



Jeffrey Modell
Foundation

Curing Pl. Worldwide.



Jeffrey Modell
Foundation

Primary Immunodeficiency Diseases

Report in Sacramento, CA

July, 2010

The Mission

JMF's Mission continues to reach undiagnosed patients through:

- **Physician & Patient Education**
 - **Patient Support**
- **Public Awareness**
 - **Basic & Clinical Research**
- **Advocacy**



Primary Immunodeficiency

The Issue:

Under-Diagnosis

“70% to 90% of all PI patients in the United States and other regions of the world are undiagnosed.”¹

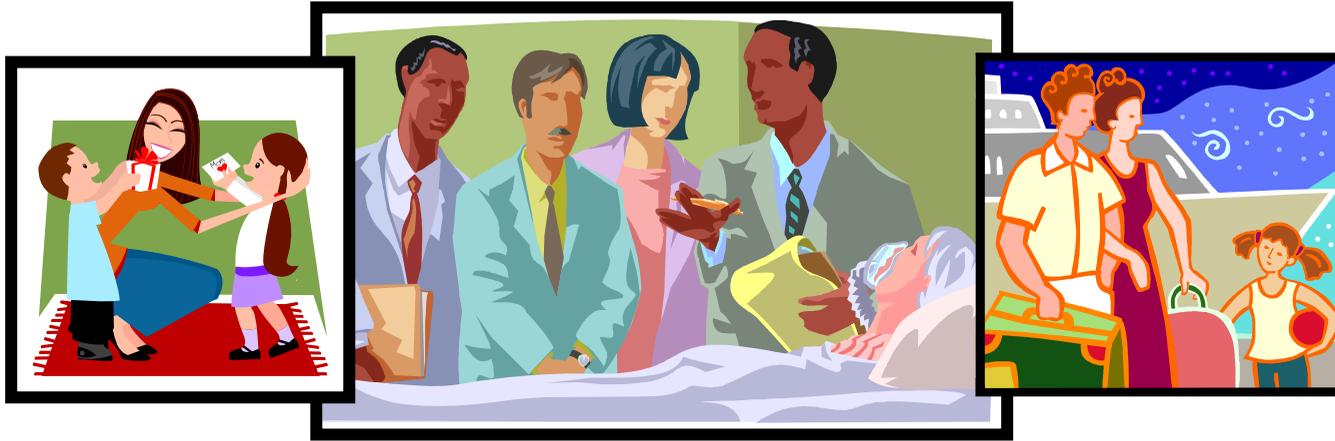
¹ Luigi Notarangelo, MD. Past President of the European Society for Immunodeficiencies (ESID) and Director of the Expert Committee on PI for the World Health Organization/IUIS Expert Committee, in a report to the EU Parliament.



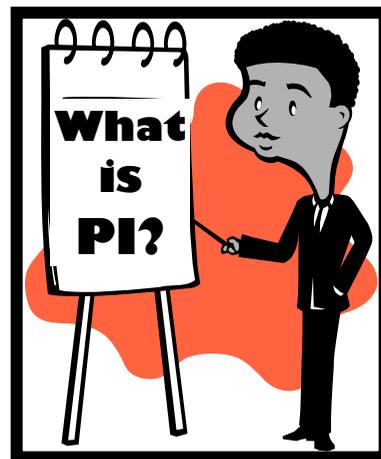
How Do We Address The Issue?

Physician Education and Public Awareness

- Identify suspected and “at risk” patients.
- Refer to JMF Referral Centers Network.
- Provide early and appropriate diagnosis.
- Generate effective intervention and treatment for lifetime management.

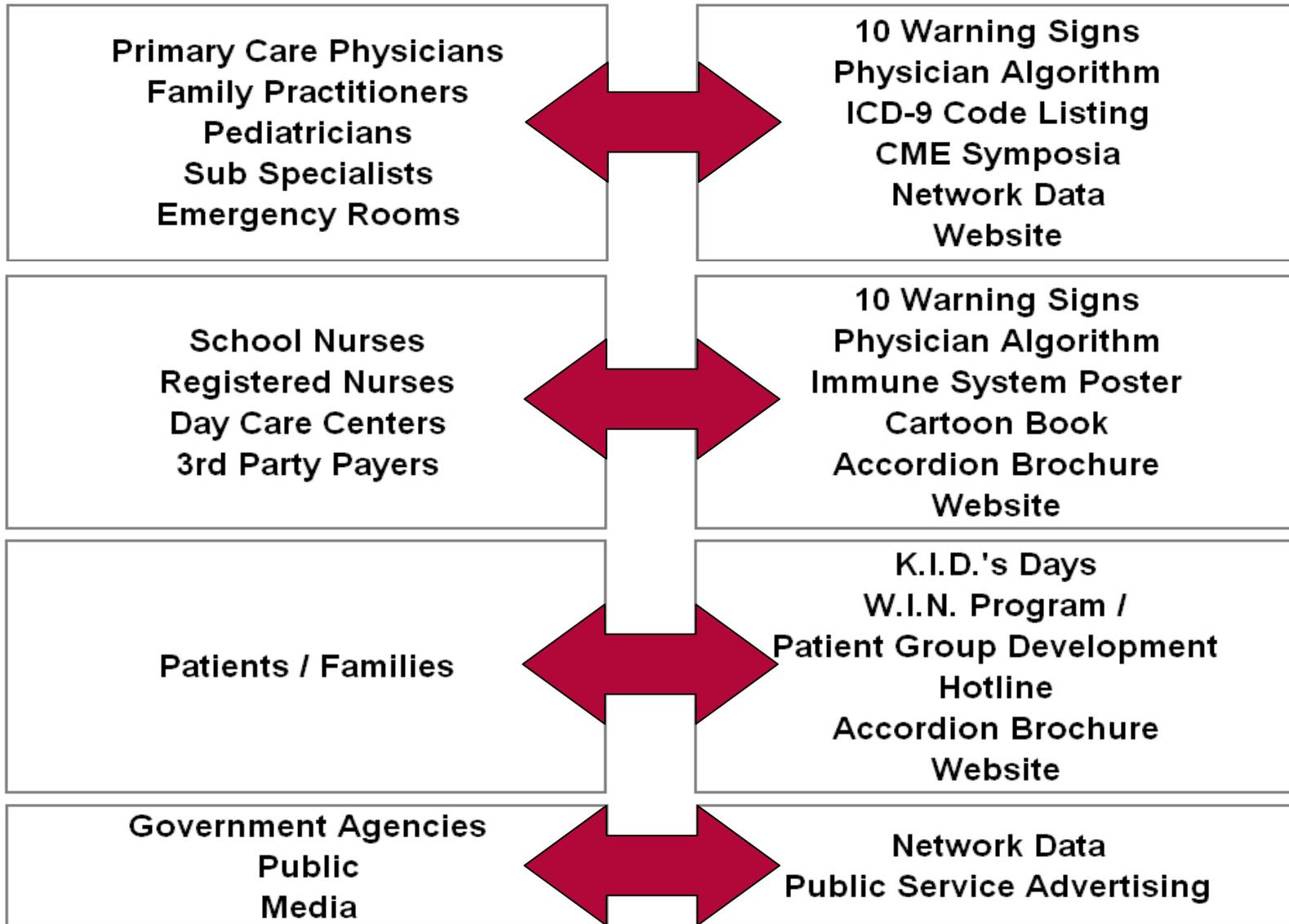


Who Do We Reach and How Do We Reach Them?



Target Audiences

Components



Educational Posters to Physicians

10 Warning Signs of Primary Immunodeficiency

Primary immunodeficiency (PI) causes children and adults to have infections that come back frequently or are unusually hard to cure. 1,000 persons are affected by one of the known Primary Immunodeficiencies. If you or someone you know is affected by two or more of the following Warning Signs, speak to a physician about the possible presence of an underlying Primary Immunodeficiency.

- 1 Four or more new ear infections within 1 year.
- 2 Two or more serious sinus infections within 1 year.
- 3 Two or more months of antibiotics with little effect.
- 4 Two or more pneumonias within 1 year.
- 5 Failure of an infant to gain weight or grow normally.
- 6 Recurrent, deep skin or organ abscesses.
- 7 Persistent thrush in mouth or fungal infection on skin.
- 8 Need for intravenous antibiotics to clear infections.
- 9 Two or more deep-seated infections including septicemia.
- 10 A family history of PI.

Presented as a public service by:



These warning signs were developed by the Jeffrey Modell Foundation Medical Advisory Board. Consultation with Primary Immunodeficiency experts is strongly suggested. © 2009 Jeffrey Modell Foundation. For information or referrals, contact the Jeffrey Modell Foundation: 800-PICO-411 | JmF.org

4 Stages of Testing for Primary Immunodeficiency

- 1
 - History and physical examination, height and weight
 - CBC and differential
 - Quantitative Immunoglobulin levels (IgG, IgM, IgA (related to age))
- 2
 - Specific antibody responses (tetanus, diphtheria)
 - Response to pneumococcal vaccine (pre/post) (for ages 3 and up)
 - IgG subclass analysis
- 3
 - Candida and Tetanus skin tests
 - Lymphocyte surface markers CD3/CD4/CD8/CD19/CD16/CD56
 - Mononuclear lymphocyte proliferation studies (using mitogen and antigen stimulation)
 - Neutrophil oxidation burst (if indicated)
- 4
 - Complement screening CH50, C3, C4
 - Enzyme measurements (adenosine deaminase, purine nucleoside phosphorylase)
 - Phagocyte studies (surface glycoproteins, mobility, phagocytosis)
 - NK cytotoxicity studies
 - Further complement studies AH50
 - Neo antigen to test antibody production
 - Other surface/cytoplasmic molecules
 - Cytokine receptor studies
 - Family/genetic studies

Presented as a public service by:



These recommended serologic tests reflect a consensus of the Jeffrey Modell Foundation Medical Advisory Board. Consultation with Primary Immunodeficiency experts is strongly suggested. © 2009 Jeffrey Modell Foundation. For information or referrals, contact the Jeffrey Modell Foundation: 800-PICO-411 | JmF.org

10 Warning Signs of Primary Immunodeficiency FOR ADULTS

Primary immunodeficiency (PI) causes children and adults to have infections that come back frequently or are unusually hard to cure. 1,000 persons are affected by one of the known Primary Immunodeficiencies. If you or someone you know is affected by two or more of the following Warning Signs, speak to a physician about the possible presence of an underlying Primary Immunodeficiency.

- 1 Two or more new ear infections within 1 year.
- 2 Two or more new sinus infections within 1 year, in the absence of allergy.
- 3 One pneumonia per year for more than 1 year.
- 4 Chronic diarrhea with weight loss.
- 5 Recurrent viral infections (colds, herpes, warts, condyloma).
- 6 Recurrent need for intravenous antibiotics to clear infections.
- 7 Recurrent, deep abscesses of the skin or internal organs.
- 8 Persistent thrush or fungal infection on skin or elsewhere.
- 9 Infection with normally harmless tuberculosis-like bacteria.
- 10 A family history of PI.

