged 30 or older. One problem for early diagnosis is that the vast majority of patients have no family history of immune deficiency disease. Nine out of ten patients report repeated, serious or unusual infections prior to diagnosis. Indeed, earlier surveys have found that most patients report that they were initially tested for immune deficiency because of repeated infections, serious infections or unusual infections. Unfortunately, the average time between the onset of symptoms and initial diagnosis as immune deficient in the 2007 survey was 12.4 years for this patient population.

The cost of late diagnosis is a heavy burden of disease on the patient. Nearly half of immune deficient patients (49%) report suffering permanent functional impairments prior to diagnosis. The likelihood of permanent impairment of lung function, mobility, digestive function, vision and hearing is related to the time between symptom onset and initial diagnosis of immune deficiency.

Only three out five persons with primary immunodeficiency diseases (61%) describe their current health as good, very good or excellent. Most (63%) say their health causes no limitations or only slight limitations on work, play and other activities. Nonetheless, the general health, activity limitation and hospitalization rates for persons with primary immunodeficiency disease are measurably poorer than the general public. A significant proportion of this difference is related to permanent functional impairments suffered prior to diagnosis and treatment as immune deficient.

The most common form of treatment for primary immunodeficiency diseases is immunoglobulin (IgG) therapy, which is the standard of care for most PIDD antibody deficiencies. More than four out of five patients with PIDD (85%) in the Third National Patient Survey report being treated with IVIG or SCIG on a regular basis for their condition. However, only 74% are currently being treated with either form of IgG therapy.

Almost all patients with PIDD are currently covered by some form of health insurance or health plan, most commonly through employer group insurance. Nonetheless, a significant proportion of those who have discontinued IG therapy have done so as a result of cost or coverage. In addition, many immune deficient patients report having had problems in obtaining treatment as a result of product availability or reimbursement.

Despite a generally positive outlook after diagnosis for most patients with primary immunodeficiency diseases, the time to diagnosis after symptom onset is much too long even today. Delayed diagnosis after symptom onset produces functional impairments as a result of infections in many patients, which unnecessarily limits their general health status and activities after treatment for their immune deficiency disorder. The long-term outlook for most patients with primary immunodeficiency diseases, while good, could be greatly improved by earlier diagnosis and better access to appropriate care and treatment.