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Celebrating Rare Disease Day - A look into Rare Disease research

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Section 6:
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28th February is Rare Disease Day, which is an international advocacy day to help raise awareness with the public about rare diseases, the challenges encountered by those affected, the importance of research to develop diagnostics and treatments, and the impact of these diseases on patients' lives.

Rare Disease Day was first observed in Europe in 2008. It was established by EURORDIS, the European Rare Disease Organization. In 2009, NORD partnered with EURORDIS in this initiative and sponsored Rare Disease Day in the United States. Since then, the concept has continued to expand beyond the US and Europe. In 2013, more than 70 countries participated.

Rare diseases collectively affect millions of people of all ages globally, of which approximately 18-25 million Americans. They are often serious and life altering; many are life threatening or fatal. In Europe a disease is considered rare when it affects no more than 5 individuals among 10,000 persons, whereas the US considers a disease to be rare when it affects less than 200,000 Americans. Since each of the roughly 7000 rare diseases affect only a relatively small population, it can be challenging to develop drugs and medical devices to prevent, diagnose, and treat these conditions. In general there is a lack of understanding of the underlying molecular mechanisms or even the cause or of many rare diseases. Hence, countries across the globe should share experiences and work together to help address these challenges successfully.

Country/Region/ Institute	Publications
Worldwide	5,879
Europe	2,679
United States	905
Germany	518
France	495
Université Paris 5	77
Harvard University	61
University of Munich	45

Table 1: Scholarly Output for 'Rare Disease' research in 2009-2013 at different levels.

SciVal is a ready-to-use tool to analyze the world of research. It is based on Scopus data and primarily developed for research organizations to help establish, execute and evaluate their strategies within the context of their peers (through benchmarking) and collaborators (through collaboration networks). The solution also allows users to set up research areas to analyze contributors within the field and their corresponding publication and citation statistics.

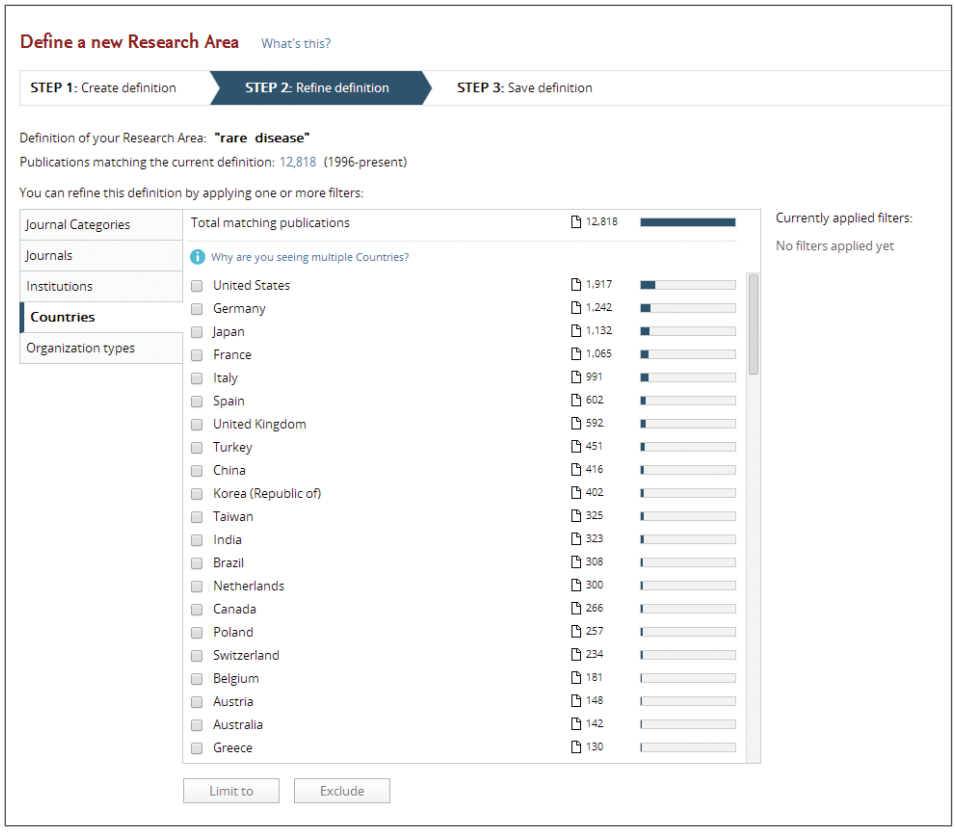

Figure 1: Defining a research area in SciVal for 'Rare Disease' research.

