**MARCIA BOYLE**

Marcia Boyle is the President and Founder of the Immune Deficiency Foundation, the national non-profit patient organization dedicated to improving the diagnosis, treatment and quality of life of persons with primary immunodeficiency diseases through advocacy, education and research.

Marcia has been a passionate patient advocate after starting IDF in 1980 in reaction to the diagnosis of her son, John, with X-linked Agammaglobulinemia. She oversees all aspects of IDF's programs and services and has been instrumental in developing new resources to meet the needs of patients with primary immunodeficiencies in an ever-changing world.

Marcia spends a great deal of her time on issues designed to improve the lives of patients, including education and resources for patients and families to manage their lives and health, expanded research, and education for physicians to improve the rate of diagnosis and optimal care.

Since 2005 when Marcia returned as president of IDF, Marcia has made a personal commitment to advocacy for issues that impact patient care. Marcia represents the community in public forums, making statements to federal and state legislators, regulators and committees regarding IDF's position on issues that affect patient access to care. In creating and leading IDF, Marcia gave a voice to a community that did not have one and created opportunities for patients to prepare to be their own best advocates. Her ultimate goal is to help patients see that these disorders do not define them and cannot be allowed to limit what they can achieve in life.

Previous professional experience: As the co-founder of IDF in 1980, Marcia served as the chair and president until 1995, as chair until 2001, and has continued as a member of the Board of Trustees since that time. During her earlier tenure as president and CEO, Marcia developed many of the patient and medical programs for which IDF is known. She was also a co-founder of IPOPI, the International Patient Organization for Primary Immunodeficiencies in 1992 and presently serves on its board.

Prior to returning to IDF in 2005 as the president, Marcia held the positions of Director of Departmental Programs and Capital Projects and the Director of Principal Gifts for the Fund for Johns Hopkins Medicine, and had served as Director of Development for the Wilmer Eye Institute and Director of Development, Neurology and Brain Sciences at Johns Hopkins Medicine. Earlier, Marcia served as a research librarian at Reader's Digest and Columbia University.

Marcia received a B.A. from Skidmore College and an M.S. in Library Service from Columbia University. She also did graduate work through a National Endowment for the Arts Fellowship in American Studies at George Washington University.

# 2016 PPTA Regulatory Workshop

Marcia Boyle

IDF President & Founder

June 13, 2016

# Mission Statement

Founded in 1980, the Immune Deficiency Foundation is the national patient organization in the United States dedicated to improving the diagnosis, treatment and quality of life of persons with primary immunodeficiency diseases through advocacy, education and research.

www.primaryimmune.org

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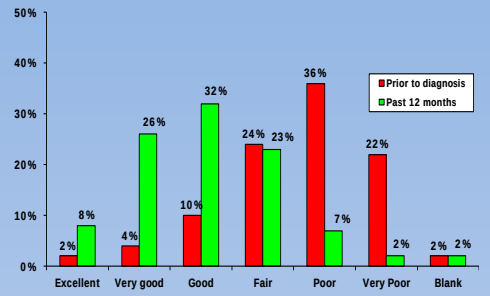


# Survey Research

## Better Information for Better Outcomes

## More than 35 surveys of patients and medical professionals since 1995

Highlights include:

- National Patient Surveys (1996, 2002, 2007, 2012)
- National Treatment Surveys (1997, 2003, 2008, 2013)
  - 2009 IDF Patient Survey (Web-based)
- Prevalence Survey (2005)
- National Internet Treatment Survey of PIDD in the U.S. (2010)
- Medicare Access to Care Surveys: Patients, Physicians, Hospital Pharmacist Directors (2006, 2007)
- Physician Surveys
  - Pediatrician (2007), Family Practitioner(2009), Pulmonologist (2011)
  - Use of IVIG in Treatment of PI – IDF and AAAAI (2009)
- Early vs. Delayed Diagnosis of SCID (2010)
- Primary Immunodeficiency & Women's Reproductive Health Survey (2012)
- Health Insurance & Primary immunodeficiency (2014 - 2016)

