fills the decade before the diagnosis of diabetes with empirical data.

Does this mean that we can find those who are about to get diabetes—perhaps even 3 or 4 years ahead? We fear not. The sensitivity and specificity of the forward predictions would be poor. However, we might at last begin to use insulin concentrations interpreted into β-cell function and insulin resistance as another marker of risk—and we know that we have proven advice and therapies that we can give. Now the hunt has to be intensified for the pathology that causes the decompensation that precipitates diabetes.

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Primary immunodeficiency diseases: the J Project

Primary immunodeficiency diseases have long been neglected as medical conditions, but are now recognised as a worldwide health problem. The rapid progress of research in this field has widened the gap between cutting-edge medical care and the lack of appropriate diagnosis and treatment of these conditions in most countries, especially in those with poor socioeconomic conditions.

Primary immunodeficiencies are a group of more than 200 clinically and immunologically defined disorders of various degrees of severity.[1–3] Almost 150 such disorders have been defined at the molecular genetic level, and new disease-causing genes are often being identified.[4] The characterisation of disease-related genes is crucial not only for the definitive diagnosis of disease in affected individuals but also for genetic counselling, family screening, and prenatal and early neonatal diagnosis.[5] Identification of the underlying genetic defect might also have implications for treatment, because gene therapy (gene-modified autologous stem-cell transplantation) has recently emerged as a possible option for patients with severe combined immunodeficiency and no available HLA-matched donor for allogeneic stem-cell transplantation.[6,7]

By contrast with the progress of molecular genetics and the continuing discovery of new primary immunodeficiency disorders, many patients continue to be ill and die early because of misdiagnosis and inadequate treatment. Thus rapid advances in cutting-edge research into the pathogenesis, diagnosis, and treatment of these disorders seem to have widened the gap between knowledge accumulated (and available at few centres worldwide) and the application of this knowledge in everyday clinical practice elsewhere. This situation shows how research and development can fail to be converted into practice, in terms of the use of new knowledge for the benefit of patients, in most countries worldwide and even in some regions of the most developed countries. Awareness about primary immunodeficiency disorders and availability of diagnosis and treatment need to be increased, particularly in countries with poor socioeconomic conditions.

An initiative in eastern and central Europe suggests that a joint effort by health professionals, scientific societies, and patients' associations can make a difference. A physicians' education campaign—the J Project—was started in March, 2004, and since then has

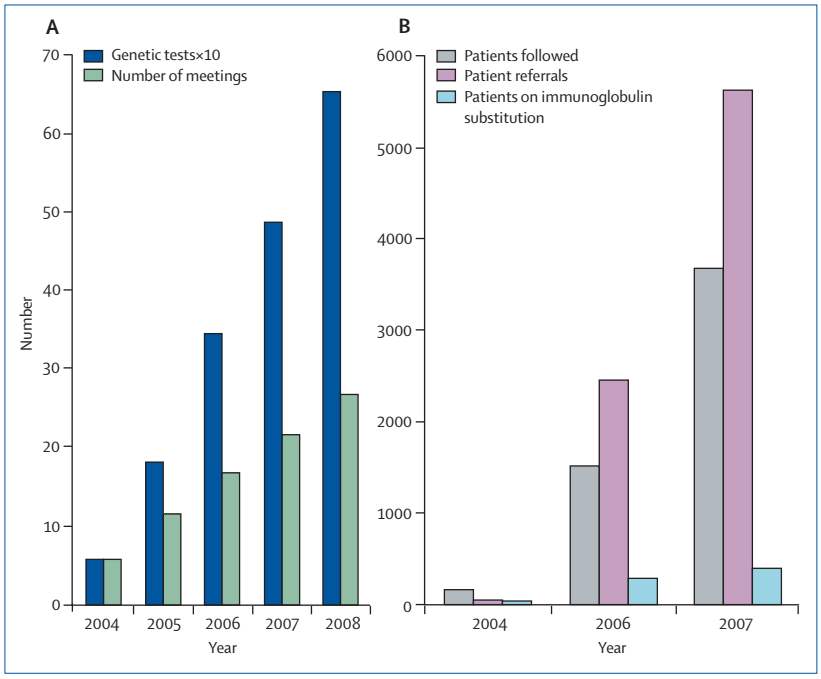

Figure: **Primary immunodeficiency diseases**
(A) Awareness meetings for J Project, and number of genetic tests, for primary immunodeficiency disorders. (B) Survey results from eastern and central Europe on cumulative primary immunodeficiency diseases (data from Jeffrey Modell Foundation).

established itself as a successful awareness programme for primary immunodeficiency disorders. The project originated from the critical analysis of data in the registry of the European Society for Immunodeficiency (ESID) before 2002, which showed that most eastern European countries had reported less than ten patients with such disorders. These data suggested that these disorders have probably been both under-reported and underdiagnosed in eastern Europe. Because of its mission of improving care for patients affected by primary immunodeficiency disorders, ESID set up the J Project to educate physicians. Over the past 5 years, 27 awareness meetings on these disorders have been organised in countries formerly controlled by the Soviet Union, including Macedonia, Bulgaria, Romania, Moldova, Ukraine, Belarus, Latvia, Russia, Poland, Czech Republic, Slovenia, Bosnia and Herzegovina, Serbia, and Hungary. These meetings have been organised with local opinion leaders, and were attended by hundreds of professionals, including general practitioners, paediatricians, infectious-disease specialists, geneticists, and laboratory experts. Representatives of national and local governments were also invited to take part and to transmit important messages.