There are many challenges faced by these types of diseases, as they are often not well defined or characterized. Rarity also means that recruitment for trials is usually quite difficult, study populations are widely dispersed, and there are few expert centers for diagnosis, management and research. This is often accompanied by a lack of high-quality evidence available to guide treatment.

At Research Trends we were curious to learn more about the subject and to highlight some of the key institutions and authors that are contributing to the field of rare disease. To do this we examined the field by looking at publication trends using SciVal. To begin with we created a research area in SciVal based on the keyword search 'rare disease'.

The keyword search searches through titles, abstracts and keywords of research papers within Scopus.

Setting up a research area in SciVal is fairly simple and can be completed in three easy steps. Figure 1 shows that for this search query a set of 12,818 publications were published between 1996 to present, where the US, Germany, Japan and France were the most prolific.

The SciVal research area focuses its analysis on the last five years of publications for which we found the pool of research papers in this area was is fairly small. Over the course of 5 years (2009-2013) close to 5900 publications containing 'rare disease' were published around the globe, of which less than 20% originated from the US, see Table 1 (data date stamp 21 January 2014).

One of the reasons why this set of research papers is small can be contributed to the simplicity of the search terms used. In the approach presented in this paper relevant articles were selected on the basis of the occurrence of the term 'rare disease' without including the names of the 7000 rare diseases themselves. We can therefore assume that papers related to many rare diseases would not be included in this set as not all papers related to specific diseases will include 'rare disease' in their abstract, keywords or title. In a follow-up study we could look into including search terms related to particular rare diseases to provide a more complete picture of this research field.

Institution	Country	Publications in this Research Area	Publications in this Research Area (growth %)	Citations	Authors	Citations per Publication
Université Paris 5	France	77	23.1	740	11	9.6
INSERM	France	71	133.3	420	4	5.9
Harvard University	United States	61	0	726	10	11.9
Université Paris 6	France	49	300	312	22	6.4
University of Munich	Germany	45	42.9	206	3	4.6

Table 2: Most Prolific Institutions for 'Rare Disease' research in 2009-2013.

Despite this small sample set, we took a look at a number of institutions, and a number of authors that were the most prolific in this area. When looking at the three most prolific institutions around the globe they all originate from either France or the US, bar one from Germany. Hence, this article focuses on the two most prolific from both countries, namely University Paris 5 and Harvard, see Table 1 and Table 2.

Insitutional Collaboration maps for Harvard, Paris 5 and Munich

Using SciVal we took a closer look at the collaboration patterns of three individual intitutions, Harvard University, Université Paris 5 and University of Munich in 'rare disease' research. SciVal allows you to drill down from a worldwide, to a regional and right down to a country level view of the institutional collaborations.

As can be seen from Figure 2, Harvard University collaborated with 171 institutions worldwide on a total of 39 co-authored publications of its total of 61 publications, with the majority of the collaborations taking place with authors within the US and Europe. The average number of insitutions per paper are 4,38. You can also see here that out of the 61 articles 39 are co-authored with other North American research organizations. In fact, Harvard's top 20 collaborating institutions on 'rare disease' research are mainly from the US, only three were international cross-border collaborations, namely with Canada, UK and Switzerland. When one looks at the general collaboration trends exhibited by Harvard they seem inline with the trends exhibited within the area of 'rare disease' where the top collaborations are all national institutions with few international collaborating institutions from abroad featuring in the top 40.

You can see from Figure 3 that Université Paris 5 collaborated with 215 institutions worldwide on 62 co-authored publications out of its 77 total publications, resulting in an average of 3,48 institutions involved in each paper. From Figure 4 you can see that the majority of collaborating institutions are from France (72). In fact, there are only three non-French institutional collaborators amongst their top 20 rare disease collaborators, namely Canada, UK and Germany.

Figure 2: Worldwide collaboration by Harvard University in 'Rare Disease' research.