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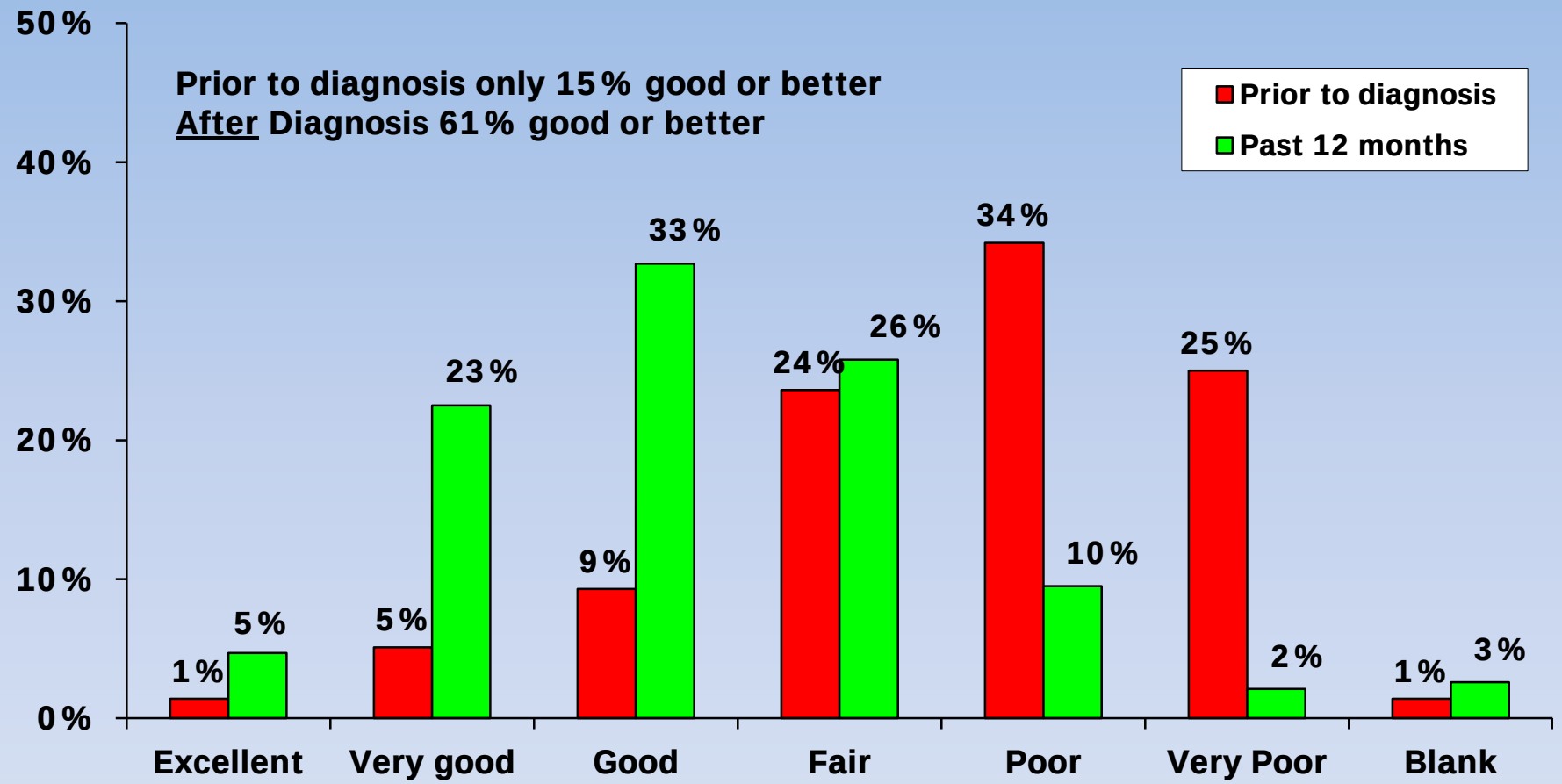
# Health Status Improves after IG Therapy




Q9. Would you describe his/her health in the 12 months prior to diagnosis.....? BASE: Those who are currently using IVIG or SCIG Therapy N=1,428

Q61. Would you describe his/her health in the past 12 months as.....? BASE: Those who are currently using IVIG or SCIG Therapy N=1,428