Presented as a public service by:



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NEW!

Posters for Pediatricians!

10 Warning Signs of Primary Immunodeficiency

Primary Immunodeficiency (PI) causes children and adults to have infections that come back frequently or are unusually hard to cure. 1:500 persons are affected by one of the known Primary Immunodeficiencies. If you or someone you know is affected by two or more of the following Warning Signs, speak to a physician about the possible presence of an underlying Primary Immunodeficiency.

- 1  Four or more new ear infections within one year.
- 2  Two or more serious sinus infections with little effect.
- 3  Two or more months on antibiotics with little effect.
- 4  Two or more pneumonias within one year.
- 5  Failure of an infant to gain weight or grow normally.
- 6  Recurrent, deep skin or organ abscesses.
- 7  Persistent thrush in mouth or fungal infection on skin.
- 8  Need for intravenous antibiotics to clear infections.
- 9  Two or more deep-seated infections including septicemia.
- 10  A family history of PI.

Presented as a public service by:



These warning signs were developed by the Jeffrey Modell Foundation Medical Advisory Board. Consultation with Primary Immunodeficiency experts is strongly suggested. © 2010 Jeffrey Modell Foundation. For information or referrals, contact the Jeffrey Modell Foundation: 866INFO4PI | info4pi.org

10 Señales de Peligro de la Inmunodeficiencia Primaria

La inmunodeficiencia primaria (Primary Immunodeficiency, PI) hace que los niños y los adultos tengan infecciones que reaparecen con frecuencia y que son inusualmente difíciles de curar. 1:500 personas están afectadas por una de las inmunodeficiencias primarias conocidas.

Si usted o alguien a quien usted conoce está afectado por dos o más de las siguientes señales de peligro, hable con un médico acerca de la posible presencia de la inmunodeficiencia primaria subyacente.

- 1  Cuatro o más infecciones de oídos nuevas en un año.
- 2  Dos o más infecciones de senos paranasales graves en un año.
- 3  Dos meses o más de tratamiento con antibióticos con escaso efecto.
- 4  Dos neumonías o más en un año.
- 5  Dificultad de un bebé o niño pequeño para aumentar de peso y crecer normalmente.
- 6  Abscesos en órganos o abscesos cutáneos profundos recurrentes.
- 7  Aftas persistentes en la boca o infecciones micóticas en la piel.
- 8  Necesidad de recibir antibióticos intravenosos para eliminar las infecciones.
- 9  Dos infecciones profundas o más, incluida la septicemia.
- 10  Antecedentes familiares de PI.

Presentado como servicio público por:



Estos señales de peligro fueron presentadas por el Comité de Asesoramiento Médico de la Fundación Jeffrey Modell. Se recomienda antes de comenzar la consulta a especialistas de inmunodeficiencia primaria. Para obtener más información o referencias, comuníquese con la Fundación Jeffrey Modell: 866INFO4PI | info4pi.org

10 Warning Signs Posters Around the World

China

Finland

France

Germany

Greece

Hungary

Israel

Italy

Iran

Japan

Netherlands

Acht of meer nieuwe oorntstekingen binnen één jaar	Terugkerende diepe huidabscessen, of abscessen in organen zoals bijvoorbeeld de lever
Twee of meer serieuze kaakholte- of/neusbijholtenontstekingen binnen één jaar	Hardnekkige schimmelinfecties (spruw) in de mond of op de huid
Twee of meer maanden achtereen antibiotica met weinig effect	Hardnekkige of terugkerende darminfectie
Twee of meer longontstekingen binnen één jaar	Twee of meer ernstige infecties zoals hersenvliesontsteking, of bloedvergiftiging
Groei achterblijft bij uw kind	In de familie één of meer patiënten met primaire afweerstoornissen

Poland

Portugal

Os 10 Sinais de Alerta para Imunodeficiência Primária na Criança adaptados para o nosso meio são:

1. Duas ou mais Pneumonias no último ano
2. Oito ou mais Otites no último ano
3. Estomatites de repetição ou Monilíase por mais de dois meses
4. Abscessos de repetição ou ectima
5. Um episódio de infecção sistêmica grave (meningite, osteoartrite, septicemia)
6. Infecções intestinais de repetição / diarreia crônica
7. Asma grave, Doença do colágeno ou Doença auto-imune
8. Efeito adverso ao BCG e/ou infecção por Micobactéria
9. Fenótipo clínico sugestivo de síndrome associada a Imunodeficiência
10. História familiar de imunodeficiência

Adaptado da Fundação Jeffrey Modell e Cruz Vermelha Americana

Russia

Spain

Sweden

Posters for School Nurses & Day Care Centers

Your Body's Best Defense

Every day, your body fights off infections, germs, bacteria and parasites. It is destroying these invaders, called *pathogens*, with the help of its number one defense: the *immune system*.

The immune system's job is to keep your body healthy. This requires many different parts of the body to work together against pathogens. Here are the main components of your immune system:

- 1 Tonsils** - Located in the back of your throat, the tonsils protect the entrance to your respiratory and digestive systems by destroying bacteria with the help of white blood cells.
- 2 Thymus Gland** - Located underneath the middle of your breastbone and above your heart, the thymus gland stores white blood cells until they are mature, and then provides them with specific jobs.
- 3 Lymph Nodes** - Small, bean-shaped nodules on the lymphatic vessels, lymph nodes are located primarily in your armpits and groin regions. They filter pathogens out of the lymphatic system.
- 4 Bone Marrow** - Located inside your body's bones, it produces red and white blood cells. Red blood cells carry oxygen to other cells and body parts, and remove carbon dioxide. White blood cells look for and destroy pathogens. The different types of white blood cells are phagocytes, B cells and T cells.
- 5 Spleen** - The largest lymphoid organ in the lymphatic system, the spleen is located to the left of your stomach. The spleen removes pathogens from the blood as it passes through.
- 6 Liver** - Your body's largest internal organ, the liver contains white blood cells. These cells destroy bacteria in the blood as it passes through the liver. It also processes nutrients found in the blood and produces bile used in digestion.
- 7 Blood** - Red and white cells travel throughout your body's blood vessels. White blood cells defend against pathogens, your red blood cells nourish your body.

Some people are born with immune systems that don't work as well as others. This might be caused by a genetic disorder called Primary Immunodeficiency (PI), which might cause a person to be sick a little more often. For more information, visit the Jeffrey Modell Foundation's Web site at www.info4pi.org or call 1-866-info-4-pi.

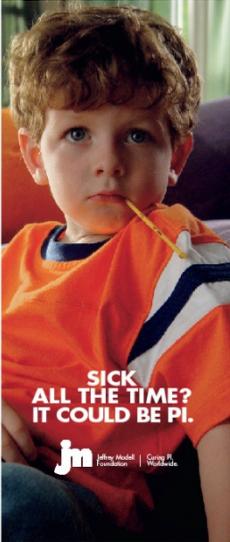
Now that you know how your immune system works, do your part to help it by keeping your body healthy with proper nutrition and exercise.

JM Lifetime Learning Systems, Inc.
A Division of Newly Reader
Jeffrey Modell Foundation

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Immune System Poster

Brochures for Patients



info4pi.org
866.INFO.4.PI

Visit info4pi.org and click **Find an Expert** to find a qualified and experienced immunologist in your area.

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Jeffrey Modell Foundation | 727 Third Avenue, NY, NY 10017
T 212.810.0200 | F 212.764.4180

THE IMMUNE SYSTEM

It's our only defense... but it doesn't work for everyone.

Every day, your body fights off infections, germs, bacteria, and viruses. The body destroys these invaders, called pathogens, with the help of its number one defense, the immune system.

Some people are born with immune systems that don't work as well as others. This could be due to a Primary Immunodeficiency (PI), which might cause a person to be sick a little more often than others.

WHAT IS PI?

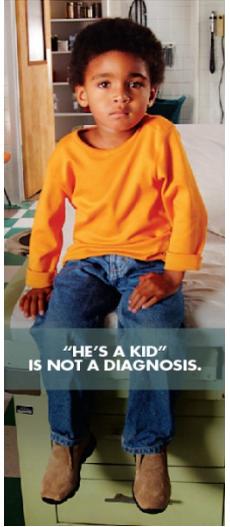
- ▶ PI causes children and adults to have infections that come back frequently and that are unusually hard to cure.
- ▶ The more than 150 different types of PI affect as many as 1 million Americans and 10 million people worldwide.
- ▶ Early diagnosis and treatment are essential to preventing recurring infections from causing permanent damage.

info4pi.org

10 WARNING SIGNS OF PI

- 1 Four or more new ear infections within 1 year.
- 2 Two or more serious sinus infections within 1 year.
- 3 Two or more months of antibiotics with little effect.
- 4 Two or more pneumonias within 1 year.
- 5 Failure of an infant to gain weight or grow normally.
- 6 Recurrent, deep skin or organ abscesses.
- 7 Persistent thrush in mouth or fungal infection on skin.
- 8 Need for intravenous antibiotics to clear infections.
- 9 Two or more deep-seated infections including septicemia.
- 10 A family history of PI.

info4pi.org



"HE'S A KID" IS NOT A DIAGNOSIS.

info4pi.org

ABOUT THE JEFFREY MODELL FOUNDATION

The Jeffrey Modell Foundation is a nonprofit organization established in 1987 by Fred and Vicki Modell in memory of their son, Jeffrey, who died at the age of 15 from Primary Immunodeficiency.

JEFFREY MODELL CENTERS NETWORK

Comprised of Jeffrey Modell Diagnostic Centers and a referral network of hundreds of Expert Immunologists at academic teaching hospitals and medical schools the world over, the Jeffrey Modell Centers Network reaches all corners of the globe.

OUR MISSION

The early and precise diagnosis, meaningful treatment, and ultimate cure, of PI.

MAKING LIVES BETTER

- ▶ Today, patients with PI are able to gain and maintain control of their lives with treatment intervention.
- ▶ They're able to participate in work, school, family and social activities.
- ▶ They see fewer and less severe infections.
- ▶ They face few, if any, side effects from medications and other treatments.
- ▶ They feel good about their treatment programs and, most importantly, themselves.



EVERY DAY BEGINS WITH "WE'LL SEE HOW YOU FEEL."

info4pi.org



VISITA AL MEDICO MAS QUE A SU MEJOR AMIGA.

10 SIGNOS DE ALERTA DE LA PI

- 1 Cuatro o más infecciones de oídos nuevas en 1 año.
- 2 Dos o más infecciones de senos paranasales graves en 1 año.
- 3 Dos meses o más de tratamiento con antibióticos con escaso efecto.
- 4 Dos neumonías o más en 1 año.
- 5 Dificultad de un bebé o niño pequeño para aumentar de peso y crecer normalmente.
- 6 Abscesos en órganos o abscesos cutáneos profundos recurrentes.
- 7 Aftas persistentes en la boca o infecciones micóticas en la piel.
- 8 Necesidad de recibir antibióticos intravenosos para eliminar las infecciones.
- 9 Dos infecciones profundas o más, incluida la septicemia.
- 10 Antecedentes familiares de PI.

