National Organization for Rare Disorders (NORD)
Rare Diseases & Orphan Products
Breakthrough Summit
Arlington, VA

Special Training for Rare-Disease Patient Advocates

October 23, 2015
The Natural History of Disease: The Trump Card?
Presenters

Jacqueline Kraska, MA
Research Programs Manager
National Organization for Rare Disorders

Ilene Sussman, PhD
Executive Director
VHL Alliance

Eleanor M. Perfetto, PhD, MS
Professor, University of Maryland School of Pharmacy
Senior Vice President of Strategic Initiatives, National Health Council
Acknowledgements

• Foundation for Prader-Willi Research (FPWR)
• National PKU Alliance (NPKUA)
• Congenital Hyperinsulinism International (CHI)
• FDA NHS Committee Members
• Reta Honey-Hiers, R.N., C., *Tarlov Cyst Disease Foundation*
• Christopher Scarchunes, *Immune Deficiency Foundation*
• Suzanne Nylander, OD, *VHL Alliance*
Learning Objectives

At the end of this session, participants will be able to:

• Describe the natural history of disease and its treatment as a leverageable asset of patient groups

• Identify how data sources (e.g., registry, database, focus groups, surveys) could be optimized to support PCOR partnerships
Session Overview

1. Natural History of Disease
   - Jacqueline Kraska, National Organization for Rare Disorders

2. Leveraging Assets
   - Jacqueline Kraska, National Organization for Rare Disorders

3. Case examples of optimizing natural history of disease resources
   - Eleanor Perfetto, University of Maryland School of Pharmacy
   - Illene Sussman, VHL Alliance

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“There’s an old saying: Know what you know, and know what you don’t know. With these rare diseases, we don’t even know what we don’t know. The way to find that out is to develop these longitudinal registries (also known as natural history studies).”

Marshall L. Summar, MD
Division of Genetics & Metabolism
Children’s National Medical Center


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What do we know?

✓ 7,000 different types of rare diseases
✓ Affects approx. 350 million people globally
✓ NIH estimates 50% affect children
✓ Approx. only 5% of rare diseases have FDA-approved treatments
✓ Rare diseases are unique and complex in nature
✓ Serious and life altering; many life threatening or fatal
✓ Low prevalence in patient populations poses challenges to understanding, diagnosing, treating & preventing rare diseases
What do we not know?

• A LOT!

“It's a very rare disease—it doesn't have a cure. It doesn't even have a spokesperson.”

“Your symptoms are completely alien to me.”
Natural History of Disease

“The natural course of a disease from the time immediately prior to its inception, progressing through its pre-symptomatic phase and different clinical stages to the point where it has ended and the patient is either cured, chronically disabled, or dead without external intervention.”

Posada de la Paz M; Groft SC. 2010. Rare disease epidemiology. Vol 686
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Natural History Study Data

• The cause, range of manifestations, and progression of rare diseases
• Identify demographic, genetic, environmental, and other variables that correlate with disease and outcomes
• Can yield information on biomarkers and other correlates of clinical outcomes
• Can inform drug development, care management and policy

http://www.fda.gov/ForIndustry/DevelopingProductsforRareDiseasesConditions/OOPDNewsArchive/ucm292294.htm
Huml RA. FSH Society’s 2014 Biennial FSHD Connect Meeting: Natural History Studies. August 2014

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Patient Registry

• An organized online system that collects uniform data to evaluate specified outcomes for a population defined by a particular disease, condition, or exposure.

• Collects NHS data.

• May also include the collection of diagnostic reports & patient clinical samples (such as tissue and blood).
Patient Registries Uses

– Learn about a specific disease/condition
– Learn about population behavior patterns and their association with disease development
– Recruit patients for clinical trials
– Develop therapeutics
– Develop research hypotheses
– Improve and monitor quality of health care
– Monitor outcomes
– Study best practices in care or treatment

Workman TA. Engaging patients in information sharing and data collection: The role of patient-powered registries and research networks prepared for AHRQ.

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Research-Generated Patient Registries

- Registries established by research, academic, or clinical institutions
- Purpose: observational data collection for a specific research agenda
- Funded by private or federal funds

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Patient-Powered Patient Registries

- Registries established by a one or more patient organizations
- Purpose: tool for patient organization to engage in research to support their objectives
- Patients /patient advocacy organizations “power” the registry
  - set, manage and control research agenda, data collection, and analysis/dissemination of research findings

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Other Opportunities for Leveraging Your Assets

- Survey data
- Interview data
- Focus group data
- Registry data
- Natural History study data
How do you Leverage Partnerships Along the way?

