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Letter to the Editor

Development of the global schizophrenia research under epidemiological and socio-economic influences

E. Lammer, D. Klingelhöfer *, M.H.K. Bendels, D. Ohlendorf, M. Spallek, D.A. Groneberg

Institute of Occupational, Social and Environmental Medicine, Goethe University Frankfurt, Germany, Theodor-Stern-Kai 7, 60590 Frankfurt

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Dear Editor

According to the World Health Organization (WHO), about 21 million people were affected by schizophrenia in 2016 (WHO, 2016). It is one of the most serious mental illnesses in the world (Oertel-Knochel et al., 2011). In 2001, the World Health Report ranked schizophrenia as one of the ten main causes of *disability-adjusted life years* (DALYs). Of 1000 people worldwide, approximately 7.2 suffer from schizophrenia in the course of their lives, with prevalence rates varying from country to country (USA: 12-month prevalence of 1,1% of the US adult population) (NIMH, 2016). The disease is associated with massive stigmatization, discrimination (Wolwer et al., 2006) and enormous social and economic costs (WHO, 2001) (Kompetenznetz-Schizophrenie, 2017).

Since the introduction of the concept of schizophrenia in 1911 by Bleuler (Bleuler and Bleuler, 1986), there has been constant research on this topic. This has led to a continuous development of the conceptualization of this disease. However, central aspects have not yet been conclusively clarified. Recent technical developments have enabled new insights into the etiopathogenesis of the disease. Problems that arise in practical patient care are not scientifically investigated and little progress has been made in the development of new drugs in recent decades.

In view of the enormous burden of the disease for the affected persons as well as the socio-economic impact of the disease on society, it is essential to gather information on the global structure of research in this field. Increased networking of the global research architecture is likely to have a positive long-term impact on the gain of knowledge and the implementation of this knowledge in clinical practice and should be specifically promoted.

Therefore, the aim of our study was to contribute to the targeted management of science and the optimization of research coordination – and thus contributes to the promotion of science. In order to optimize the scientific basis for this disease, its treatment and to reduce the burden of disease, detailed knowledge of the research structures is essential. Initiated within the framework of the bibliometric NewQIS platform (New Quality and Quantity Indices in Science) (Groneberg-Kloft et al., 2009a) (Groneberg-Kloft et al., 2009b), we analyzed the WoS listed Schizophrenia related articles both quantitatively and semi-qualitatively by assessing various citation parameters.

Since the conceptualization of the disease, there has been an increasing number of research into schizophrenia as the analysis results show. The increasing volume of publications reflects inter alia the disease-related knowledge gained over the years and reflects the typical course of events. It is assumed that the number of scientific publications worldwide will double every nine years (Noorden, 2014). All in all, we detected 42,491 publications in the Web of Science Core Collection from 1900 unit 2015. The analysis of the influence of the publication year on the volume of publications revealed that also the disease-specific gains in knowledge directly influence the chronological development of the volume of publications. The first application of electroconvulsive therapy in 1938 caused a relatively high volume of publications in 1938/39, and the increase in publications between 1961 and 1991 is due to elementary discoveries on the etiology and therapy of the disease. The dopamine hypothesis, the introduction of the first atypical drug (Clozapine 1970s) (Crilly, 2007) and further developments on a psychosocial level (e.g. psychoeducation) are examples of this.

The results are consistent with the results of scientometric work on other topics and reflect the strong monetary dependence of biomedical research. As the in-depth analysis of the year 2015 shows, other countries, especially China, are, however, catching up on the USA in this respect. The importance of China's contribution to the schizophrenia-specific research might increase even more in the years to come (Shi and Rao, 2010). A look at the country-specific number of articles of 2016 and 2017 confirms this. In these years, China reached already the second position after the USA and is pushing further (OECD, 2015).

The picture is, however, different with regards to the parameters that put publication performance in relation to the number of citations or socio-economic indices. In terms of population, countries such as Iceland, Bulgaria and Ireland are among the leaders and have published several important articles (Table 1).

The high ranking is, however, also based on the methodology used. Nevertheless, the small population numbers of these countries contribute their part to these results.

* Corresponding author.
E-mail addresses: klingelhoefer@med.uni-frankfurt.de, (D. Klingelhöfer), bendels@med.uni-frankfurt.de, (M.H.K. Bendels), ohlendorf@med.uni-frankfurt.de, (D. Ohlendorf), spallek@med.uni-frankfurt.de, (M. Spallek), groneberg@med.uni-frankfurt.de (D.A. Groneberg).