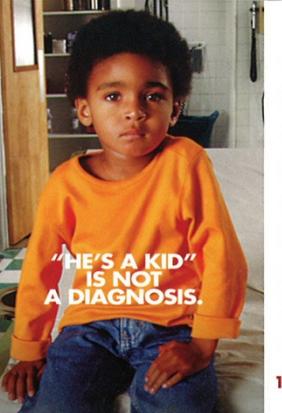


"ES UN NIÑO", NO ES UN DIAGNÓSTICO.

AND



SICK ALL THE TIME? IT COULD BE PI.



"HE'S A KID" IS NOT A DIAGNOSIS.

10 WARNING SIGNS OF PI

- 1 Four or more new ear infections within 1 year.
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Public Service Advertising

- JMF created the first ever Public Service Advertising Campaign on Primary Immunodeficiencies. The campaign reaches the general public through television, radio, print, web and airport advertising.
- To date, the campaign has generated over **\$130 million** in donated media.
- The program is supported by the U.S. Congress, the National Institutes of Health (NIH), and the U.S. Centers for Disease Control and Prevention (CDC).



As Seen In...



As Seen On...



AND MANY MORE...

Airports, Shopping Malls, and High Traffic Billboards!



AND MANY MORE...



What was the Impact?

More than 11 million
Hits to JMF Website in the Past Year

More than 500,000
Visits to JMF Website in the Past Year

More than 17,000
Calls to JMF Hotline

More than 24,000
Patients Registered in JMF Database



The Jeffrey Modell Centers Network

**As a result of this Awareness
Campaign, JMF created a network of
expert physicians to accommodate
referrals, known as the
Jeffrey Modell Centers Network
(JMCN).**



The Jeffrey Modell Centers Network

448 Physicians at
189 Academic Institutions in
191 Cities and
55 Countries Spanning
6 Continents

Where are the JMF Centers in the U.S.?

9 of the Top 10 and 24 of the Top 30
Pediatric Hospitals*



(*Best Pediatric Hospitals 2010. *U.S. News & World Report*, June 4, 2010)

What Does the Network Look Like Worldwide?



AFRICA

Algeria
Bénin
Burkina Faso
Chad
Egypt
Gabon
Guinea
Mali
Mauritania
Morocco
Niger
Senegal
South Africa
Togo
Tunisia

ASIA

China
Hong Kong
India
Japan
Malaysia
Singapore

CANADA

Calgary
Edmonton
Halifax
Hamilton
Montreal
Quebec
Toronto
Vancouver
Winnipeg
Albania
Belarus
Bosnia-Herzegovina
Bulgaria
Czech Republic
Croatia
Estonia
Hungary
Latvia
Lithuania
Macedonia
Moldova

EUROPE

Austria
Belgium
Canary Islands
Denmark
England
Finland
France
Germany
Greece
Ireland
Italy
Netherlands
Norway
Portugal
Spain
Sweden
Switzerland

LATIN AMERICA

Argentina
Brazil
Chile
Colombia

Kuwait
Lebanon
Oman
Saudi Arabia
United Arab Emirates

UNITED STATES

Alabama
Arizona
Arkansas
California
Colorado
District of Colombia
Florida
Georgia
Illinois
Indiana
Louisiana
Maryland
Massachusetts
Michigan
Minnesota
Missouri
Nebraska

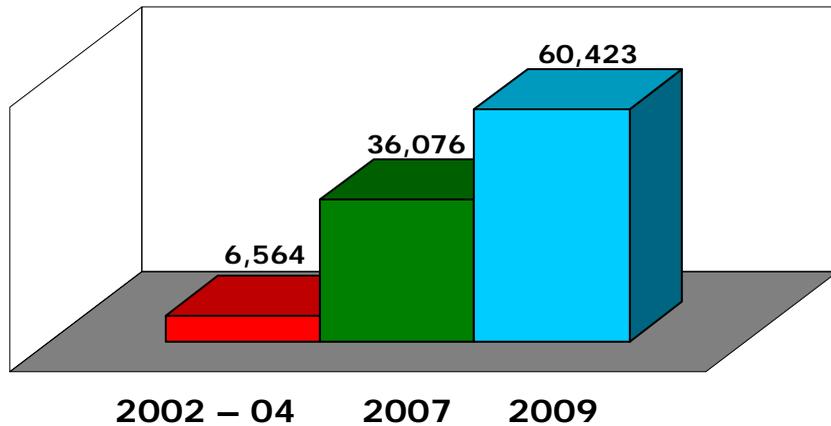
EASTERN/CENTRAL EUROPE



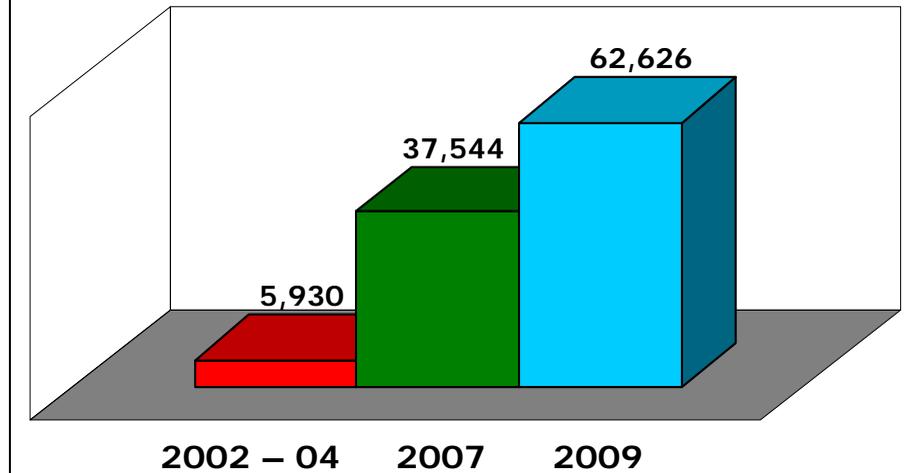
What Has Been the Impact of the Campaign on Early Diagnosis and Management of Primary Immunodeficiencies?

2010 Jeffrey Modell Centers Survey

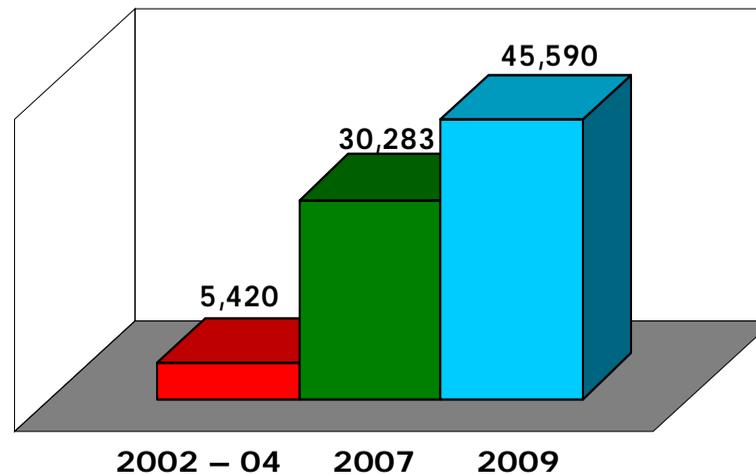
Number of Patients Referred



Number of Patients Followed



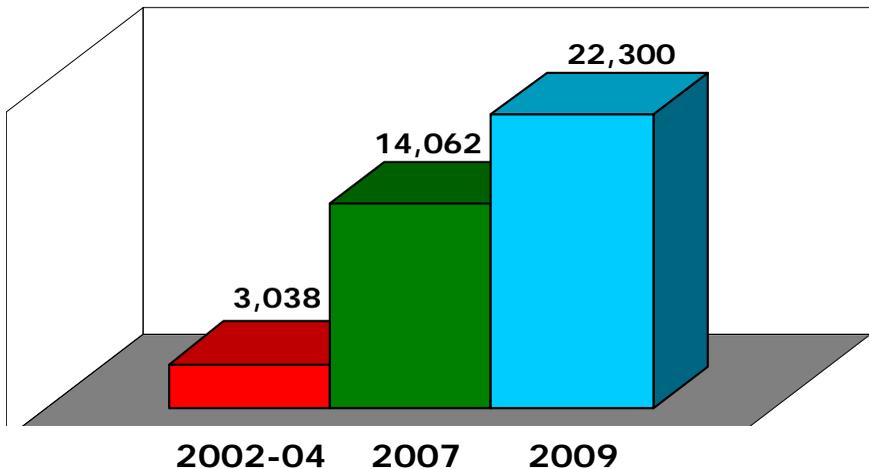
Number of Patients with Identified PI Defects



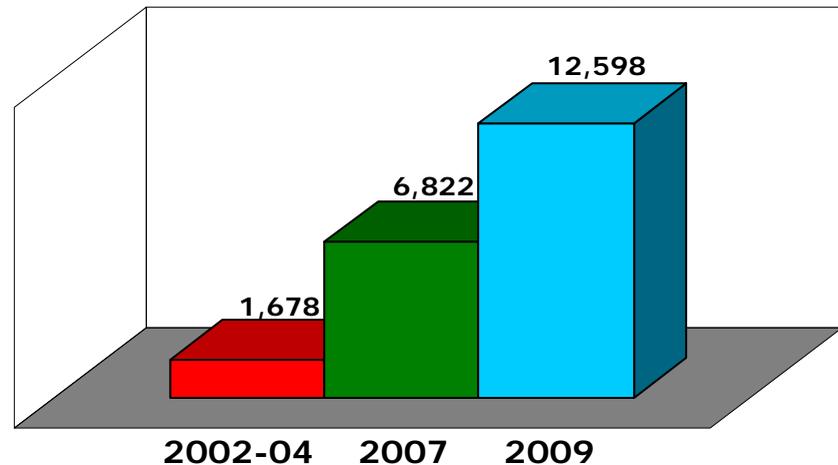
2010 Jeffrey Modell Centers Survey

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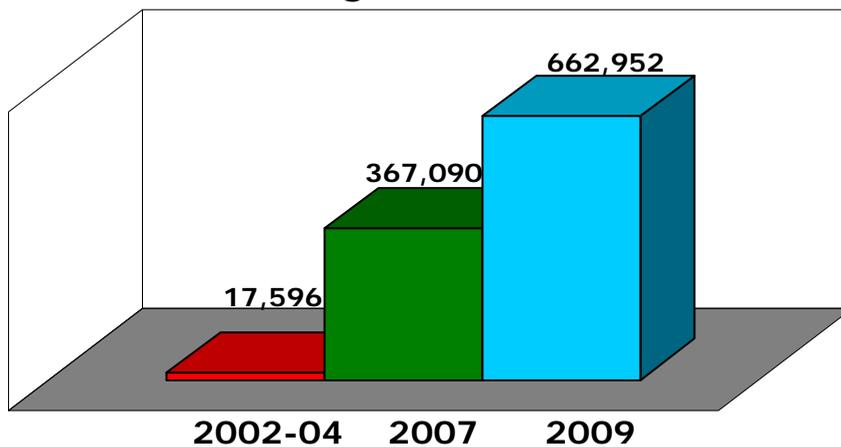
Number of Patients Receiving Treatment