Source: 2013 IDF National Patient Treatment Survey

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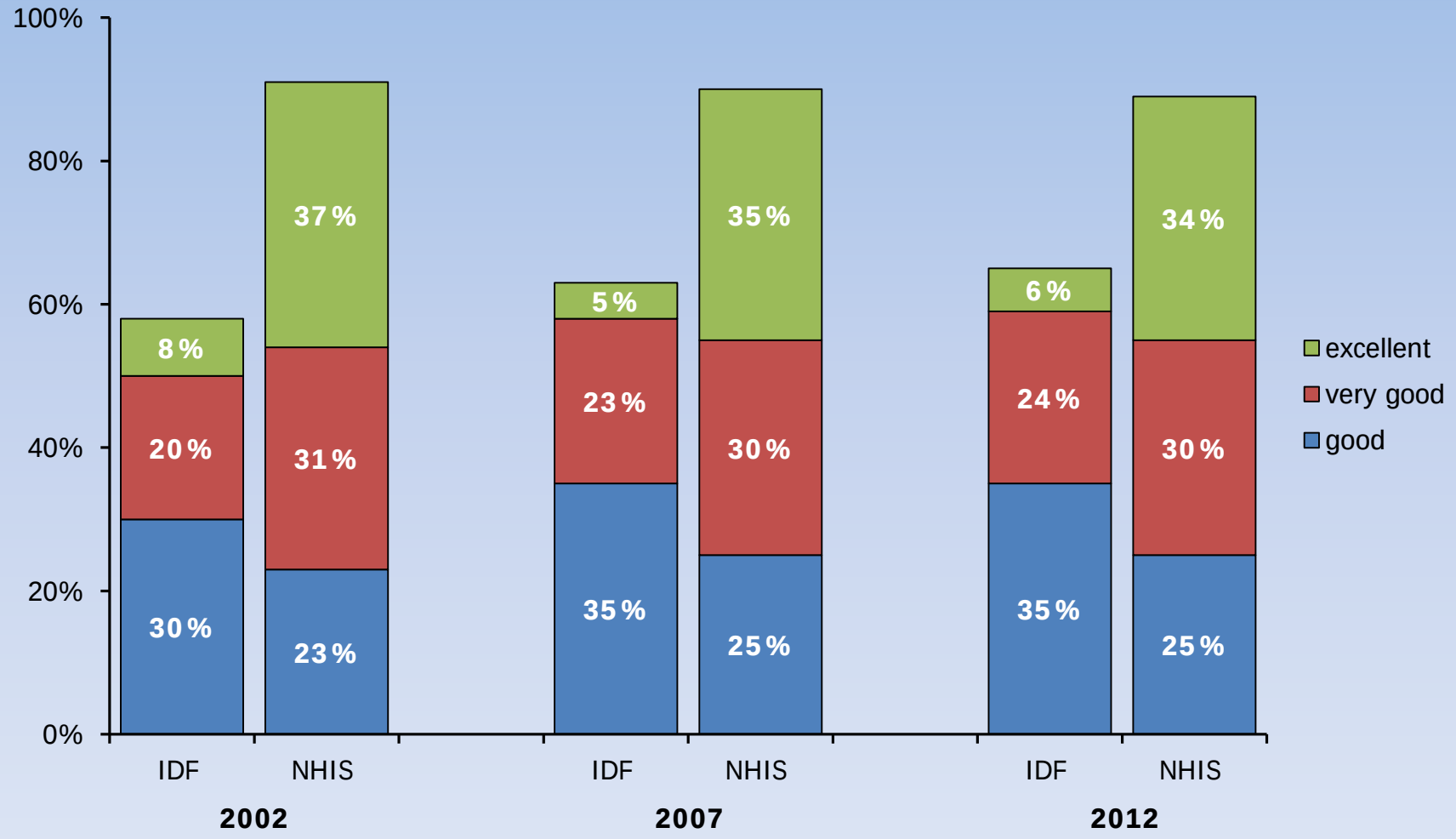
# Current Health Status: Good or Better
# Patients Currently Receiving IG Therapy




Sources: 2002, 2007 & 2012 IDF National Patient Surveys/ 2002, 2007 & 2011 National Health Interview Survey (NHIS)

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J Clin Immunol
DOI 10.1007/s10875-015-0196-7

ORIGINAL RESEARCH

# Perceived Health in Patients with Primary Immune Deficiency

Filiz Odabasi Seeborg[1] · Roann Seay[2] · Marcia Boyle[3] · John Boyle[3] · Christopher Scalchunes[3] · Jordan Scott Orange[1]

- IDF 2002 National Patient Survey
- Published February 2015
- Chronic disease strong predictor of poor PH
- Hospital admissions in past year is a driver of poor PH
- Limitations in physical activity predictor of poor PH
- Regular Ig Therapy associated with better PH

