



The Konya Declaration for Patients with Primary Immunodeficiencies

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Introduction

Every year since 2004 when the J Project was launched, the growing interest and activity of devoted clinicians and scientists in Eastern and Central Europe (ECE) and elsewhere and their efforts to make a difference in the care of patients with primary immunodeficiencies (PIDs) in their regions and countries are clear [1]. A few Central European countries have now progressed to such an extent that they are approaching the professional standards of Western Europe in terms of diagnosis, clinical care, and education [2]. By contrast, in some countries, particularly in Central Asia, PID diagnostics and care are no further advanced than they were in Central Europe 30–40 years ago. There are also remarkable regional differences in patient management, particularly in large countries, such as Russia. One of the biggest challenges facing us now is providing differential assistance to achieve advances throughout the whole J Project area (Fig. 1), which currently has markedly different levels of complex PID care. Maybe we can take inspiration from the Turkish dervishes. During their unique dancing performance, they hold one of their extended arms with the palm up, suggesting receiving, and the other arm with the palm facing downwards, suggesting giving. We must continually encourage those centers

and groups with advanced levels of PID care to share their knowledge with those most in need of it.

Fifteen years have passed since we embarked on the exciting professional journey that is the J Project [1–7]. Every year has been demanding, but in different ways, with the continual addition of new centers and countries. The 237 physician education meetings till December 2019, the J Project congresses organized in Turkey, and the Antalya Declaration issued in 2014 have greatly contributed to our joint success. Major reasons to revise the Antalya declaration included that revision was scheduled for 2020 when it was issued and several changes in the field of PIDs, like the number of diseases, more widely use of next generation technology and newborn screening, and more JP member countries and more SC members who wanted to be part of a new JP Declaration. The Konya Declaration endeavoring to express the conceptual framework, the vision, and mission of the J Project is admittedly more demanding and critical. The challenges surrounding the rapidly growing field of PIDs must be met all over the world by health care providers and call for urgent and decisive actions. We believe that the better management of PIDs can help us to understand immunology and human diseases better and to serve patients with more humility. The past 15 years provided an excellent opportunity to build up a professional community in many countries in Eastern and Central Europe and elsewhere in order to provide a better care of patient with PIDs. Devoted PID working groups were established and developed, and remarkable number of new patients were diagnosed and started on treatment. Among great successes should be mentioned the international meetings called J Project Congresses and the establishment of a growing collaboration with other international societies especially the ESID. The unequal distribution of knowledge in different countries

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Fig. 1 Schematic map of 30 J Project (JP) countries (green) and J Daughter countries (beige) that have joint the JP between 2004 and 2019 from Eurasia and Africa. Three countries in preparation to join are shown in stripes

and regions, especially in Central Asia, might be mentioned as pitfalls and challenges in future work. To this end the J Project should strengthen collaboration and start specific programs with the recently launched European Reference Network (ERN) program.

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Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflict of interest.

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The Konya Declaration

Primary immunodeficiency (PID) disorders constitute a major and growing health problem in individuals of all ages, worldwide. They may lead to severe, life-threatening diseases and death in early childhood or prolonged diseases with a later onset. Much has been accomplished in Eastern and Central Europe (ECE) over the last 15 years, under the auspices of the J PROJECT and in collaboration with national and international organizations. The major aims of this project were to increase awareness of these conditions among physicians and to improve medical training in this domain. However, much remains to be done if we are to achieve all the goals outlined in 2004. The last decade has seen an unprecedented increase in our knowledge of the clinical, immunological, and genetic features of PID disorders. The number of known PID disorders now exceeds 450, and more than 400 PID disorder-causing genes have been described.

PID expert representatives of the J PROJECT met in Konya, Turkey, on December 4–7, 2019, for the 3rd J PROJECT Congress. They unanimously agreed on a revision of the recommendations of the J PROJECT laid down in the Antalya Declaration, 2014, urging an update of their presentation and approval for implementation in ECE countries and elsewhere, throughout the world. The participants at the Konya Congress as well as the J Project Steering Committee expressed their long-term commitment and determination to achieve the goals defined below.

National governments and health departments should take sole responsibility for supporting healthcare providers, thereby facilitating the diagnosis and treatment of PID disorders early in life, to decrease the heavy burden of disease and mortality rates. Specific plans and programs for the prevention, diagnosis, and treatment of PID disorders and their infectious and noninfectious complications, such as cancer, inflammatory and autoimmune diseases, and allergy, should be formulated at national and regional levels. Such programs should be implemented through partnerships between professional organizations, patient groups, and healthcare providers.

The Konya Declaration calls for prompt and effective action to ensure the application of current knowledge to the diagnosis and treatment of patients with PID disorders, thereby considerably improving the quality of life of these patients. To this end, the following five objectives have been targeted for attainment by the end of 2025:

- (1) *The education* of medical students and healthcare professionals, especially nurses should continue to be improved, with the inclusion of PID diseases in the curriculum, as an emerging and increasingly important field of clinical medicine. Continuing medical education is also required for physicians practicing in primary care settings and hospitals. PID should be an integral part of the nationally acknowledged clinical immunology specialty.
- (2) *Public awareness* should be raised, as most PID patients remain undiagnosed and untreated. Such activities should take place year-round rather than specifically on PID awareness days or at occasional meetings, and interactions with patients' organizations should be improved at both national and international levels.
- (3) *PID genetic diagnosis* should be available in each of the J PROJECT countries and should include the use of next-generation sequencing technologies. Diagnostics should be improved by implementation of newborn screening for PIDs.
- (4) A *PID register* should be established in every J PROJECT country and, following diagnosis, data for all patients with proven PID disorders should be entered into national and international databases, primarily to the ESID Registry.
- (5) *Personalized immunoglobulin replacement and hematopoietic stem cell transplantation* should be made available to PID patients, without constraints related to funding or infrastructure.

Physician education and clinical research collaboration programs in the domain of PID should receive preferential support from national funding agencies or bodies to help achieve these goals. These recommendations should be endorsed by national health departments, PID-related professional societies, and patient groups. Stakeholders should regularly come together to discuss openly the way of support they may provide to achieve the highly desirable goals described in the Declaration. All the points outlined above should result in a measurable reduction of comorbidity and mortality in patients with PID disorders. They should also result in a shorter time lag between the first manifestation and the definitive diagnosis and appropriate treatment of PID disorders.

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