Number of Patients Receiving IgG Therapy



Number of Diagnostic Tests Performed



Survey of Jeffrey Modell Centers Global 2010

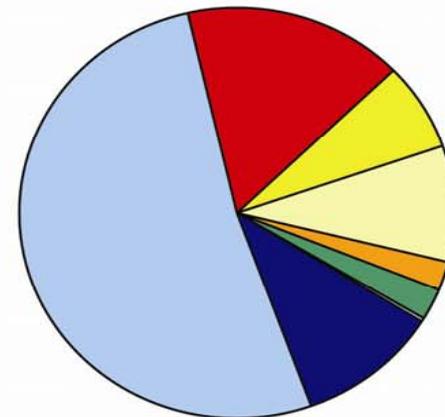
Classification of Immunodeficiency Diseases:

Agammaglobulinemia, AR	372
Agammaglobulinemia, X-linked	1,773
ALPS	425
Antibody Deficiency, Selective	2,510
APECED	105
Ataxia Telangiectasia	1,806
Cartilage-hair Hypoplasia	86
Chediak-Higashi Syndrome	165
Chronic Granulomatous Disease	1,629
Chronic Mucocutaneous Candidiasis	456
Common Variable	7,181
Complement Deficiencies	1,098
DiGeorge Syndrome	3,973
Griscelli Syndrome	98
Hyper IgE Syndrome	809
Hyper IgM, AR	337
Hyper IgM, X-linked	439
Hypogammaglobulinemia of Infancy, Transient	2,261
IgA Deficiency, Selective	5,419
IgG Subclass Deficiency	3,857
IPEX	92
MHC Class I / II Deficiency	195

NEMO	116
Nijmegen Breakage Syndrome	218
Neutropenia	1,488
Leukocyte Adhesion Deficiency	201
Severe Combined:	n=2,547
<i>ADA Deficiency</i>	245
<i>Artemis Defect</i>	87
<i>CD3 δ Deficiency</i>	9
<i>CD3 ϵ Deficiency</i>	4
<i>CD45 Deficiency</i>	2
<i>IL-2R α Deficiency</i>	23
<i>IL-7R α Deficiency</i>	97
<i>JAK3 Deficiency</i>	96
<i>Omenn Syndrome</i>	217
<i>PNP Deficiency</i>	21
<i>RAG-1/2 Deficiency</i>	254
<i>X-Linked Severe Combined</i>	478
<i>ZAP-70 Deficiency</i>	75
<i>Other SCID</i>	939
WHIM Syndrome	49
Wiskott Aldrich	885
X-Linked Lymphoproliferative	223
Any Other	4,777

Major Immunodeficiency Groups:

Predominantly Antibody Deficiencies	(n= 23,710)	52.0%
Cellular Immunodeficiencies	(n= 7,424)	16.3%
Combined Immunodeficiencies	(n= 3,181)	7.0%
Defects of Phagocytic Function	(n= 4,127)	9.1%
Disease of Immune Dysregulation	(n= 1,108)	2.4%
Complement Deficiencies	(n= 1,098)	2.4%
Defects in Innate Immunity	(n= 165)	0.4%
Other Immunodeficiencies	(n= 4,777)	10.5%



Total = 45,590

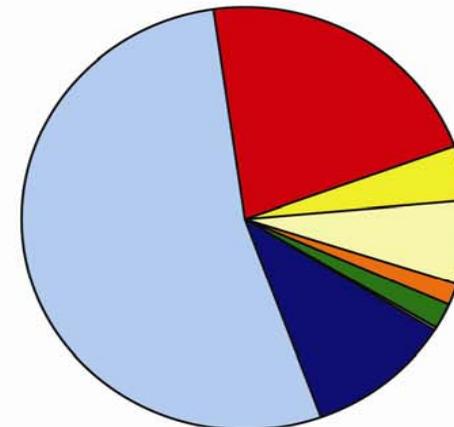
Survey of Jeffrey Modell Centers United States 2010

Classification of Immunodeficiency Diseases:

Agammaglobulinemia, AR	101	NEMO	60
Agammaglobulinemia, X-linked	408	Nijmegen Breakage Syndrome	34
ALPS	76	Neutropenia	337
Antibody Deficiency, Selective	1,569	Leukocyte Adhesion Deficiency	27
APECED	25	Severe Combined:	n=473
Ataxia Telangiectasia	819	ADA Deficiency	64
Cartilage-hair Hypoplasia	20	Artemis Defect	15
Chediak-Higashi Syndrome	20	CD3 δ Deficiency	0
Chronic Granulomatous Disease	283	CD3 ϵ Deficiency	0
Chronic Mucocutaneous Candidiasis	147	CD45 Deficiency	0
Common Variable	2,740	IL-2R α Deficiency	6
Complement Deficiencies	233	IL-7R α Deficiency	29
DiGeorge Syndrome	1,691	JAK3 Deficiency	24
Griscelli Syndrome	6	Omenn Syndrome	51
Hyper IgE Syndrome	186	PNP Deficiency	0
Hyper IgM, AR	60	RAG-1/2 Deficiency	30
Hyper IgM, X-linked	88	X-Linked Severe Combined	136
Hypogammaglobulinemia of Infancy, Transient	554	ZAP-70 Deficiency	19
IgA Deficiency, Selective	1,114	Other SCID	99
IgG Subclass Deficiency	579	WHIM Syndrome	9
IPEX	46	Wiskott Aldrich	179
MHC Class I / II Deficiency	12	X-Linked Lymphoproliferative	62
		Any Other	1,394

Major Immunodeficiency Groups:

Predominantly Antibody Deficiencies	(n= 7,125)	53.4%
Cellular Immunodeficiencies	(n= 2,890)	21.6%
Combined Immunodeficiencies	(n= 573)	4.3%
Defects of Phagocytic Function	(n= 833)	6.2%
Disease of Immune Dysregulation	(n= 235)	1.8%
Complement Deficiencies	(n= 233)	1.7%
Defects in Innate Immunity	(n= 69)	0.5%
Other Immunodeficiencies	(n= 1,394)	10.4%



Total = 13,352

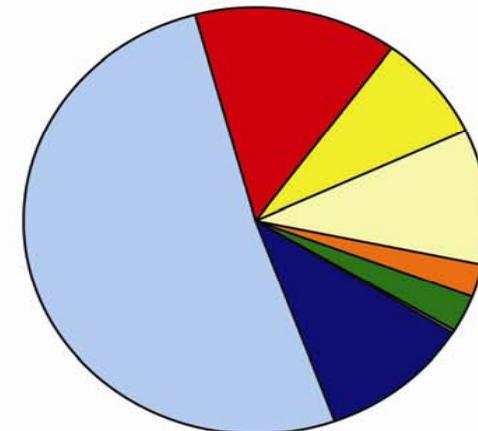
Survey of Jeffrey Modell Centers International 2010

Classification of Immunodeficiency Diseases:

Agammaglobulinemia, AR	271	NEMO	56
Agammaglobulinemia, X-linked	1,365	Nijmegen Breakage Syndrome	184
ALPS	349	Neutropenia	1,151
Antibody Deficiency, Selective	941	Leukocyte Adhesion Deficiency	174
APECED	80	Severe Combined:	n=2,074
Ataxia Telangiectasia	987	<i>ADA Deficiency</i>	181
Cartilage-hair Hypoplasia	66	<i>Artemis Defect</i>	72
Chediak-Higashi Syndrome	145	<i>CD3 δ Deficiency</i>	9
Chronic Granulomatous Disease	1,346	<i>CD3 ϵ Deficiency</i>	4
Chronic Mucocutaneous Candidiasis	309	<i>CD45 Deficiency</i>	2
Common Variable	4,441	<i>IL-2R α Deficiency</i>	17
Complement Deficiencies	865	<i>IL-7R α Deficiency</i>	68
DiGeorge Syndrome	2,282	<i>JAK3 Deficiency</i>	72
Griscelli Syndrome	92	<i>Omenn Syndrome</i>	166
Hyper IgE Syndrome	623	<i>PNP Deficiency</i>	21
Hyper IgM, AR	277	<i>RAG-1/2 Deficiency</i>	224
Hyper IgM, X-linked	351	<i>X-Linked Severe Combined</i>	342
Hypogammaglobulinemia of Infancy, Transient	1,707	<i>ZAP-70 Deficiency</i>	56
IgA Deficiency, Selective	4,305	<i>Other SCID</i>	840
IgG Subclass Deficiency	3,278	WHIM Syndrome	40
IPEX	46	Wiskott Aldrich	706
MHC Class I / II Deficiency	183	X-Linked Lymphoproliferative	161
		Any Other	3,383

Major Immunodeficiency Groups:

Predominantly Antibody Deficiencies	(n= 16,585)	51.4%
Cellular Immunodeficiencies	(n= 4,534)	14.1%
Combined Immunodeficiencies	(n= 2,608)	8.1%
Defects of Phagocytic Function	(n= 3,294)	10.2%
Disease of Immune Dysregulation	(n= 873)	2.7%
Complement Deficiencies	(n= 865)	2.7%
Defects in Innate Immunity	(n= 96)	0.3%
Other Immunodeficiencies	(n= 3,383)	10.5%



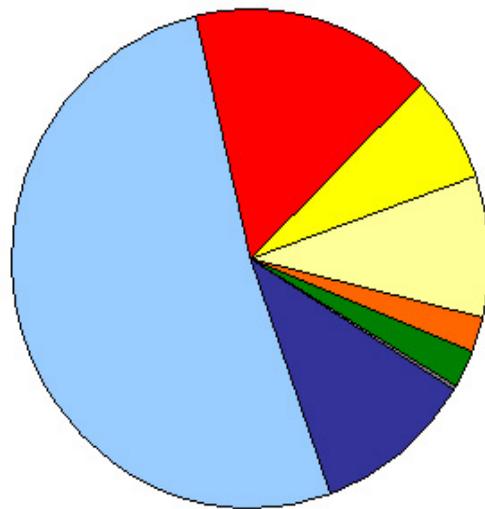
Total = 32,283

Survey of Jeffrey Modell Centers

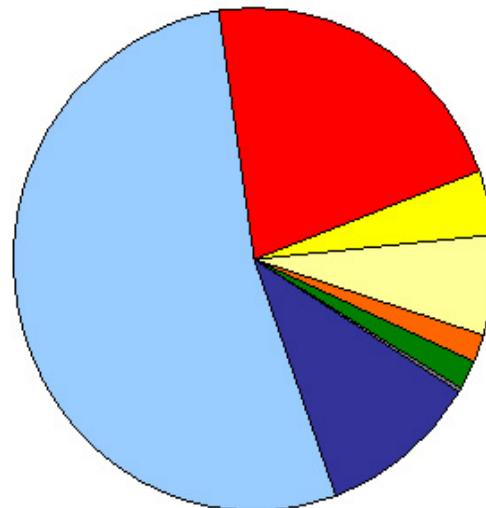
8 Major Categories of Primary Immunodeficiencies