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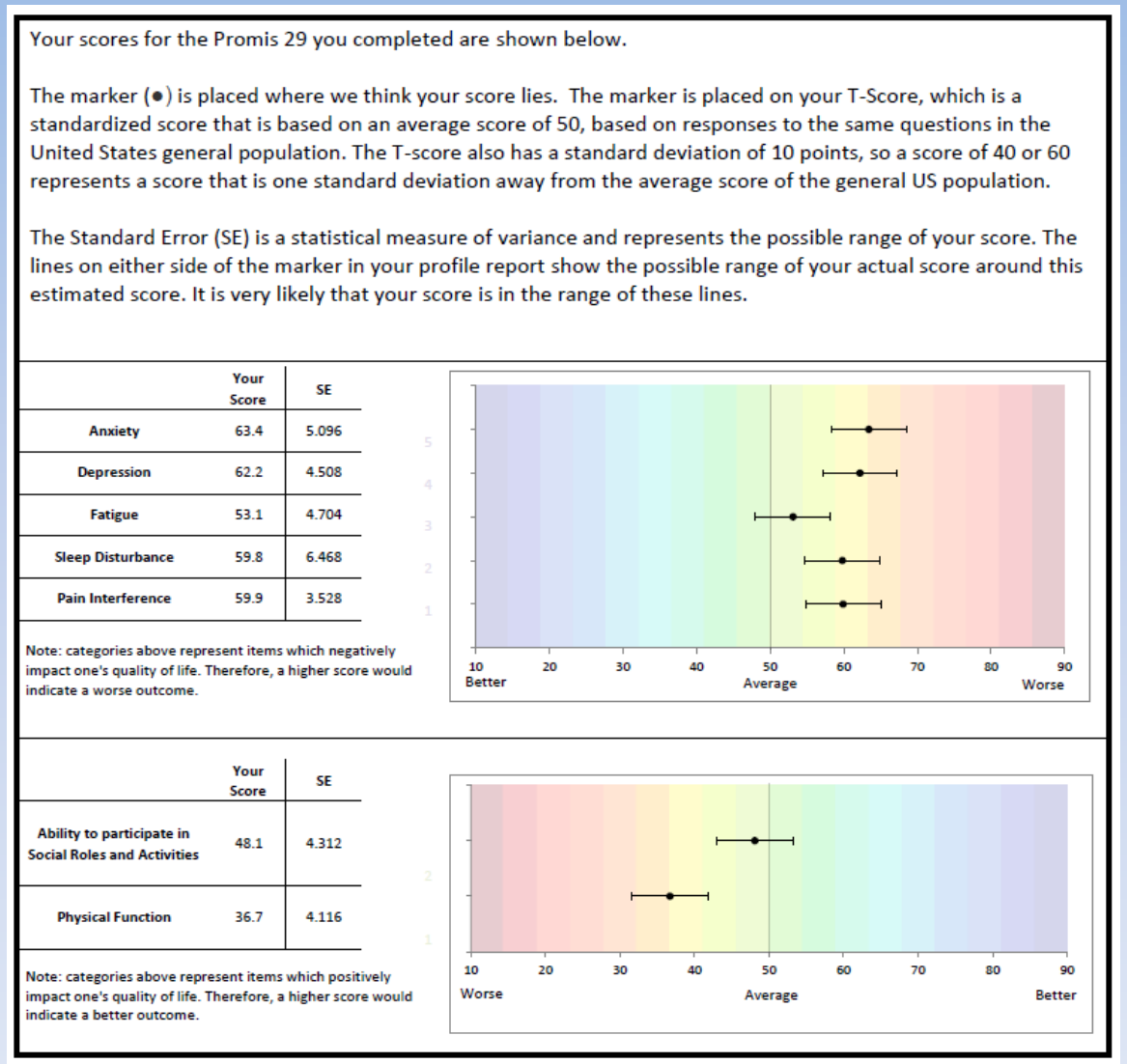
# IDF 2013 Treatment Survey: SF-12 Scores


- SF-12 added to the 2013 IDF National Treatment Survey
- 75 other main questions in survey
- Manuscript in progress
  - Jordan Orange, MD, PhD
  - Nicholas L. Rider, DO

Source: IDF 2013 National Treatment Survey

# IDF ePHR: Customized Patient PROMIS-29 QoL Report

- In the field November 2015
  - Patients can print
  - Stays in the record
  - Shared with USIDNET (consented)
- IDF will perform every 6 months
- Second iteration May 2016
  - PGH-7 also included
    - Pediatric 8-17 years of age



Your scores for the Promis 29 you completed are shown below.

The marker (●) is placed where we think your score lies. The marker is placed on your T-Score, which is a standardized score that is based on an average score of 50, based on responses to the same questions in the United States general population. The T-score also has a standard deviation of 10 points, so a score of 40 or 60 represents a score that is one standard deviation away from the average score of the general US population.

The Standard Error (SE) is a statistical measure of variance and represents the possible range of your score. The lines on either side of the marker in your profile report show the possible range of your actual score around this estimated score. It is very likely that your score is in the range of these lines.

| | Your Score | SE |
|---|---|---|
| Anxiety | 63.4 | 5.096 |
| Depression | 62.2 | 4.508 |
| Fatigue | 53.1 | 4.704 |
| Sleep Disturbance | 59.8 | 6.468 |
| Pain Interference | 59.9 | 3.528 |

