Opportunities and challenges in rheumatology research in Central Europe

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Abstract
The Central European Congress of Rheumatology (CECR) has been organized by seven Central European countries: Austria, Croatia, Czech Republic, Hungary, Poland, Slovakia, and Slovenia. These countries have lots of similarities, but also differences, with respect to rheumatology research. In this paper, based on questionnaires, we wish to demonstrate achievements and difficulties in rheumatology research performed in our region.

Keywords: Central Europe, Rheumatology, Research, Funding, Arthritis, Collaboration

Background
Central European countries have common geopolitical backgrounds and numerous similarities with respect to history and development including medical care and research. Here we will deal with the seven official organizers of the Central-Eastern Congress of Rheumatology (CECR): Austria, Croatia, Czech Republic, Hungary, Poland, Slovakia, and Slovenia. There are significant differences between the countries with respect to gross domestic product (GDP), organization of healthcare, and research funding.

In this brief review, we wish to describe the recent developments and present the current situation of clinical rheumatology and research in Central Europe. For this purpose, we sent out a questionnaire to the presidents of the national societies.

Some indicators of rheumatology care
In order to understand rheumatological research in these countries, first we should assess postgraduate training and the definition of rheumatologists. In some countries, such as Austria and Czech Republic, most rheumatologists are also internists. On the other hand, in Hungary, about 70% of rheumatologists are not internists so many of them do not treat connective tissue diseases.

There are between 2 and 75 rheumatology hospitals/departments in these countries. Where internists treat rheumatic patients, most outpatient and inpatient care is of course performed in internal medicine units. There are variable numbers of patients treated with biologics (Table 1).

Description of rheumatology research
As seen in Table 1, significant research in the field of arthritides, osteoporosis, and connective tissue diseases has been carried out over the past years. Our rheumatologists have been involved in the development of international recommendations (e.g. management of rheumatoid arthritis (RA), early RA, spondyloarthropathies, systemic sclerosis, systemic lupus erythematosus (SLE), myositis, Sjögren’s syndrome, polymyalgia rheumatica, vasculitides, osteoporosis, alkaptonuria, cardiovascular comorbidities, and ultrasound) [1–13]. There have been active members of EULAR, EUSTAR, GRAPPA, ASAS, EUROPHOSPHOLIPD, MYONET, and several other working groups. Although there have been significant limitations in funding of research, recently our countries have been involved in large European Union (EU), Horizon2020, Foreum, and other collaborative projects.

The Central European Congress of Rheumatology
CECR congresses started in 1996 in Piestany (Slovakia), and were followed by meetings every other year in Warsaw (1998), Bratislava (2000), Baden (2002),
Table 1: Key figures in the seven countries

| Population (millions) | Austria | Croatia | Czech Republic | Hungary | Poland | Slovakia | Slovenia |
|-----------------------|---------|---------|----------------|---------|--------|----------|---------|
|                       | 8.3     | 4.4     | 10.4           | 10.0    | 38.5   | 5.4      | 20      |

| GDP per capita (IMF, 2016, Int$) | Austria | Croatia | Czech Republic | Hungary | Poland | Slovakia | Slovenia |
|----------------------------------|---------|---------|----------------|---------|--------|----------|---------|
|                                  | 47,800  | 22,400  | 33,200         | 27,200  | 27,700 | 31,200   | 32,000  |

| No. of rheumatologists | Austria | Croatia | Czech Republic | Hungary | Poland | Slovakia | Slovenia |
|------------------------|---------|---------|----------------|---------|--------|----------|---------|
|                        | 324     | 47      | 350            | 800     | -1300  | 71       | 21      |

| No. of rheumatology departments/hospitals | Austria | Croatia | Czech Republic | Hungary | Poland | Slovakia | Slovenia |
|-----------------------------------------|---------|---------|----------------|---------|--------|----------|---------|
|                                        | 10/2    | 18      | 12             | 31      | 75     | 1+ ***   | 7       |

| No. arthritis patients on biologics | Austria | Croatia | Czech Republic | Hungary | Poland | Slovakia | Slovenia |
|------------------------------------|---------|---------|----------------|---------|--------|----------|---------|
|                                    | N/A     | 1800    | 5700           | 8500    | -8000  | 2200     | 2200    |

| No. of research centres (with international publications) | Austria | Croatia | Czech Republic | Hungary | Poland | Slovakia | Slovenia |
|----------------------------------------------------------|---------|---------|----------------|---------|--------|----------|---------|
|                                                          | 20      | 7       | 5              | 21      | 15     | 6        | 2       |

| No. of research groups | Austria | Croatia | Czech Republic | Hungary | Poland | Slovakia | Slovenia |
|------------------------|---------|---------|----------------|---------|--------|----------|---------|
|                         | 20      | 7       | 13             | 21      | 15     | 6        | 2       |

