TRENDS

The Global Market For ADHD Medications

The United States is an outlier among developed countries in its high usage rates of these medications among children.

by Richard M. Scheffler, Stephen P. Hinshaw, Sepideh Modrek, and Peter Levine

ABSTRACT: Little is known about the global use and cost of medications for attention deficit hyperactivity disorder (ADHD). Global use of ADHD medications rose threefold from 1993 through 2003, whereas global spending (U.S. $2.4 billion in 2003) rose ninefold, adjusting for inflation. Per capita gross domestic product (GDP) robustly predicted use across countries, but the United States, Canada, and Australia showed significantly higher-than-predicted use. Use and spending grew in both developed and developing countries, but spending growth was concentrated in developed countries, which adopted more costly, long-acting formulations. Promoting optimal prescription and monitoring should be a priority. [*Health Affairs* 26, no. 2 (2007): 450–457; 10.1377/hlthaff.26.2.450]

ATTENTION DEFICIT hyperactivity disorder (ADHD), a psychiatric condition first evident in childhood, is the subject of great clinical interest and strong scientific investigation.[1] The prevalence of ADHD is 5–8 percent of U.S. children and adolescents, and its impairments are likely to persist into adolescence and adulthood.[2] A syndrome with strong neurobiological origins, ADHD has major importance for public health, given the marked academic, social, familial, and accidental injury–related impairments with which it is associated.[3]

First used for youth in the 1930s, psychostimulant medications enhance dopaminergic and noradrenergic neurotransmission and provide symptom improvement in the clear majority of people who receive them.[4] Several key issues are salient. First, objective tests for ADHD are lacking, a problem shared with most other psychiatric conditions. Guidelines for proper diagnosis must be followed, so that disorders with similar symptoms (such as conduct disorder or bipolar disorder) do not receive inappropriate stimulant treatment.[5] Second, prescription rates of stimulants (and other psychotropic medications) have greatly increased, at least in the United States, even for preschoolers.[6] About half of U.S. children and adolescents diagnosed with ADHD receive stimulant medications or related agents.[7] Third, unintended side effects may accompany stimulant use. Most are mild, but public health concerns have arisen about the potential for negative cardiovascular effects and suicidal thoughts.[8] Fourth, questions abound

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about the potential for "diversion" of prescription stimulants to people without ADHD, related to improvement of study skills and possible euphoriant effects.[9]

Since the 1960s, methylphenidate and dextroamphetamine have been the mainstays of stimulant prescriptions for ADHD. New formulations, as well as efficacious nonstimulants, have taken up an increasingly large U.S. market share since the late 1990s.[10] Given the increasing recognition that ADHD is a problem of worldwide scope, diffusion of ADHD medications outside the United States may well be occurring, but the extent to which global use includes these newer and more costly formulations is unknown.[11]

Countries with different diagnostic traditions, such as the United Kingdom, have had lower prevalence rates than the United States.[12] However, ADHD appears in multiple nations and cultures at similar prevalence rates.[13] Less well documented are international treatment patterns, including rates of use and associated costs. Our objectives are to (1) describe global trends in ADHD-related medication use, the types of medications used, and medication spending over the past decade; (2) make a preliminary determination of the factors that explain diffusion of ADHD medications globally; and (3) discuss relevant policy issues.

Study Data And Methods

We used the IMS Health MIDAS database to analyze trends in the global market for ADHD medications from 1993 to 2003. We classified ADHD medications as those in the "ATC=N6B Psychostimulants" category, along with the nonamphetaminelike stimulant modafinil (Provigil, Cephalon) and the nonstimulant atomoxetine HCL (Strattera, Lilly). Each medication (name brand and generic) was classified into one of four categories, along the dimensions of (1) stimulant versus nonstimulant medications and (2) long-acting (formulations that remain active for at least eight hours) versus short-acting (fewer than eight hours). We further classified stimulants by active pharmacologic agent: methylphenidate, amphetamine, or other stimulant (Exhibit 1). To analyze changes in medication mix, we then generated a three-level categorization of short-acting stimulants, long-acting medications that received approval from the Food and Drug Administration (FDA) during the study period, and other long-acting medications. As a proxy for dose, IMS Health calibrated each product form into a common metric known as a standard unit (SU). For example, one standard unit is equivalent to a 5 mg tablet or 5 ml of a liquid.