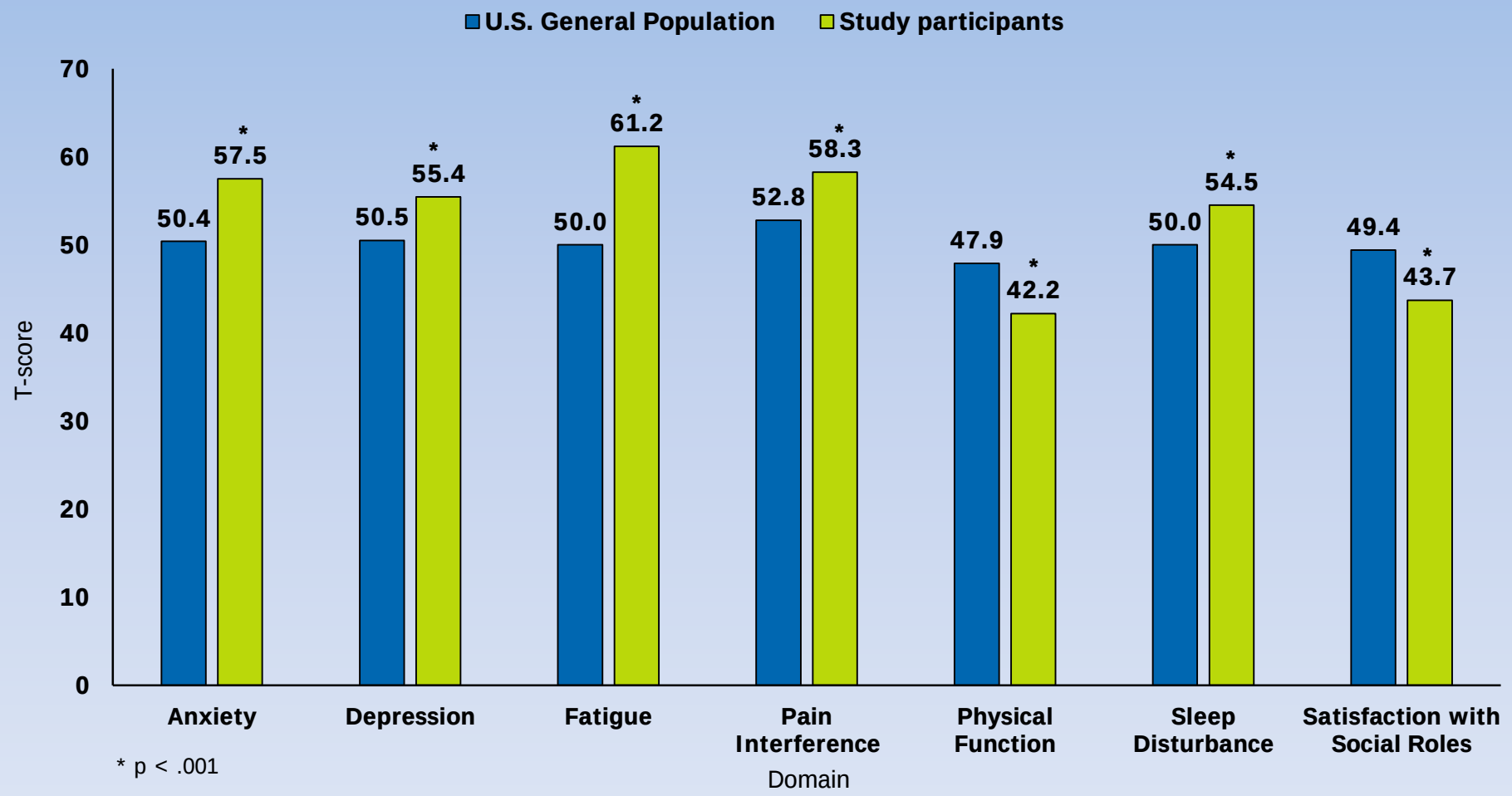
Note: categories above represent items which negatively impact one's quality of life. Therefore, a higher score would indicate a worse outcome.



| | Your Score | SE |
|---|---|---|
| Ability to participate in Social Roles and Activities | 48.1 | 4.312 |
| Physical Function | 36.7 | 4.116 |

Note: categories above represent items which positively impact one's quality of life. Therefore, a higher score would indicate a better outcome.

# PROMIS-29 QoL Scores: Study vs. U.S. Comparison




* p < .001

N= 311

Source: IDF ePHR Fall 2015 PROMIS-29 QoL Survey

# Reported Infections in Past 12 Months

| Infection Type | Percent | Mean # of infections |
|---|---|---|
| Sinusitis | 62% | 5.7 |
| Bronchitis | 34% | 2.3 |
| Diarrhea (repeated) | 31% | 31.4 |
| Other infection | 17% | N/A |
| Ear Infection | 17% | 3.5 |
| Skin Infection | 16% | 9.1 |
| Candida | 15% | 8.0 |
| Pneumonia | 12% | 1.6 |
| Eye Infection | 11% | 3.4 |
| Abscess | 6% | 2.0 |
| Sepsis | 2% | 1.4 |
| NO INFECTIONS | 8% | N/A |

Q54a.-l. Did the patient experience any of the following infections during the **past 12 months?**
Base: Patients reporting current use of IG therapy, N= 1,439