	<u>Global</u>		<u>USA</u>		<u>International</u>	
 Predominately Antibody Deficiencies	n= 23,710	52.0%	n= 7,125	53.4%	n= 16,585	51.4%
 Cellular Immunodeficiencies	n= 7,424	16.3%	n= 2,890	21.6%	n= 4,534	14.1%
 Combined Immunodeficiencies	n= 3,181	7.0%	n= 573	4.3%	n= 2,608	8.1%
 Defects of Phagocytic Function	n= 4,127	9.1%	n= 833	6.2%	n= 3,294	10.2%
 Disease of Immune Dysregulation	n= 1,108	2.4%	n= 235	1.8%	n= 873	2.7%
 Complement Deficiencies	n= 1,098	2.4%	n= 233	1.7%	n= 865	2.7%
 Defects in Innate Immunity	n= 165	0.4%	n= 69	0.5%	n= 96	0.3%
 Other Immunodeficiencies	n= 4,777	10.5%	n= 1,394	10.4%	n= 3,383	10.5%
Total	n= 45,590	100.0%	n= 13,352	100.0%	n= 32,238	100.0%

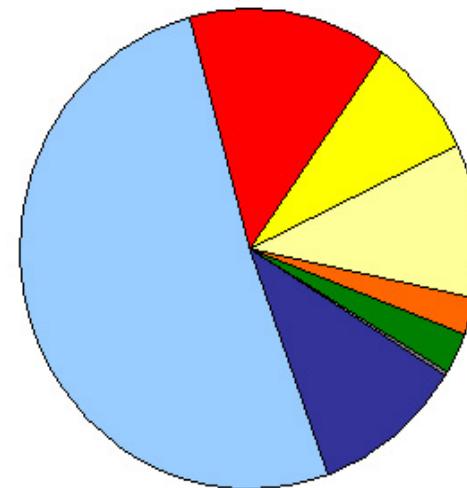
Global



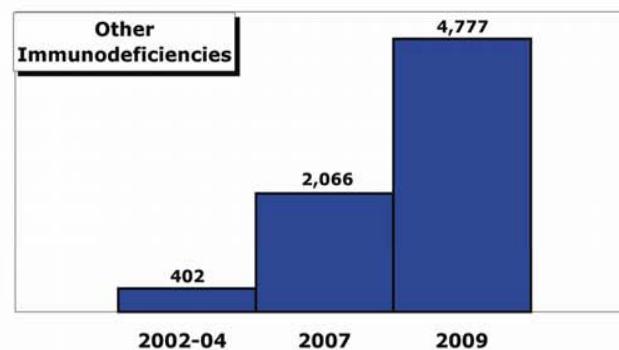
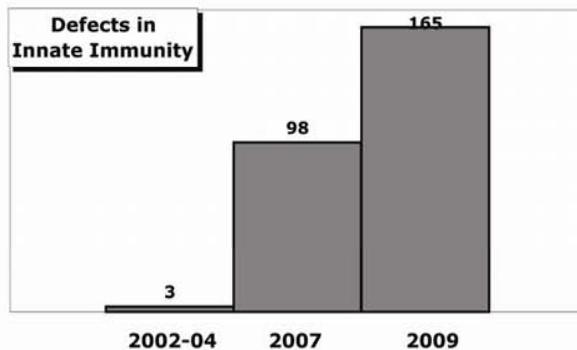
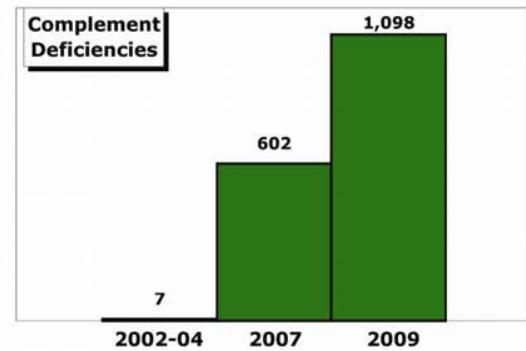
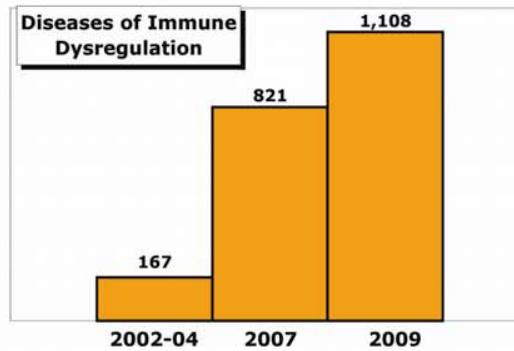
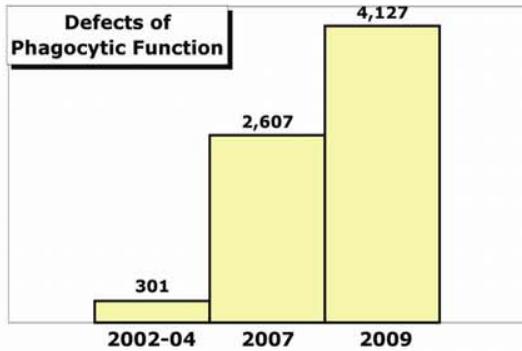
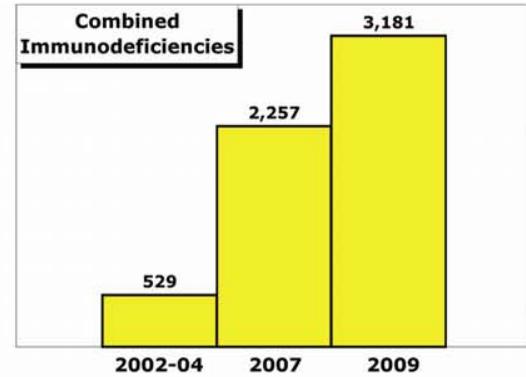
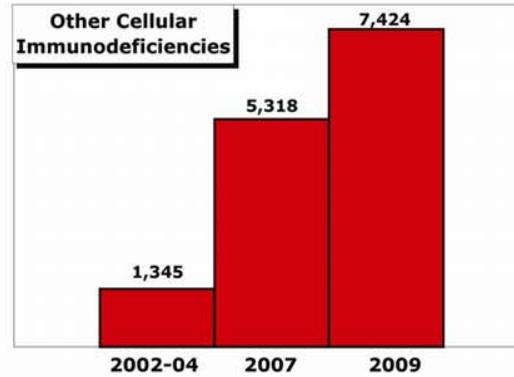
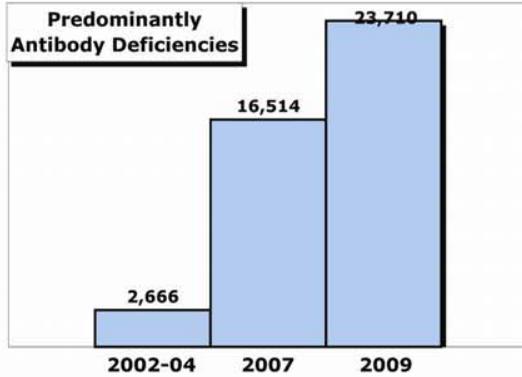
USA



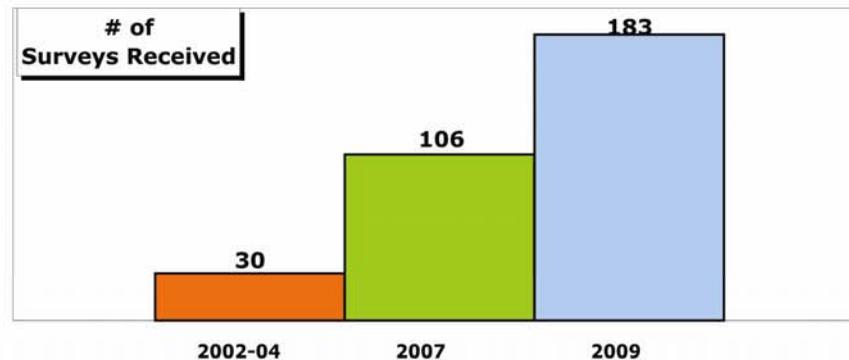
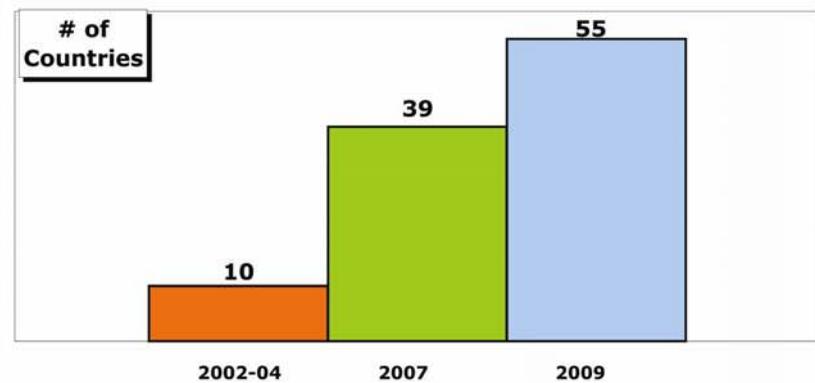
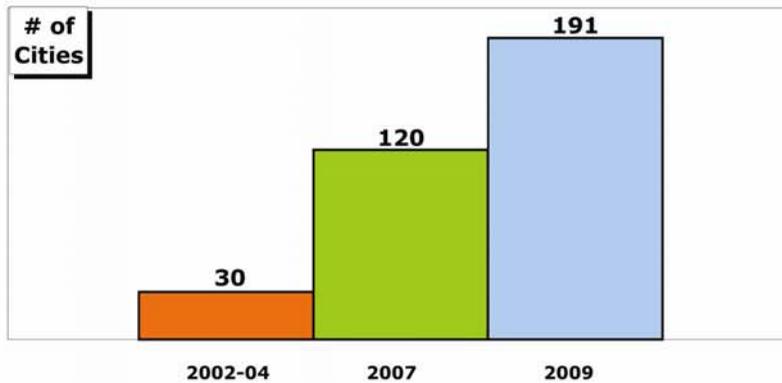
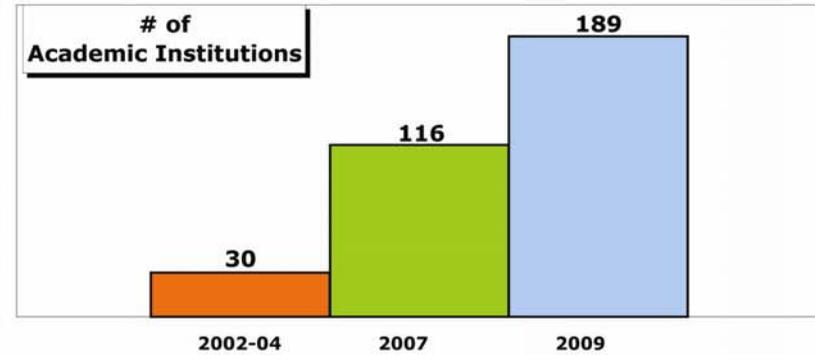
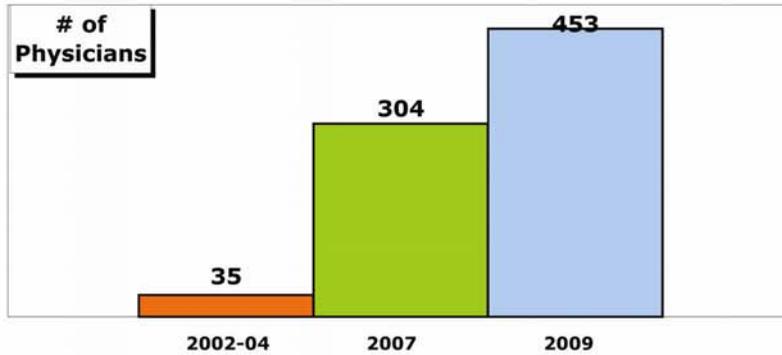
International