• Step 1 – partnerships with patient, family and caregivers to collect data

• Step 2 – patient organization use partnerships with patient community to discern gaps in knowledge, form an advisory committee, develop protocol and launch data collection

• Step 3 – patient organization use partnership with patient community, advisory board, and external collaborators to engage in PCOR
Case Examples
Leveraging Your Assets

• **Case 1**
  – Asset: Engaged patient, family member, caregiver or organization
  – Collect data via website, questionnaire, database, spreadsheet

• **Case 2**
  – Asset: Engaged patient organization
  – Formalize data collection as per a project protocol and develop and launch registry

• **Case 3**
  – Asset: Engaged patient organization conducting research
  – Actively collecting data, managing registry and data, including data sharing and collaborations
Leveraging Your Assets

• Case 1:
  – Asset: Engaged patient, family member, caregiver, or organization
  – Collect data via website, questionnaire, database, or spreadsheet
  – Case Example:
    • Tarlov Cyst Disease Foundation
Tarlov Cyst Disease Foundation

• Small rare-disease patient advocacy organization
• Mission:
  – Volunteer-based, 501(c)(3) non-profit foundation
  – Dedicated to the research, improved diagnosis and development of successful treatments and outcomes for symptomatic Tarlov cysts and improving education surrounding Tarlov Cyst disease
• Incorporated exclusively for scientific, educational, and charitable purposes
• Seeks to improve the level of understanding, diagnosis and treatment of Tarlov cysts.
• President/Executive Director - Reta Honey Hiers, R.N., C.
Tarlov Cyst Disease Foundation Patient Survey History

- Initiating the survey
  - Began collecting data from patients and providers
  - Survey drafted by the Founder, an RN
  - Survey put on Foundation website
  - Patients voluntarily complete

- Concerted outreach effort by Founder
  - Phone calls to providers, sent letters, etc.
  - Established important connections and partnerships with clinicians and researchers
Tarlov Cyst Disease Foundation

Patient Survey Today

• Now a Funded Survey!
  – Members contribute
  – Grant funding supports

• Data collection to date:
  – Ongoing data collection (over 3500 Responses)
  – Survey evolving over time with patient, physician, and researcher input
  – Partnerships established with a physician and researcher at Harvard/Mass General Hospital for encoding and data retrieval

• New research opportunities
  – Professorship for Tarlov Cyst Disease established
    • Focus on development of an integrated Maryland Tarlov Cyst Initiative that will advance research and clinical care

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Overcoming Barriers

• Lack of resources and staff
  – Started small, grown over time
  – Used existing infrastructure (e.g., website)
  – Tapped friends and acquaintances with clinical and research experience

• Survey development
  – Drafted by founder
  – Evolved over time with help from research experts
  – Foundational for natural history data

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Leveraging Your Assets

• Case 2
  – Asset: Engaged patient organization
  – Formalize data collection as per project protocol/summary, source funding,
  – Develop and launch registry
  – Case Example:
    • Immune Deficiency Foundation
Immune Deficiency Foundation

- Founded in 1980
- National patient organization dedicated to improving the diagnosis, treatment, and quality of life of persons with Primary Immune (PI) deficiency diseases through advocacy, education, and research
- Consists of a group of about 250 rare diseases representing approximately 250,000 diagnosed in the United States
Two Paths to One Registry

1980: First “registry”—index card catalog, then moved to a spreadsheet

1988: IDF “Get Connected”—Patient contact forms at every patient meeting, family retreat, patient calls, etc.

1990: IDF “Get Connected” Online form added

1992: NIH/NIAID partnership to develop CGD registry

1995: Physician Survey

1998: CGD registry expanded to include 8 other PI diseases

1999: “Get Connected” Online form added

2000: USIDNET research consortium formed; proposal accepted by NIAID

2011: IDF eHealth Record Launched

2014: Funding renewed for USIDNET registry project

2014: Launch of PI Connect

2014: USIDNET data integrated with IDF ePHR through PI Connect

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Growing IDF Patient Database: Physician & National Patient Survey

• Desired to conduct a national patient survey
  – rare diseases were not understood or described well at the national level
• Conducted first survey of physicians, specifically those likely to see persons with primary immune deficiency diseases
  – Immunologists/Allergists
  – Pediatricians
  – Infectious disease
  – Registry physicians
• Asked physicians to distribute a survey questionnaire to their patients with primary immune deficiency diseases
• Provided a significant increase to IDF patient database
Growing IDF Patient Database: IDF eHealth Record

- Discussions began in 2008, officially launched in 2011
- IDF patients needed something to help them stay organized and keep track of all of their paperwork and notes
  - Lab results
  - Diagnoses
  - Insurance information
  - Medications
  - Infusion
Expansion Through Partnerships: USIDNET

- United States Immunodeficiency Network (USIDNET) oversees a registry of patients with primary immune deficiency
- Funded by NIH/NIAD
- Physician advisory committee approached IDF in 1992 to develop a registry for patients with CGD
  - Registry later expanded to include 8 additional immunodeficiency disorders
- Physician-validated clinical data
  - Lab results
  - Genetic and molecular information
  - Diagnostic criteria
  - Longitudinal data included
Gaps in Data Remain..