| Main research topics | Austria | Croatia | Czech Republic | Hungary | Poland | Slovakia | Slovenia |
|----------------------|---------|---------|----------------|---------|--------|----------|---------|
|                      | Several clinical trials in arthritides, SLE,etc | Epidemiology of SLE | Cardiovascular comorbidities | SpA | Systemic sclerosis | Early arthritis | Osteoporosis | Urate transporters | mIRNA | JIA | Registries | Comorbidities (CV, malignancies) | RA | Pregnancy | Systemic sclerosis | Stem cell transplantation | Ultrasoundography | GCA | Fibromyalgia | Immunopathology | SpA | Ped. rheumatology | Osteoporosis | RA | Pregnancy | Systemic sclerosis | Stem cell transplantation | Ultrasoundography | GCA | Fibromyalgia | Immunopathology | SpA | Ped. rheumatology | Osteoporosis |
|                      | EULAR-related activities, recommendations | SpA | Systemic sclerosis | Early arthritis | Osteoporosis | Urate transporters | mIRNA | JIA | Registries | Comorbidities (CV, malignancies) | RA | Pregnancy | Systemic sclerosis | Stem cell transplantation | Ultrasoundography | GCA | Fibromyalgia | Immunopathology | SpA | Ped. rheumatology | Osteoporosis | RA | Pregnancy | Systemic sclerosis | Stem cell transplantation | Ultrasoundography | GCA | Fibromyalgia | Immunopathology | SpA | Ped. rheumatology | Osteoporosis |
|                      | Registers (BiOREG), databases, biobanking | Autoantibodies | Bone/osteoimmunology | Experimental arthritis | Experimental lupus | Outcomes research (PA, PsA, SLE, OA) | Sclerosis | Ultrasoundography | Osteoarthritis | Psoriatic arthritis | PMR | Health services research | RA | Pregnancy | Systemic sclerosis | Stem cell transplantation | Ultrasoundography | GCA | Fibromyalgia | Immunopathology | SpA | Ped. rheumatology | Osteoporosis | RA | Pregnancy | Systemic sclerosis | Stem cell transplantation | Ultrasoundography | GCA | Fibromyalgia | Immunopathology | SpA | Ped. rheumatology | Osteoporosis |
|                      | Autoantibodies | Bone/osteoimmunology | Experimental arthritis | Experimental lupus | Outcomes research (PA, PsA, SLE, OA) | Sclerosis | Ultrasoundography | Osteoarthritis | Psoriatic arthritis | PMR | Health services research | RA | Pregnancy | Systemic sclerosis | Stem cell transplantation | Ultrasoundography | GCA | Fibromyalgia | Immunopathology | SpA | Ped. rheumatology | Osteoporosis | RA | Pregnancy | Systemic sclerosis | Stem cell transplantation | Ultrasoundography | GCA | Fibromyalgia | Immunopathology | SpA | Ped. rheumatology | Osteoporosis |
|                      | Falk and colleagues | Research groups | Main topics | Main topics | Main topics | Main topics | Main topics | Main topics | Main topics | Main topics | Main topics | Main topics | Main topics | Main topics | Main topics | Main topics | Main topics | Main topics | Main topics | Main topics | Main topics | Main topics | Main topics | Main topics | Main topics | Main topics | Main topics |

| Number of publications with IF (2012–2016) | Austria | Croatia | Czech Republic | Hungary | Poland | Slovakia | Slovenia |
|-------------------------------------------|---------|---------|----------------|---------|--------|----------|---------|
|                                           | 278*    | 90      | 250            | 315     | 663    | 55       | 21      |

| National journal | Austria | Croatia | Czech Republic | Hungary | Poland | Slovakia | Slovenia |
|------------------|---------|---------|----------------|---------|--------|----------|---------|
| Zeitschrift für Rheumatologie (Germany) | Reumatizam | Czech Rheumatology | Magyar Reumatológia (Hungarian Rheumatology) | Reumatologia (Rheumatology) (bimonthly; in English) | Forum Reumatologiczne (quarterly; in Polish) | Rheumatologia | None |

| No. of PhD theses in rheumatology | Austria | Croatia | Czech Republic | Hungary | Poland | Slovakia | Slovenia |
|-----------------------------------|---------|---------|----------------|---------|--------|----------|---------|
|                                   | 4**     | 10      | 9              | 16      | 7      | 0        | 0       |

| No. of research grants awarded | Austria | Croatia | Czech Republic | Hungary | Poland | Slovakia | Slovenia |
|--------------------------------|---------|---------|----------------|---------|--------|----------|---------|
|                                | 16      | 8       | 17             | 43      | N/A    | 3        | 0       |

*First or last authorship
**Associate Professorship
***Many arthritis and autoimmune patients are treated in internal medicine departments
CV cardiovascular, GCA giant cell arteritis, GDP gross domestic product, IF impact factor, JIA juvenile idiopathic arthritis, MCTD mixed connective tissue disease, mIRNA microRNA, N/A not available, OA osteoarthritis, PET-CT positron emission tomography-computed tomography, PMR polymyalgia rheumatica, PsA psoriatic arthritis, RA rheumatoid arthritis, SLE systemic lupus erythematosus, SpA spondyloarthropathy
Budapest (2004), Bled (2006), Prague (2008), Sopron (2010), Krakow (2012), Vienna (2014), and again Prague (2016). Croatia joined "the club" in 2016 and the next meeting will be in Zagreb in 2018.