2010 - 8 Major Immunodeficiency Groups



2010 Jeffrey Modell Centers Survey Participants



JMCN Comparison with ESID

Major Primary Immunodeficiencies Categories:		JMCN 2010		ESID 2010	
Predominantly Antibody Deficiencies		23,710	52.0%	6,063	55.0%
Cellular Immunodeficiencies		7,424	16.3%	1,788	16.2%
Combined Immunodeficiencies		3,181	7.0%	905	8.2%
Defects of Phagocytic Function		4,127	9.1%	1,211	11.0%
Disease of Immune Dysregulation		1,108	2.4%	157	1.4%
Complement Deficiencies		1,098	2.4%	569	5.2%
Defects In Innate Immunity		165	0.4%	135	1.2%
Other Immunodeficiencies		4,777	10.5%	189	1.7%
TOTAL		45,590	100%	11,017	100%

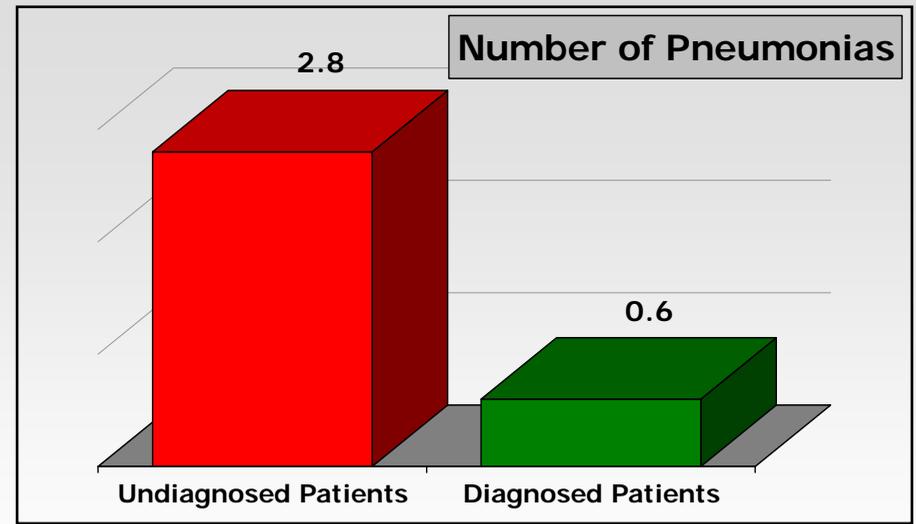
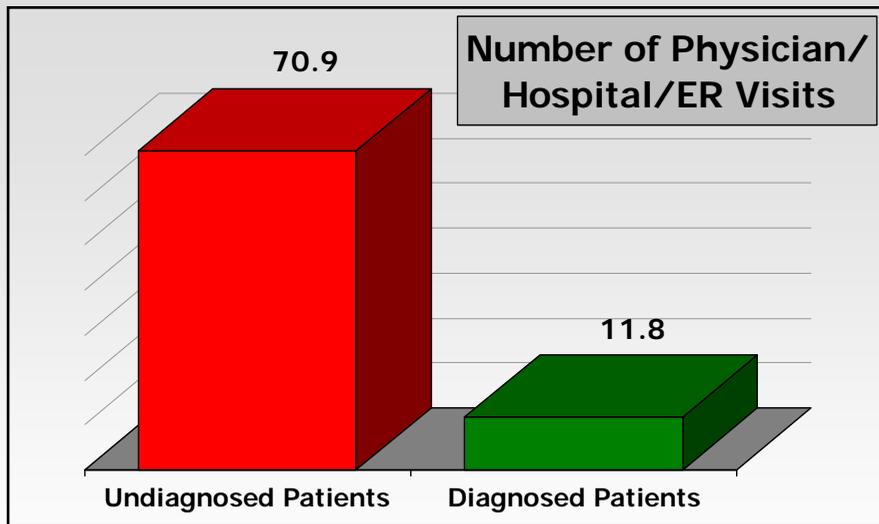
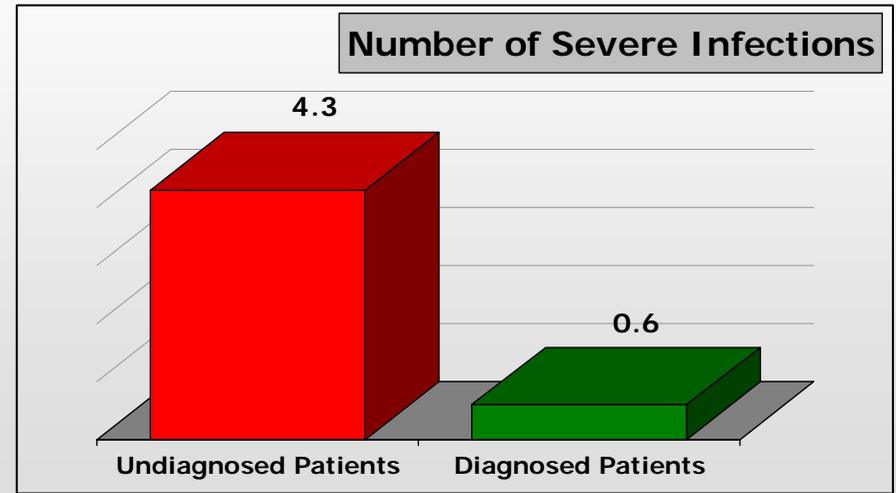
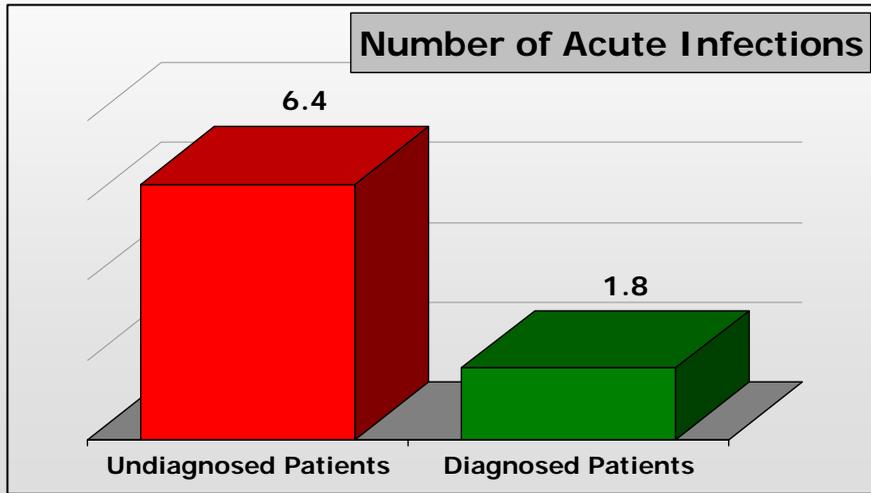


What Does This Data Tell Us?