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Table 1
Socio-economic ranking of country-specific publication performance for countries with ≥30 published articles. (Source: World Bank 2014). Ranked by Articles/GDP in trill. USD. GDP = Gross Domestic Product, USD = US-Dollar.

Country	Articles	GDP in bn USD	Population in mill.	Articles/GDP in trill. UDS	Rank 1	Articles/population in mill.	Rank 2
Iceland	81	16.69	0.31	4853.21	1	261.29	1
Israel	933	303.8	7.82	3071.10	2	119.31	3
Croatia	116	57.16	4.47	2029.39	3	25.95	17
Denmark	683	340.8	5.56	2004.11	4	122.84	2
Finland	498	271.2	5.26	1836.28	5	94.68	5
Ireland	439	246.4	4.83	1781.66	6	90.89	6
UK	4555	2945	63.74	1546.69	7	71.46	8
Sweden	873	570.1	9.72	1531.31	8	89.81	7
Hungary	194	137.1	9.91	1415.03	9	19.58	19
Taiwan	674	529.6	23.35	1272.66	10	28.87	16
Canada	2189	1789	34.83	1223.59	11	62.85	10
Czech Republic	242	205.7	10.62	1176.47	12	22.79	18
Switzerland	816	712.1	8.06	1145.91	13	101.24	4
Netherlands	964	866.4	16.87	1112.65	14	57.14	11
Australia	1548	1444	22.5	1072.02	15	68.80	9
Germany	3862	3860	80.99	1000.52	16	47.68	14
Austria	418	437.1	8.22	956.30	17	50.85	12
USA	15,476	17,420	318.9	888.40	18	48.53	13
Greece	210	238	10.77	882.35	19	19.50	20
Belgium	421	534.7	10.44	787.36	20	40.33	15

This also reflects the high publication performance of the Scandinavian countries with their well-developed research structure. It was also possible to ascertain that Iceland, Israel and Croatia are characterized by a high publication participation in relation to country-specific GDP. This correlates with the headquarters of the important biopharmaceutical company deCODE genetics in Iceland and the increased prevalence of the disease in Israel and Croatia (Jablensky, 1997).

The inherited disposition to develop Schizophrenia stood often in the focus of Icelandic publications. The gene Neuregulin 1 (NRG1) has been isolated in Iceland and can be taken as an example for the isolation of a gene in a small population that can have relevance in larger populations, e.g. England, Ireland and China as well. Several studies showed the highly significant association between NRG1 and schizophrenia (Stefansson et al., 2003). Already in 1988, the partly dominant mechanisms of the heredity of schizophrenia were found in an Icelandic study that evaluated a large data base (Stefansson et al., 2003). A genealogical database that reaches back to the 9th century (IslendigaBoks) keeps the data of all Icelanders that are born in the 20th century and nearly all of them born in the 19th century. It is funded by deCODE Genetics a Genetic Research Institute in Reykjavik.

Evidence shows that international cooperation is particularly important because different countries have varying research priorities due to structural reasons. Europe has comprehensive, multi-year centralized data registers on the disease (e. g. at the Institute of Psychiatry at Maudsley Hospital). This allows e.g. to carry out extensive epidemiological studies. Due to the sectoral healthcare system, this is not possible in the US (SRF, 2005).

In addition, the importance of targeted programs for networking on schizophrenia-specific research could be demonstrated, e.g. through the number of publications resulting from collaborations within the Research on Asian Psychotropic Prescription Pattern (REAP) and the German *Kompetenznetz Schizophrenie*.

The high citation numbers of the study *Biological insights from 108 schizophrenia-associated genetic loci* (Schizophrenia Working Group of the Psychiatric Genomics, 2014) with the participation of 27 countries showed exemplarily that national and international collaborations, contribute decisively to the gain of knowledge, despite their complexity. This study has been cited 312 times. The publication was based on a genome-wide association study of the Psychiatric Genomics Consortium (PGC) conducted by the Schizophrenia Working Group, in which 83 new risk markers for the disease were identified and replicating 25 existing markers (PGC, 2016).

Prevalence studies can help to understand the reasons and the risks for the pathogenesis of schizophrenia, but the emphasizing of cultural, socio-economic and educational issues often goes short. Therefore, this study stresses the importance of international epidemiological research networks and illustrates their research success. Especially, the ambiguous data base of developing countries should emphasize the need for closer co-operations.

Conflict of interest
The authors declare that there are no competing interests existing.

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Contributors
DK, DAG contributed to conception, design and analyses. EL, DK, MHKB, DO, MS, DAG contributed to the interpretation of data. EL drafted the article. DK EL, DK, MHKB, DO, MS, DAG revised the article and have participated in the final approve of the manuscript.

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Appendix A. Supplementary data

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