• Lessons learned from XLA Disease Workgroup Project\(^1\)
  – Discovered gaps in registry data that only patients could fill in
• Gap: Need for Real Life Data in PI
• Data gathered from patient input:
  – Paper records
  – ePHR
  – Drawbacks: lack clinical records, missing data
• Data from HCPs input for patient registries:
  – USIDNET, ESID, and others
  – Drawbacks: lacks patient perspective; missing data points from other physicians not contributing to registry

• A patient-researcher collaboration for primary immune deficiencies
• Empowers users to help others living with PI by simply logging experiences and joining the conversation
• Includes access to an exclusive research forum where patients can discuss and offer opinions about PI research
• Gives patients a seat at the research table

Funded through Patient-Centered Outcomes Research Institute (PCORI)
http://www.pcori.org/research-results/2013/pi-patient-research-connection-pi-connect

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We’ve Come A Long Way: Lessons Learned

• Researchers initially did not appreciate patient involvement, but now understand power of patient’s voice

• Getting patients to think differently:
  – Willing to participate in focus groups and complete surveys but less likely to participate in governance committees due to lack of expertise
  – Crowd sourcing: identify patient research leaders and provide training so they can contribute more effectively
IDF PI CONNECT Team

Christopher Scalchunes
Vice-President of Research

cscalchunes@primaryimmune.org
Leveraging Your Assets

• Case 3
  – Asset: Engaged patient organization conducting research
  – Actively collecting data, managing registry and data—including deciding uses for data, PCOR collaborations, and further funding
  – VHL Alliance
VHL Alliance

• Small 501(c)3 patient advocacy organization (currently 4 FTE)

• **VISION:** VHLA envisions a cure for VHL

• **MISSION:** VHLA is dedicated to research, education, and support to improve awareness, diagnosis, treatment, and quality of life for those affected by VHL.

• Organizational structure includes:
  – Clinical Advisory Council
  – Research Council
  – Clinical Care Centers
  – Executive Director, PhD in biochemistry
  – Director of Wellness, experience in surveys

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The Birth of CGIP

- Relatively good understanding of natural history
  - Based on institutional clinical databases → geographic differences

- 2012: Research Council instructed VHIL to “invest in itself” set-up and launch patient databank/registry

- Result: Cancer in Our Genes International Patient (CGIP) Databank a collaboration/partnership between patients and researchers
Identifying Goals

• Maintain privacy and confidentiality
• Complement not replace other existing institutional databanks
  – Collecting information best told by patient
  – Lifestyle: Nutrition, Exercise, Mood, Sleep, Oral Health
• Expedite clinical trials
• Remove geographic differences
• Identify correlation between lifestyle and tumor growth
• Recognize and share best practices of treatment
• Share de-identified data
Development Process

• Identifying Software Provider
  – Priorities
    o Meeting the needs of extensive surveys, including branching logic
    o Ease of use
    o Equivalent priorities: collaboration
  – Comprehensive review of existing providers
    o For-profit, academic, providers, non profit providers
    o Equivalent vision, objectives, and priorities

• Survey Question Development
  – Input from clinical researcher—Patient Registry Task Force
  – Draft by Staff
  – Evaluation from FDA
  – Extensive review from researchers and patients
  – Continuous process based on responses and feedback
Challenges

• Funding
  – Current part of annual budget
    o Lack of interest from industry: rare disease with no pharmacologic indication
    o Providing important information for cancer in general

• Global support and participation by researchers

• Increased awareness among patients

• Increasing participation

• Patient follow-through
  – Surveys
  – Medical information
Questions?
Resources

• National Organization for Rare Disorders. Patient Registry Platform: [http://rarediseases.org/for-industry/education-research-programs/natural-histories-patient-registry/]


Resources (continued)

- PSC Partners--Registry Video:  [https://youtu.be/a6DNMAAm_zRw](https://youtu.be/a6DNMAAm_zRw) PSC Partners Patient Registry video at  [https://pscpartnersregistry.org](https://pscpartnersregistry.org)

- Workman TA. Engaging patients in information sharing and data collection: The role of patient-powered registries and research networks prepared for AHRQ. Available at:  [http://www.effectivehealthcare.ahrq.gov/ehc/assets/File/Patient-Powered-Registries-white-paper-130911.pdf](http://www.effectivehealthcare.ahrq.gov/ehc/assets/File/Patient-Powered-Registries-white-paper-130911.pdf)

- Patient Crossroads  [https://www.patientcrossroads.com/registry-partners.html](https://www.patientcrossroads.com/registry-partners.html)