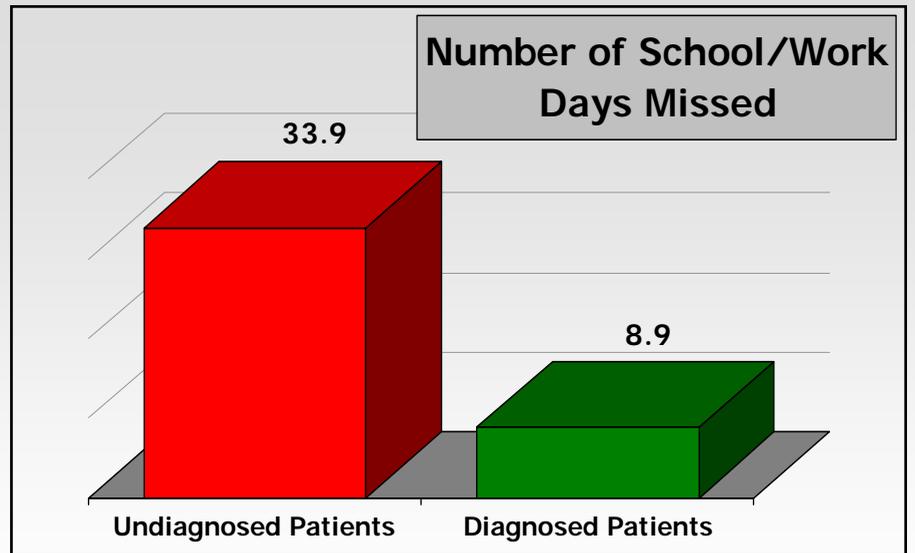
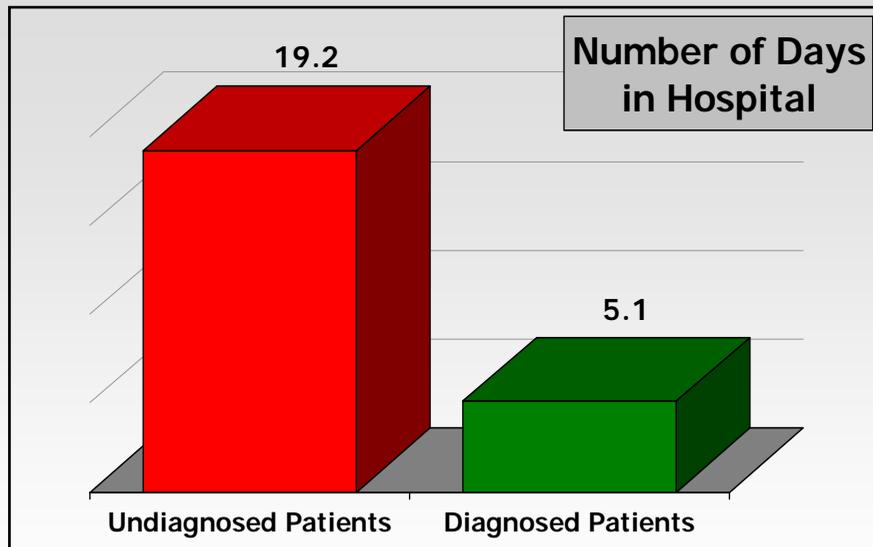
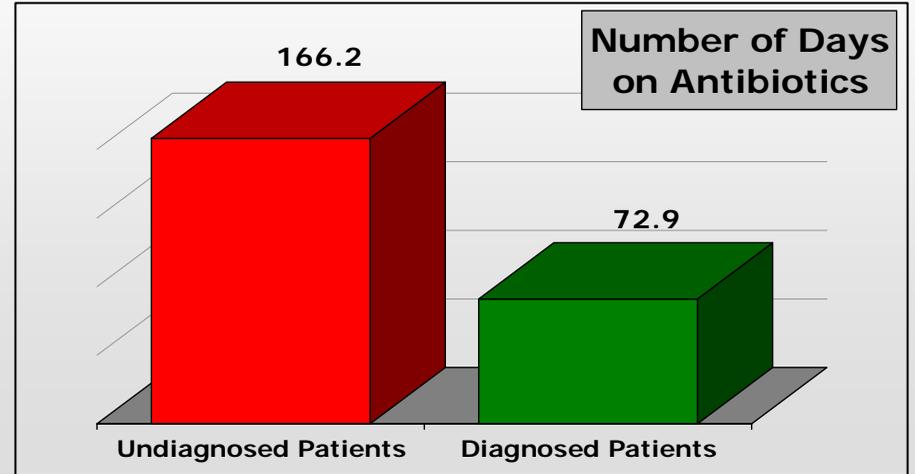
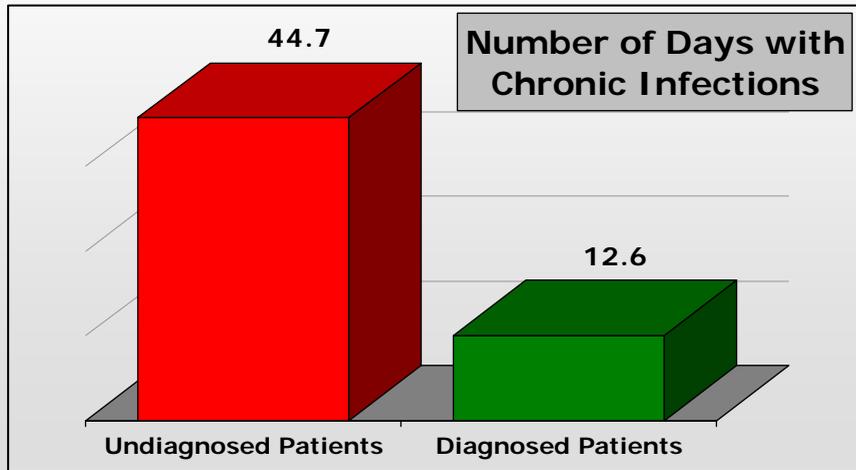
- Specific defects of **45,590** patients!
- **Where** they are being treated!
- **Who** is treating them!
- **How** they are being treated!

What about the Quality of Life for Diagnosed vs. Undiagnosed?

Quality of Life Impact



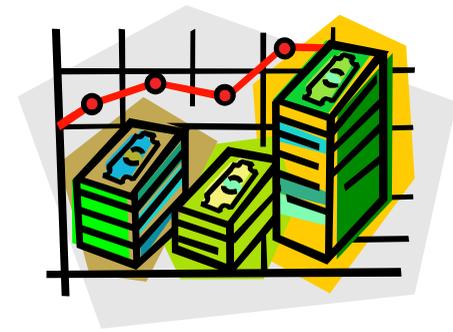
Quality of Life Impact (Continued...)



What is the Economic Impact?

Condition	Cost per patient per episode/day	Pre Diagnosis		Post Diagnosis		Annual savings per patient
		# of episodes	Annual cost per patient	# of episodes	Annual cost per patient	
Chronic infections	\$36.33 (per day)	44.7	\$1,623	12.6	\$457	\$1,166
Acute infections	\$2,950 (per episode)	6.4	\$18,880	1.8	\$5,310	\$13,570
Severe infections	\$5,708 (per episode)	4.3	\$25,544	0.6	\$3,424	\$21,119
Bacterial pneumonias	\$7,529 (per episode)	2.8	\$21,081	0.6	\$4,517	\$16,564
Hospitalizations	\$1,158 (per day)	19.2	\$22,223	5.1	\$5,905	\$16,328
Physician/Hospital/ER visits	\$125 (per visit)	70.9	\$8,862	11.8	\$1,475	\$7,387
Antibiotics	\$4.25 (per day)	166.2	\$706	72.9	\$309	\$397
School/Work days missed	\$136.40 (per day)	33.9	\$4,632	8.9	\$1,213	\$3,410
Totals per patient		\$102,552		\$22,610		\$79,942

Sources for Economic Study



- **Hospital Costs and Utilization Project (HCUP) Data**, was employed for hospital charges and length of stay under the Agency for Healthcare Research and Quality (AHRQ).
- **Centers for Medical and Medicaid Services (CMS)** provided hospital billings.
- **AETNA website** provided outpatient charges based on “in network” centers.
- The study does not include costs of patients/parents lost wages, transportation, or quality adjusted life years benefits for diagnosed and treated patients.



Physicians' Conclusion on Quality of Life & Economic Impact On Diagnosed Patients

The physicians in the Jeffrey Modell Centers Network (JMCN) reported an average annual decrease of **70%** in the number of severe infections, physician, hospital and emergency room visits, pneumonias, school/work days missed, days in the hospital, acute infections, and days with chronic infections.



Physicians' Conclusion on Quality of Life & Economic Impact On Diagnosed Patients

- **The physician reports reflect overall cost savings to the healthcare system comparing undiagnosed and diagnosed/ treated PI patients.**
- **Cost savings average \$80,000 per patient, per year.**
- **This data translates to a cost savings of \$40 billion annually to the healthcare system in the United States.**

All of this Data was published in a Scientific Peer Reviewed Journal:

Modell, F., Puente, D., Modell, V. *From genotype to phenotype. Further studies measuring the impact of a Physician Education and Public Awareness Campaign on early diagnosis and management of Primary Immunodeficiencies. Immunologic Research. Humana Press, an imprint of Springer Publishing. 2009. 44(1-3):132-49*



JMF Program Accomplishments in the Past 12 Months

- **52% increase in the number of funded Jeffrey Modell Diagnostic and Research Centers, expanding from 50 to 76.**
- **25% increase in the number of physicians participating in the JMCN from 357 to 448**
- **The number of academic institutions in the network increased from 157 to 189**
- **27% increase in the number of patients identified in the network with specific defects from 35, 695 to 45,590.**



JMF Program Accomplishments in the Past 12 Months

- **\$18 million of donated media contributed to the Awareness Campaign with an overall average of \$1.5 million per month.**
- **Production of new 10 Warning Signs Poster, Adult 10 Warning Signs Poster, “Cartoon Version” in English and Spanish, Slim Jim, Accordion Folder in English and Spanish and New Immune System Poster Kit.**
- **Distribution of newly published materials to 30,000 pediatricians, as well as sub specialists in emergency medicine, infectious disease, and pulmonary disease.**
- **Distribution of newly published materials to 18,000 physicians in internal medicine and family practitioners, as well as 15,000 school nurses and day care centers, nationwide.**



JMF Program Accomplishments in the Past 12 Months

- **22 Kid's Days** in regions across the US. Featuring Major League Baseball Games, Visits to the Zoo, Harbor Cruise, Football games, museums, and more!
- **34% increase** in new WIN grants to patient organizations worldwide, bringing the total WIN Grants awarded to 104.
- **8 Peer Reviewed Fellowships** awarded through – the Jeffrey Modell Centers Network (**4**) as well as Seattle Children's Hospital (**1**) and Mount Sinai School of Medicine (**3**), totaling \$500,000 in the past year.
- Fellowship funding is provided to the brightest investigators around the world with focus on Primary Immunodeficiencies.



JMF Program Accomplishments in the Past 12 Months

- Each awarded Fellow from the Jeffrey Modell Centers Network will be mentored at a leading institution by our expert investigators.
- Endowed Chair dedicated at Children's Hospital Boston, MA.
- Jeffrey Modell Centers Network peer reviewed research awards totaling \$250,000 in the past year. This program is a collaboration with the National Institutes of Health (NIH).
- Jeffrey Modell Immunology Center at Harvard Medical School, continuing academic programs, symposia, and seminars, throughout 2009-2010.

EU Parliament

- JMF's initiative at the EU Parliament "Call to Action" has generated 121 signatories to-date.
- "HOPE" Hospital System is a signatory covering 15,000 leading hospitals throughout Europe.
- World Health Organization is in discussion with the JMF for a collaboration going forward.

Newborn Screening

- Secretary of HHS adds SCID to the Federal Core Panel for Newborn Screening.
- JMF has advocated for this program over past 9½ years. This is the first defect to be added to the core panel.
- The State of Wisconsin identified and cured the first Newborn screened with SCID.



Newborn Screening

- Late diagnosis of SCID costs an average of \$2.2 million according to the Children's Hospital in Wisconsin.
- Early diagnosis & treatment, in the first 3 months of life, ranges in cost from \$10,000 to \$100,000.
- Cost to screen using TREC's assay is \$4-\$5 per baby
- 10 States are implementing screening programs for SCID at this time.
- JMF has reached out to ALL Governors and State Public Health Commissioners, urging startup of newborn screening programs for SCID.



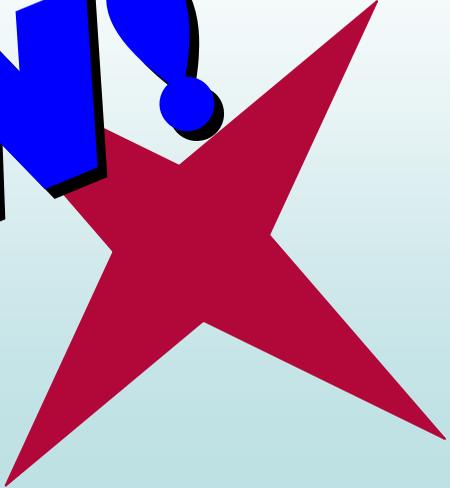
NEW!



NEW!



NEW!



NEW!

TRACE PROGRAM

**Tracking of Reported
Activity
for Clinical Evaluation**

TRACE

Program Studies

NEW!