Source: IDF 2013 National Treatment Survey

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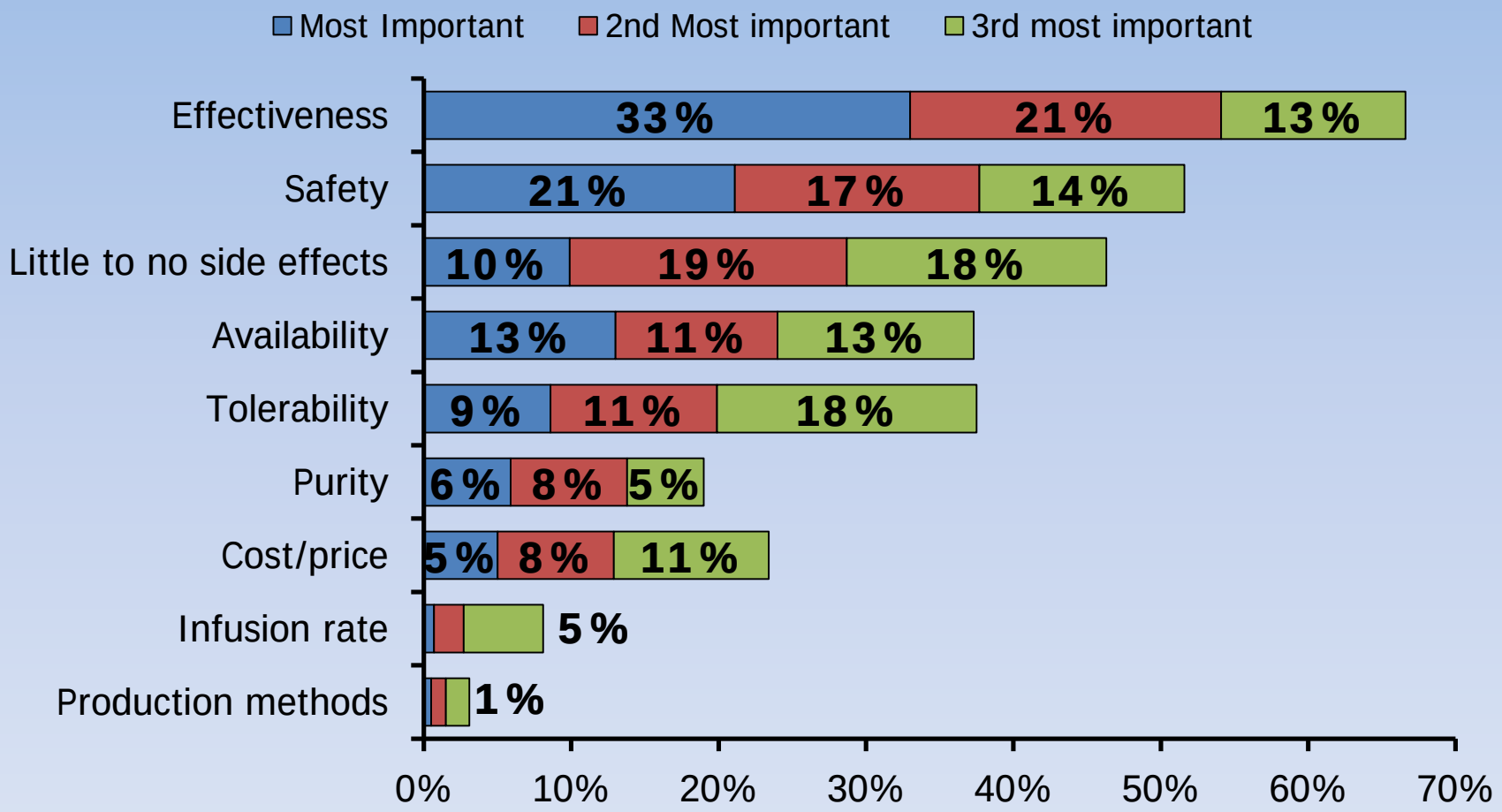
# Most Important Properties of IG Therapy Ranked According to Importance




Q23. What are the THREE most important things when considering an IG therapy product?
Base: Those reporting current IG Therapy use., N= 882, multiple selection