Soon after the project was started, it became clear that awareness meetings alone might not be effective because many countries faced the major issue of lack of facilities for genetic diagnosis. A Jeffrey Modell diagnostic laboratory was therefore established in Debrecen, Hungary, to serve as a molecular diagnostics laboratory for eastern and central Europe. This laboratory was challenged by an increasing number of samples for the analysis of genes related to primary immunodeficiency disorders (figure A). Although awareness meetings have continued, and reached a record number of 12 scheduled meetings in 2009, the J Project has also gradually changed from a physicians' education campaign into a collaborative research programme that aims to define the mutational spectrum of genes related to primary immunodeficiency disorders and to analyse unique genotype–phenotype relations in eastern and central Europe.[8] This transition has opened new possibilities for the establishment of clinical and genetic databases and joint research.

The J Project has created a network of physicians, biologists, and research clinicians in eastern and central Europe, which could be an important first step towards a worldwide collaboration on medical care and research for primary immunodeficiency disorders. Physicians' education campaigns encouraged by the success of the J Project are now emerging in Canada, South America, Australia, and Asia, and could spread further. Sufficient resources for a global network should include national and international funding and cross-continental awareness activities, as best exemplified by the pioneering work of the Jeffrey Modell Foundation.[9] Once established, a global network should identify the main criteria for early diagnosis of the many forms of these disorders. Genetic analysis of disease-related genes and the creation of subregistries could further develop the genetic databases first generated by the ESID registry. As soon as multiple PCR strategies for the rapid and low-cost amplification of known genes related to primary immunodeficiency disorders and neonatal screening assays become available, it will be possible to identify gene defects associated with these disorders worldwide. Knowledge dissemination by the J Project had measurable results about awareness of primary immunodeficiency disorder (figure B). However, the major challenge is now to close the gap and reduce the disparity in resources available between wealthy and poor countries.

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Strengthening health systems to promote security

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We are living through a paradoxical mix of uncertainty and opportunity. The current economic crisis is placing additional strains on a world that is already overburdened by its inability to meet the basic needs of billions of its inhabitants. Yet we also have before us the unique opportunity represented by strong interest in health systems. The political visibility of this topic has recently grown to unprecedented levels, as discussed by Michael Reich and Keizio Takemi[1] in an overview of follow-up activities on global health to the most recent G8 Summit. We must seize this opportunity by articulating concrete proposals.

The health effects of economic crises typically lead to multiple vicious cycles. Loss of income and employment generates growth in the number of uninsured people and increases in catastrophic health expenditures, further compounding income loss. At the same time, many families reduce their use of services that are erroneously considered discretionary, such as preventive care, which further deteriorates health status in a way that reduces the capacity of people to work and generate income. Many governments compound the problem by cutting health budgets, which itself aggravates the unemployment picture, while at the same time generating further reductions of services and increases in catastrophic expenditures.

For example, the 1995 financial meltdown in Mexico created the conditions for an excess of about 7000 deaths in children and 20 000 in elderly people,[2] and for a huge increase in catastrophic expenditures by poor people.[3,4] Partly in response to such evidence, Mexico broke away from the standard policy response

***Panel:* Some actions to protect health during times of crisis**

- Information systems must be sharpened for surveillance of health impacts caused by current crisis. Because economic distress increases likelihood of disease outbreaks, now is not the time to weaken epidemiological surveillance. Epidemic or pandemic would only deepen world's economic troubles.
- Health workers must be protected to offer services and perform key functions, and education budgets must be sustained to avoid future workforce crises. Short-sighted responses that reduce quantity and quality of vital services compound economic turmoil.
- Budget cuts across the board are damaging. Instead, smart budgeting calls for culling waste, improving efficiency and equity, and protecting people. In particular, preventive measures must be expanded. Even in normal times, there is wide consensus for public or publicly mandated financing in health. Yet we must earn financial support by showing better results. We need "more money for health, but also more health for the money" (V Ramalingaswami, personal communication).
- Beyond immediate response to the crisis, health security must be grounded on truly universal package of guaranteed benefits or entitlements, comprising set of essential services applied to all in the world. Such a package would empower people by making them aware of their explicit rights, through what could be termed a "health social contract" as key component of global citizenship. As has happened in successful national experiences, explicit benefits at global level would offer template for long-term planning of efforts. It would also represent a major source of global security.