- I. The TRACE program “drills down” into the JMF Survey data by specific defect. For example, if we did a TRACE Program study on CVID, we would be able to identify the following:
 1. Overall number of CVID patients globally
 2. Number of CVID patients identified in the 9 major regions
 3. Number of CVID patients identified in each country
 4. Number of CVID patients identified in each state, city, and by institution

TRACE

Program Studies

NEW!

II. In each of the 4 categories we can determine:

- 1. The number and percentage of CVID patients related to 100% of all patients.**
- 2. The number and percentage of CVID patients receiving treatment.**
- 3. The number and percentage of CVID patients receiving IG therapy.**
- 4. The number and percentage of patients with CVID compared to all other PI diseases, at the sites.**
- 5. The number and percentage of patients with CVID compared to all other antibody deficiencies other than CVID, at the sites.**
- 6. The number and percentage of patients with antibody deficiencies including CVID compared to the other 7 major Immunodeficiency categories.**

NEW!

TRACE

Program Studies

Continued

- III. A trend study, over a period of 5 years that will show the # and % of patients with CVID globally, by region, country, city, and at a particular institution, for all categories.**

- IV. This retrospective study can be applied to any of the 43 defects but our recommendation would be to initially study CVID and XLA.**

- V. A Second, Phase 2, prospective study may be considered after Phase 1.**

Genome-wide Sequencing in the Newborn Screening Program for SCID

NEW!

- The Newborn Screening program for SCID has been successful in Wisconsin and Massachusetts. Many additional states are starting new programs.
- One scenario that has arisen is that newborns with very low T cell count were picked up by TRECs assay screen but were not typical of SCID
- The baby appears to have a serious condition but not one that should necessarily require a Bone Marrow Transplant

NEW!

Genome-wide Sequencing in the Newborn Screening Program for SCID

- On the other hand, if we wait, significant and overwhelming infectious complications may occur making it too late to transplant.
- Evaluation of those newborns to find the molecular defect can take months or even years to complete.
- The Wisconsin newborn screening team believes that genome wide sequencing, is the most expeditious, informative and cost effective method to evaluate infants with profound T-cell Lymphopenia, not typical of SCID. The sequencing should provide the specific mutation.
- JMF initiated funding with the State of Wisconsin and entered an Illumina Individual Genome Sequencing Services Agreement.

NEW!

TROUGH Level Study Plans for 2011

- This is a multicenter research project
- 8 Children's Hospitals and Principal Investigators at these institutions are currently participating in this study.
- The goal is to determine biological IgG levels for patients with CVID and XLA, to remain infection free.
- The Web based program to compile data for the 8 hospital consortium has been developed and refined.
- Joint IRB approval is now underway.
- Patient data entry forms will be finalized to determine number of data fields in the questionnaire, when enrolling a patient in the study.

What is **Spirit**® ?

Software for
Primarily
Immunodeficiency
Recognition
Intervention and
Tracking

Spirit[®]'s Mission

- 1. Disease Prevention**
- 2. Electronic Medical Tracking**
- 3. Reduction of Healthcare Costs**
- 4. Improved Quality of Life for Patients**

What Data Will **Spirit**[®] Generate?

HIPAA-compliant, de-identified reports will describe the health plan's population via the following metrics related to PI:

- **Population Overview (Gender and Age)**
- **Distribution by PI Warning Sign**
- **Distribution by Risk Category and by Number of Warning Signs (High, Moderate, and Low)**
- **Antibiotic Utilization**

Spirit[®] Analyzer

Pilot Testing

Three health plans pilot tested the SPIRIT Analyzer utilizing their plans' records and provided JMF with top-level, de-identified, blinded data.

A summary comparing their results follows...

Analyzer **Spirit**[®] Data Summary From Beta Benchmark and Pilot Sites

	Benchmark Data		Pilot Site 1		Pilot Site 2		Pilot Site 3	
TOTAL PATIENT POPULATION	2,056,857		525,000		700,000		200,000	
TOTAL PATIENTS OF INTEREST	712,144 (34%)		122,085 (23%)		183,888 (26%)		91,787 (46%)	
CLAIM TYPE (All Patients of Interest)	Patients	Percent	Patients	Percent	Patients	Percent	Patients	Percent
PI warning sign diagnosis only	153,861	22	1,572	1	27,370	15	14,533	16
Antibiotic only	264,379	37	70,643	58	64,031	35	26,162	29
PI warning sign diagnosis + antibiotic	293,904	41	49,870	41	92,487	50	51,109	56
GENDER (All Patients of Interest)	Patients	Percent	Patients	Percent	Patients	Percent	Patients	Percent
Female	408,997	57	71,985	59	102,927	56	54,805	59.7
Male	303,147	43	50,100	41	80,946	44	36,982	40.3
AGE GROUP (YRS) (All Patients of Interest)	Patients	Percent	Patients	Percent	Patients	Percent	Patients	Percent
<5	78,384	11	9,373	8	33,203	18	33,738	36.8
5-10	84,154	12	9,915	8	20,846	11	16,588	18.1
11-17	80,001	11	11,792	10	18,449	10	12,508	13.6
18-25	82,121	12	12,085	10	19,706	11	8,388	9.1
26-35	97,697	14	12,412	10	27,159	15	6,905	7.5
36-60	289,787	41	58,100	48	51,589	28	7,400	8.1

Data Summary From Beta Benchmark and Pilot Sites (Continued...)

	Benchmark Data		Pilot Site 1		Pilot Site 2		Pilot Site 3	
	Patients	Percent	Patients	Percent	Patients	Percent	Patients	Percent
PI WARNING SIGNS								
WARNING SIGN 1	1,031	0.14	128	0.10	230	0.13	378	0.41
WARNING SIGN 2	953	0.13	178	0.15	212	0.12	95	1.00
WARNING SIGN 3	11,992	1.68	2,468	2.02	4,331	2.36	719	0.78
WARNING SIGN 4	1,510	0.21	220	0.18	270	0.15	346	0.38
WARNING SIGN 5	10,048	1.41	745	0.61	1,157	0.63	2,221	2.42
WARNING SIGN 6	4,984	0.7	663	0.54	714	0.39	1,423	1.55
WARNING SIGN 7	681	0.1	62	0.05	72	0.04	211	0.23
WARNING SIGN 8	283	0.04	80	0.07	203	0.11	0	0.00
WARNING SIGN 9	5,488	0.77	760	0.62	649	0.35	631	0.69
NUMBER OF PI WARNING SIGNS	Patients	Percent	Patients	Percent	Patients	Percent	Patients	Percent
2 WARNING SIGNS	1,403	0.2	257	0.21	307	0.17	346	0.38
3+ WARNING SIGNS	86	0.01	32	0.03	33	0.02	33	0.04
RISK CATEGORY	Patients	Percent	Patients	Percent	Patients	Percent	Patients	Percent
HIGH (>10 RISK POINTS)	1221	0.17	281	0.23	228	0.12	560	0.61
MODERATE (8-10 RISK POINTS)	1793	0.25	288	0.24	413	0.22	433	0.47
LOW (1-7 RISK POINTS)	307,730	43.21	4,009	3.28	6,698	3.64	4,607	5.02
PATIENTS WITH 0 RISK POINTS	401,400	56.37	117,507	96.25	176,549	96.02	86,187	93.9

Data Summary From Beta Benchmark and Pilot Sites (Continued...)

PREVALENCE	Benchmark Data	Pilot Site 1	Pilot Site 2	Pilot Site 3
2 OR MORE OF THE 10 WS	1:478	1:423	1:598	1:243
HIGH RISK CATEGORY	1:583	1:430	1:806	1:165
MODERATE RISK CATEGORY	1:235	1:428	1:445	1:212
HIGH + MODERATE CATEGORIES	1:167	1:214	1:287	1:92

All of the ratios are consistent with NIH and CDC estimates of incidence and prevalence.

What Happens To “At Risk” Patients Flagged By Spirit[®]?

- The Jeffrey Modell Centers Network continually identifies outcomes of “high risk” patients.
- A number of these “high risk” patients, even after definitive diagnosis, require periodic monitoring but no specific intervention.
- Others require the use of prophylactic antibiotics and in some cases immunoglobulin therapy.
- This data provided by the physicians and the Jeffrey Modell Centers Network is helpful as a guide to anticipated outcomes for “high” and “moderate” risk patients flagged by SPIRIT.

Anticipated Outcomes for “High Risk” patients flagged by Spirit®

(Information Derived from the Jeffrey Modell Centers Network)

100
Random sample of referred “at risk” patients

73 of 100
Identified with a PI defect

38 of 100
Patients with Antibody Deficiency

24 of 100
Patients treated with IVIG

Recently JMF Presented the SPIRIT Analyzer to members of the Managed Care Network.

Managed Care Network (MCN) includes senior executives and Medical/Pharmacy Directors at regional and national health plans. Together they represent nearly 200 million covered lives.

Spirit[®] Analyzer

When Surveyed, participants reported as follows:

- **81 % agreed or strongly agreed that “Primary Immunodeficiency is a concern that should be monitored in my health plan”**
- **75% agreed or strongly agreed that “early identification of Primary Immunodeficiencies can improve patient’s quality of life and reduce health care costs”**
- **66% agreed or strongly agreed that “JMF’s SPIRIT Analyzer represents an excellent opportunity to screen for undiagnosed patients in my health plan”**

Why is **Spirit**® Right for you?

- No cost to implement this software.
- No risk to your current database.
- Can easily do a test-run of the software with a small portion of your database.
- **Potential to save huge healthcare dollars**

Why is **Spirit**[®] **Right for you?**

- **Technical support**
- **User Guide, FAQs, and hotline contact included with software.**

No additional personnel or resources are required to make use of the SPIRIT Analyzer.

Spirit[®] Analyzer System Requirements

Hardware

Intel[®] Pentium[®] III 600MHz or equivalent
512 MB RAM (1 GB RAM or more strongly recommended)
1GB + (3 X Data file size) free disk space
32-bit Video (1024 x 768 display)

Operating System

Microsoft[®] Windows[®] 2000, XP, Vista

Software Applications

Adobe[®] Reader[®] 6.0
Microsoft[®] .NET Framework 1.1

Processing Time

Processing (run) times will vary based on computer speed and file size. The amount of computer memory (RAM) and the size of the dataset are the biggest factors affecting execution run time. Desktop computers generally run faster than notebook computers with the same technical specifications. A notebook computer with Pentium IV, 1GB RAM, and 20GB of free disk space can analyze **1,000,000 pharmacy and medical claims in approximately 30 minutes.**

How to Begin ?

There are two ways to obtain this software:

1. Online: www.info4pi.org:

- a. Scroll down to "Professional Medical Information"
- b. Click on "SPIRIT Analyzer"
- c. Complete brief request form

OR

2. Email the Jeffrey Modell Foundation at Info@JMFWorld.org with the following information:

- a. Company/Group Affiliation
- b. Your Contact Information

Let's Begin!

It's time to catch the

