regulations and restrictive allocations of financial resources. Differences in diagnostic systems, with Denmark using the ICD-10 rather than the DSM-IV classification, and a potentially less strict adherence to clinical guidelines in most European countries compared to the US, may have exerted some impact.

The main factor involved may still be represented by the different cultural attitudes towards child and adolescent mental disorders among both lay people and experts. Without having solid studies and data in this respect, one may only argue that some characteristics of the Danish society, including no marked social gradients, a stable large middle class, free public health services for citizens, and a predominant feeling of a high quality of life, may have had an impact against the tendency to over-

prescribe psychotropic medications to children and adolescents. It is also possible that the current status of Danish and European child and adolescent psychiatry is encouraging a patient-oriented assessment and treatment, beyond evidence-based guidelines. However, more detailed analyses are needed in order to understand inter-country differences in drug prescriptions in young people with mental disorders.

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Do we face the same dilemma on pediatric psychopharmacology in low and middle income countries?

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Children and adolescents constitute almost a third of the world's population, and almost 90% live in low and middle income countries (LMIC), where they form up to 50% of the population (1). Available data strongly suggest that child mental disorders occur in different cultures at the same rates as those detected in developed countries (1,2). Thus, the majority of children suffering from mental disorders live in LMIC.

Can we extend the dilemma proposed in Rapoport's paper ("too much or too little psychiatric medication?") to those children? I am afraid the answer would be no. Some years ago, we documented that a substantial proportion of children with the diagnosis of attention-deficit/hyperactivity disorder (ADHD) do not receive any kind of

treatment in several countries of Latin America (3). As an example, we studied around 100 children with ADHD presenting clear impairment from a huge non-referred school sample in Brazil. Less than 5% of them had ever received any treatment for their condition (4).

We recently highlighted a phenomenon that we called the 90/10 paradigm: only about 10% of randomized clinical mental health trials for children and adolescents come from LMIC, while almost 90% of children and adolescents live in those countries. Almost all trials assess psychopharmacological interventions, while there is a complete lack of high quality studies assessing combined treatments (1). Finally, less than 2% of the items published in child psychiatry have an author from a low or low-middle income country (5).

There is a shortage of child psychiatrists in LMIC, and the great majority of them do not have access to training in evidence-based mental health. So,

differently from the US, children with ADHD, obsessive-compulsive disorder, tics, anxiety or depressive disorders receiving medication represent a small minority in those countries. In fact, ordinarily, only those from middle-high to high-income class families have access to the few child psychiatrists in these regions by paying out of their pockets (1).

What kind of child psychopharmacology is found in LMIC? Outside the few university settings, we see children with inadequate diagnosis, being treated with ineffective doses for short periods of time, with medications not supported by empirical evidence, and frequently with polypharmacy. Most of these children are treated by non-specialists (this is not a problem *per se* in our reality; the problem is the lack of adequate training). So, the future of pediatric psychopharmacology in LMIC lies not only in the development of new drugs, but also in training more child psychiatrists and in educating more child mental health

professionals in evidence-based treatments, so that they can use appropriately the tools we already have. However, Rapoport's view that child psychiatrists are being reduced to a mechanistic role of prescribing medication should be taken as a word of advice for the kind of training to be offered globally.

Moving away from the role of a LMIC clinician and taking the perspective of a researcher in the field, I cannot be in more agreement with Rapoport's description of a sense of frustration in the field of child psychopharmacology in recent years. Despite some initiatives like testing drugs acting on the glutamatergic system for different child mental disorders, we are living in a moment of "me too" drugs. Nothing really new and effective seems to be visible in the horizon.

I share with Rapoport the excitement and expectations on potential discoveries from studies using brain cells derived from human induced pluripotent stem cells of individuals with both typical development and child neuropsychiatric conditions. However, as she points out, in order to develop new drug targets, we need to expand our knowledge on the normal trajectories of brain development and how child mental disorders impact on it (6). We need to pursue effective ways to

interfere on these trajectories as early as possible, addressing the so-called "at risk" conditions, as other medical specialties do. Some initiatives along this line are flourishing in the area of psychosis (7).

Combining the research and the clinical perspectives, one additional issue that is worth to mention is the lack of real functional outcomes as dependent variables in child psychopharmacology. The field needs to move beyond studies only documenting statistically significant reductions in psychopathological scale scores. What we really want to know, as in other areas of medicine, is how our treatments impact on the natural history of the disorders. Do antidepressants decrease suicides in adolescence? Do ADHD medications reduce school repetitions and accidents at home? Some findings are just now appearing in the literature (8).

Finally, as wisely mentioned by Rapoport, we cannot forget that child psychopharmacology means prescribing medication for individuals with a developing brain and, most of the time, for long periods. Thus, we need to improve our long-term drug surveillance by well-designed post-marketing psychopharmacology epidemiological studies.

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Child psychopharmacology: how much have we progressed?

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Since its inception, pediatric psychopharmacology has been a point of clinical interest as well as concern. While a constant attempt has been made to find the "magic pill" for psychiatric disorders, concerns regarding safety have often overshadowed new drug development. However, with double blind randomized placebo controlled trials becoming the norm, pediatric psychopharmacology has

come of age to certain extent. Rapoport reviews the evolution, current practices and future of child psychopharmacology. However, there are other important issues relevant to clinical practice across the world that we would like to discuss briefly.

To begin with, a large part of pediatric psychopharmacological literature comes from the US and European countries. Most drug trials are on homogenous populations of Caucasian individuals, often to the exclusion of other ethnic and cultural groups. However, studies

have shown that different ethnic groups metabolize drugs differently, and hence safety and efficacy in one group cannot be easily generalized to the other (1,2). This is especially important given that a huge population of today's children reside in Asia and Africa. Ideally, in the future, we should design large scale multicentric or multicountry trials to generate data which can be applicable to children and adolescents throughout the world. Additionally, diagnostic criteria for various psychiatric disorders have been developed in the Western