Source: 2009 Immune Deficiency Foundation Patient Survey

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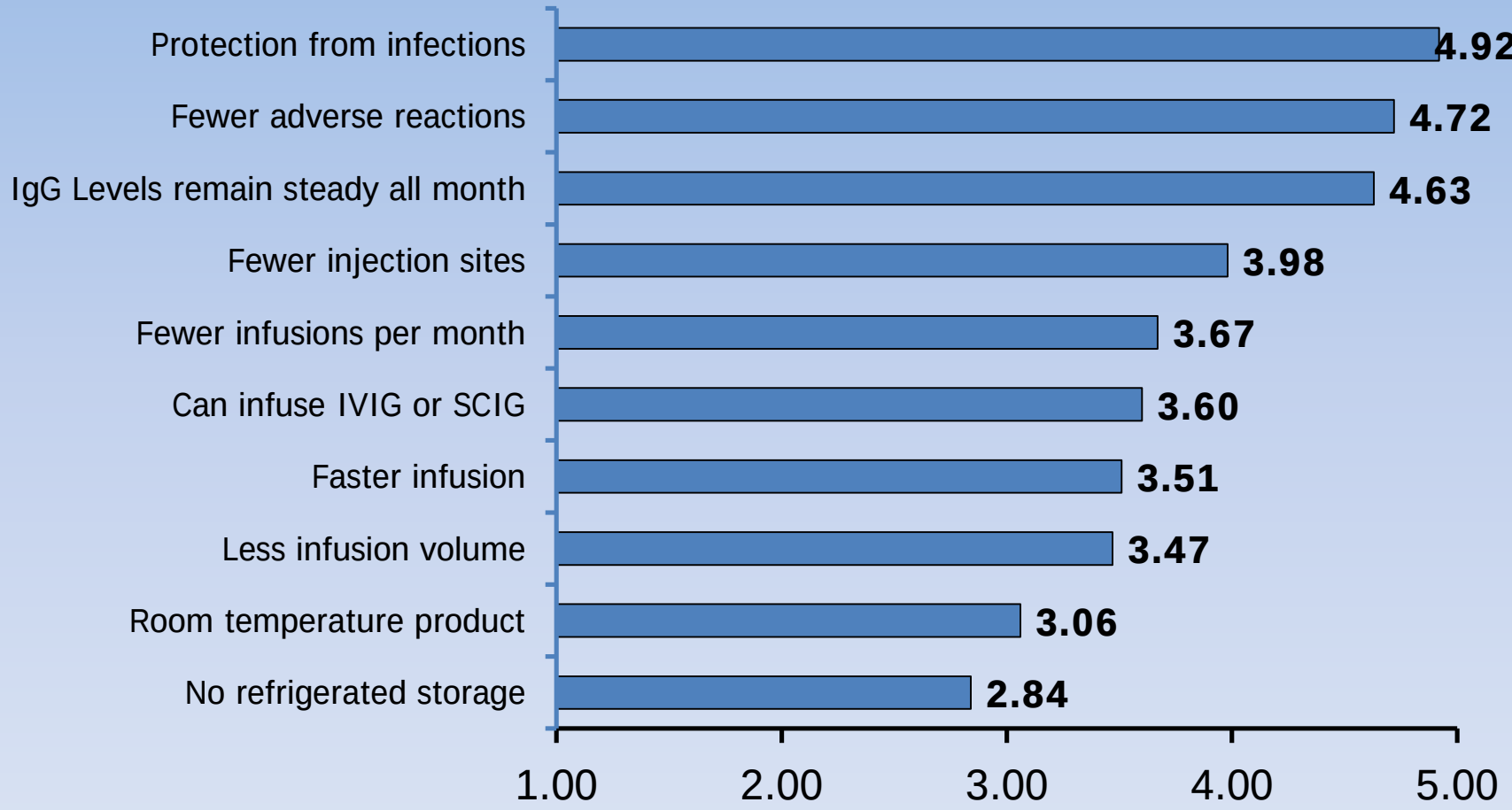
# Importance of Selected IG Therapy Properties




Q57. Please rate on a scale of 1 to 5 where 1 is “not at all important” and 5 is “Very important” Base: Current IG therapy users, N= 808

Source: 2009 Immune Deficiency Foundation Patient Survey

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# What is Important From the Patient Perspective?

- For PI Patients, IG Therapy is life saving and lifelong
- Antibody replacement
- Protection from infections is the most important quality as well as fewer adverse reactions.

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# Efficacy

- As replacement therapy, IG prevents a number of acute infections in immunocompromised individuals
- Successful with many acute bacterial infections, but not completely
- Are current products providing a protective antibody level for patients?
- Concern of lowered titers from the donor pool
- Concern of lower herd immunity
- Dose-relationship with efficacy

# Decline in Titers of Protective Antibodies

- Well publicized outbreaks:  Measles and Pertussis (vaccine not long lasting).
- Reduced titers may not only make IG products less effective, but the reduction in herd immunity may lead to more outbreaks, and less ability to control the spread of disease.
- **How are we going to protect PI patients in this situation?**

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# Emerging Pathogens

- SARS, MERS, new strains of Avian Flu, Enterovirus D-68, EBOLA, WNV, Chickungunya, Dengue, Zika:  Our community is concerned
- **For patients unable to produce protective antibodies, what plans are there to respond rapidly to the threat of an emerging pathogen in the U.S. that has not yet immunized the U.S. donor population?**

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# Outbreaks from Overseas

- **Access to Non-U.S. sourced plasma to produce IG products containing antibodies not found in the US donor population.**
- Useful for outbreaks of pathogens resident elsewhere, as well a possible outbreaks of diseases formally eradicated from the U.S. (measles, smallpox, polio).
- Would vaccinated military personnel by possible donors?