**EULAR activities**

The 70-year-old European League Against Rheumatism (EULAR) is the key organization in the field of rheumatology. The seven countries have nominated country representatives on the EULAR committees. In addition, Frantisek Lenoch (Czechoslovakia), Karl Gotsch (Austria), Béla Gömör (Hungary), and Josef Smolen (Austria) served as EULAR presidents. Karel Pavelka (Czech Republic) and László Czirják (Hungary) worked as General Secretary. Tadej Avcin (Slovenia) is currently Chairperson of the Standing Committee on Paediatric Rheumatology. Daniel Aletaha (Austria) chaired the Standing Committee for Clinical Affairs, Zoltan Szekanecz (Hungary) and Tadej Avcin are currently members of the Scientific Programme Committee of the EULAR congress. Past members of the Scientific Committee include Jiri Vencovsky and Karel Pavelka (Czech Republic), Wlodzimierz Maslinski (Poland), and Kurt Redlich (Austria). Jiri Vencovsky is currently acting as the treasurer for FOREUM.

The numbers of submitted and accepted EULAR abstracts are relevant indicators of the quality of rheumatology research. As listed in Table 2, the 7 countries together submitted 169, 152, 153, 133, and 138 abstracts to the last five EULAR congresses (2012–2016), respectively. The total number of submissions to these congresses was 3806, 3872, 4041, 4323, and 4109, respectively. Thus, our 7 countries submitted 4.4%, 3.9%, 3.8%, 3.1%, and 3.4% of all abstracts, respectively. The percentage of accepted abstracts (oral + poster tour + poster + abstract publication only) was 79.3%, 75.0%, 85.0%, 79.7%, and 77.5%, respectively.

With respect to the number of abstract submissions, in 2015 Austria, Czech Republic, Hungary, Poland, Slovakia, and Slovenia ranked 36th, 48th, 35th, 30th, 27th, 51st, and 46th, respectively, among the 84 countries with abstract submissions. In 2016, these ranks were 29th, 53rd, 32nd, 35th, 28th, 62nd, and 45th, respectively. Austria, Croatia, Czech Republic, Hungary, Poland, Slovakia, and Slovenia submitted 150, 40, 138, 150, 190, 34, and 43 abstracts, respectively, a total of 745, to the 2012–2016 congresses. The total acceptance rates were 88.0%, 77.5%, 77.5%, 72.7%, 81.6%, 55.9%, and 88.4%, respectively. Austria (n = 7), Hungary (n = 6), Poland (n = 6), and Czech Republic (n = 5) had the most oral presentations.

The seven countries have varying population numbers (Table 1) so their relative share within the whole of Europe differs. However, the seven Central European countries took a significant share (3–4%) of abstracts submissions to recent EULAR congresses with an acceptance rate of 75–85%.

**EWRR**

The first European Workshop of Rheumatology Research (EWRR) was organized in London in 1981. The idea of the annual EWRR meetings was to give a platform to mostly young researchers to present their data in basic and translational rheumatology research. To date, 37 EWRR meetings have been organized. Among our seven countries, Vienna (twice), Warsaw, Prague, and Budapest have hosted EWRR congresses. An also increasing number of presentations from Central Europe has been included in the very recent EWRR meetings.

**Problems to solve**

Maybe with the exception of Austria, our countries have experienced a significant delay in the development of rheumatology research. For many years, only Austria and Czech Republic could be part of large international projects (e.g. BeTheCure, AutoCure). In many countries, research is very much centralized to the capital (Vienna, Prague, Ljubljana, Zagreb) or to nominated centres (Piestany). It is more evenly distributed among numerous university towns in Hungary and Poland. A major problem is lack of interest of young physicians in the field of rheumatology, as well as the large workload in routine clinical practice, leaving little time for research. With the advent of new therapies and novel molecular insights, this interest will hopefully rise again over the next years. Funding has been an issue and we hope that, with development, these countries could also participate in more EU- or EULAR-related projects.

With respect to human resources, the "next generation" of rheumatologists is now slowly establishing itself in the international community.

**Conclusion**

Although, with the exception of Austria, these countries were socialist countries, significant development has been observed in rheumatology research.
Abbreviations
CECR: Central European Congress of Rheumatology; EU: European Union; EULAR: European League Against Rheumatism; EWR: European Workshop of Rheumatology Research; GDP: Gross domestic product

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