Figure 3: Worldwide collaboration Université Paris 5 in 'Rare Disease' research.

University	Single author publications (%)	Institutional collaboration (%)	National collaboration (%)	International collaboration (%)
Harvard University	9.6	20.8	31.1	38.5
Université Paris 5	8.5	13.3	40.2	37.9
University of Munich	8.1	24.1	20.7	47.1

Table 3: General collaboration trends for the three universities investigated.

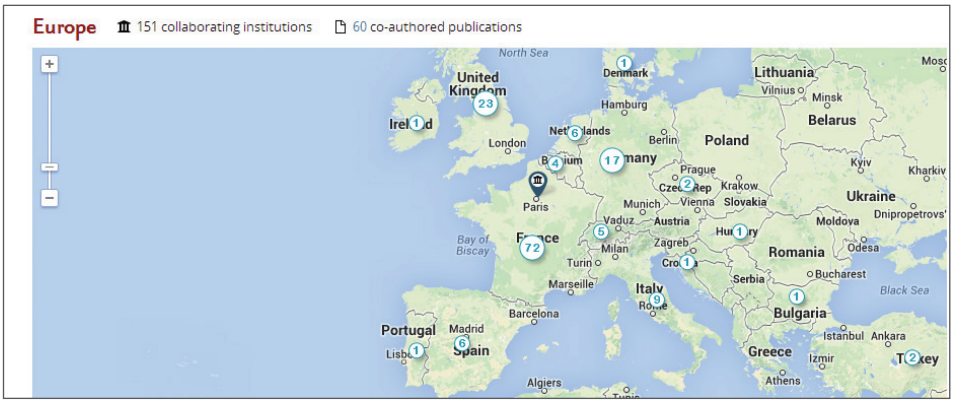

Figure 4: European collaboration by Université Paris 5 in 'Rare Disease' research.

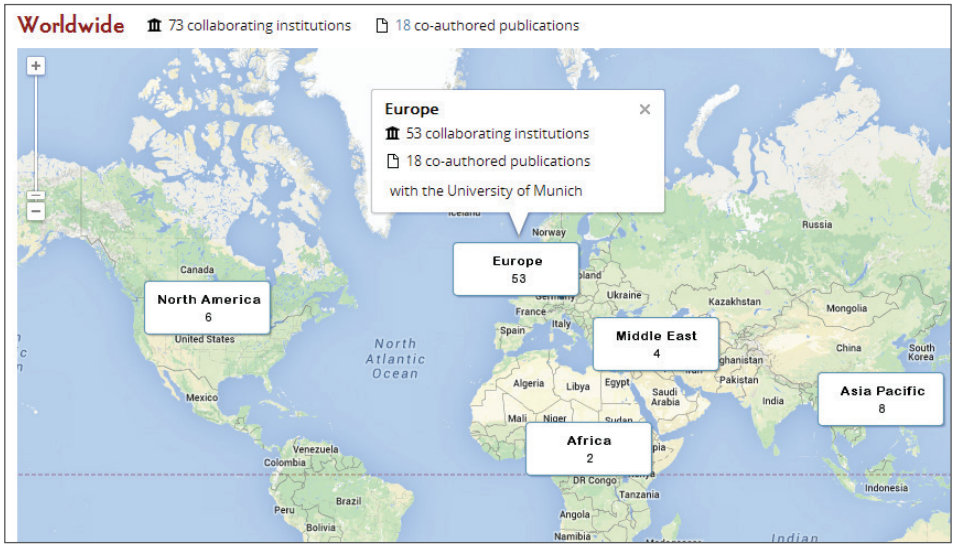

Figure 5: Worldwide collaboration by University of Munich in 'rare disease' research.

Name	Publications in this Research Area	Citations in this Research Area	Citations per Publication
Taruscio, D.	16	37	2.3
Simoens, S.	14	50	3.6
Groft, S.C.	11	53	4.8

Table 4: Most Productive Authors in 'Rare Disease' research in 2009-2013.

Here again in Figure 5 we find there are a large number of institutions that work on a number of papers, 73 institutions collaborated on 18 articles, with an average of 4 institutions per paper. The University of Munich enters into the most cross-boarder collaborations with half of its top 20 institutions coming from abroad, namely three US, two UK, two Dutch, one Canadian and one institute from the Czech Republic. It seems logical for collaboration to play a central role in 'rare disease' research, though it may be expected that cross-border collaborations would be most important to effectively propel the research forward, mainly due to the small patient numbers in each country.