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# Infections We See In Antibody Deficient Patients

Major Acute

- Pneumococcus
- Haemophilus influenza B

Other infections

- Mycoplasma, pseudomonas, streptococcus, staphylococcus aureus, staphylococcus epidermidis, Neisseria, clostridium difficile, salmonella, Moraxella, Klebsiella
- Non-bacterial: giardia and pneumocystis
- Viruses: measles, polio, CMV, VZV, Influenza A&B, parainfluenza, RSV, Adenovirus, enterovirus, Hepatitis A,B,C, WNV, EBV

# Concerns for the Future

- Occasional SBI still occur
- Non-typeable haemophilus, mycoplasma, enterovirus
- Will higher dosing prevent and clear up some of these infections?
- Will they require development of new products?
- More data is needed
  - **We don’t have a clear understanding of what is happening at the level of the pulmonary microbiome**
  - **Important information in guiding the development of future products specifically designed to help prevent the development of progressive pulmonary damage in PI patients.**
  - **Collaboration between manufacturers, FDA, PI patients and immunologists:  opportunity to generate this critical data.**

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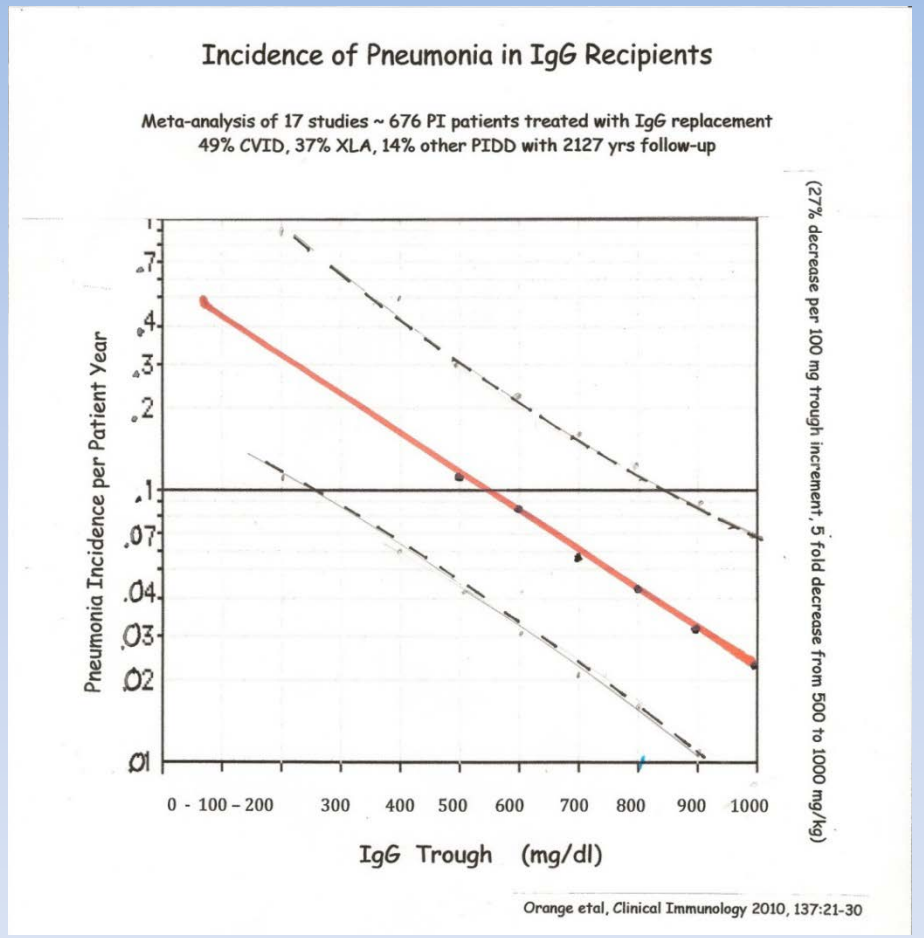
# Critical Role of Dosing

Meta analysis by Orange, et al, *Clinical Immunology* (2010) demonstrated incidence of pneumonia in PI patients fell by 80% as trough level raised from 500 to 1000 mg/dl

- What is an acceptable incidence of infection?
- Issue of insurance company willingness to pay
- Need more data supporting the value of higher dose therapy




Orange, J. S. 2011. Clinical Update in Immunoglobulin Therapy for Primary Immunodeficiency Diseases. *Clinical Focus on Primary Immunodeficiencies*

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# In Summary

- For PI, IG replacement therapy is life saving and life long
- Antibody diversity and efficacy are essential
- Changes to improve safety, yield, etc., must also take into account the critical importance of preservation of antibody efficacy
- Ig replacement therapies should be developed in response to emerging pathogens, and the discussion of non U.S. plasma needs to start
- Changes in the population regarding vaccination impact the health of our patients
- IDF recommends increased focus on issues of antibody efficacy and diversity in patients with PI

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# Potential Next Steps

- Establish a subcommittee of immunologists, IDF, FDA, PPTA and manufacturers to discuss next steps
  - Develop a workshop
  - Survey of physicians to identify serious infections in antibody deficient patients
  - Discuss how to enrich Ig therapies for emerging pathogens and breakthrough infections

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# Thank You!

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