The overal results show a large number of institutions collaborting on one paper, and it seems that Munich in general is a more internationally focused research organization from the three universitites investigated, see Table 3 for the general collaboration trends for these universities.

Highlighting the Most Prolific Authors in SciVal

By looking at the most prolific authors in the set, in addition to clicking though to the abstracts in Scopus from SciVal, we were able to get a better idea of the set of research papers we were looking at.

The most prolific authors in the dataset for 'rare disease' between 2009-2013 are: Dr. Domenica Taruscio, MD. Director at the National Centre for Rare Diseases, Instituto Superiore di Sanita, Rome, Italy; Dr. Steven Simoens, Katholieke Universiteit Leuven, Department of Pharmaceutical and Pharmacological Sciences, Leuven, Belgium; Dr. Stephen Groft, Director National Institutes of Health, Office of Rare Disease Research (see Table 4).

Dr. Domenica Taruscio MD. focuses her research on setting systems in place that can, firstly, help train and inform clinicians to make the right diagnosis and secondly, improve the dissemination of information around symptomatic treatments. She has just spent the last 30 months on a feasibility study funded by the European Commission (DG Sanco) addressing regulatory, ethical and technical issues associated with the registration of rare disease patients and with the creation of an EU platform for the collection of data on rare disease patients and their communication among qualified users.

Dr. Steven Simoens, on the other hand, does not focus his research especially on rare disease themselves. He works within Pharmaceutical Sciences with a keen interest in pharmaco-economics and ethics which is where rare disease seem to come up in his research. His publication rate is very impressive with about 15 papers per year. 'Rare disease' research is a topic of concern for this field of interest as there are debates on the economic rationale behind society supporting any part of the rare disease value chain. There was a debate in the Netherlands, for example, in 2012 related to the cost of providing medication to patients with Pompe's disease. Medication for these patients cost between 400-700,000 Euros per patient per year. The economist Dr. Marc Pomp introduced the concept of the quality-adjusted life year (QALY), where the costs of medical treatment are placed in relation to the quality of life in those years for the patient. The level considered acceptable was set at 50,000 Euro per year, far below the cost of treating a Pompe patient, while stopping their treatment would would most likely cause them to die (1).

The third most prolific researcher within our sample, Dr. Stephen Groft, received the life time achievement award for his nearly 30 years of service and commitment to advancing research and treatments for the millions of people afflicted by rare and genetic diseases. He is one of the original pioneers in the rare disease arena and is recognized globally as a leader in building collaborative relationships to improve patient treatment and care. Pham. D. Groft retired on February 8th this year. He was praised for giving thousands of rare disease patients and their families renewed hope and a collective voice. One of the organizations he set up was the National Center for Advancing Translational Science (NCATS). You can read more about his work at: http://www.ncats.nih.gov/news-and-events/features/groft.html

Each of these three individuals look at rare disease in very different ways, though all are in some way interested in the management of the research field, suggesting that our keyword search did in fact omit the research of 'rare disease' from the sample set. However, this also shows how much attention needs to be placed on attracting the public's attention for 'rare disease' and on building global awareness and a collective solidarity to support the population and their families affected by these rare and often severe diseases.

References:

1. NOS, Advies: Stop met Dure medicijnen, R. vd Brink and H. vd Parre, (Dutch) 29 July 2012, http://nos.nl/artikel/400207-advies-stop-met-dure-medicijnen.html

Related links:

ORDR – Office of Rare Diseases Research – http://rarediseases.info.nih.gov/about-ordr/pages/30/about-ordr

NORD – The National Organization for Rare Disorders (NORD) – http://www.rarediseases.org/

Eurordis – The voice of rare diseases Europe – http://www.eurordis.org/

JPA Japanese patients association – http://www.nanbyo.jp/

European Platform for Rare Diseases Registries – http://www.epirare.eu/

The next International Conferences for Rare Diseases and Orphan Drugs

(ICORD) 2014 Annual Meeting on October 8-10, 2014 in The Netherlands. More information will follow: http://icord.se