To compare countries' usage, we created a usage per capita measure (SU per child ages 5–19) to examine the relationship between use of ADHD medications and national income for each country that is a member of the Organization for Economic Cooperation and Development (OECD). We estimated a fixed-effects model to establish the relationship between per capita (ages 5–19) use and per capita GDP.[14] This method estimates parameters in panel data, which controls for variability across countries and over time.[15]

Study Results

In 1993, thirty-one countries had adopted the use of ADHD medications; by 2003, the number had grown to fifty-five.[16] Our analysis aggregated data from individual countries from the year of adoption into a global sum. Because the United States is the single largest market, we also show its use, which constitutes 83–90 percent of total market share (by volume).

■ **Global utilization.** The usage of ADHD medications increased 274 percent during the study period (Exhibit 2).[17] From 1993 to 2000, global volume increased steadily (13.2 percent per year); from 2000 to 2003, growth accelerated to 16.8 percent per year.[18] The U.S. share of the global market declined from 86.8 percent in 1993 to 83.1 percent in 2003. A more detailed analysis (not shown) reveals marked variation by country. Low-use countries exhibited growth rates as high as 46 percent per year, whereas moderate-use countries had growth rates of nearly 20 percent per year. If these rates continue, the U.S. market share should

EXHIBIT 1
Categories Of Attention Deficit Hyperactivity Disorder (ADHD) Medications

	Stimulants			
	Methylphenidates	**Amphetamines**	**Other stimulants**	**Nonstimulants**
Short-acting medications (fewer than eight hours)	Ritalin Methylin Methylphenidate Ritalin SR Methylin ER Metadate ER Focalin	Dextroamphetamine Dexedrine Desoxyn Mixed amphetamine Salts Adderall		
Long-acting medications (eight hours or more)	Ritalin LA[a] Metadate CD[a] Concerta[a]	Dexedrine Spansule[b] Adderall XR[a]	Modafinil[b] Provigil[b] Pemoline[b] Cylert[b]	Atomoxetine[a] Strattera[a]

SOURCE: Authors' classification scheme, based on the pharmacologic literature.

NOTES: These medication names are those used commonly in the United States. The equivalent preparations were determined from other countries.

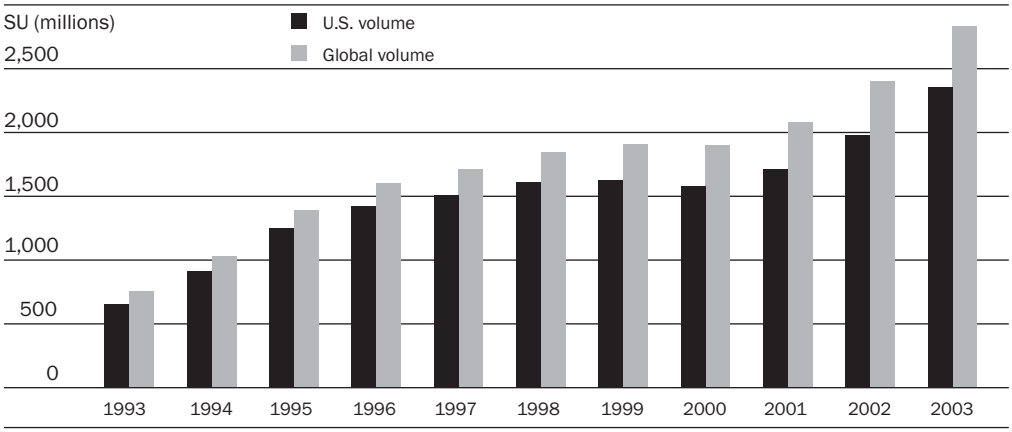
[a] Long-acting medications approved by the Food and Drug Administration (FDA) after January 1993.

[b] Other long-acting medications.

continue to fall.

We then analyzed the relationship between per capita utilization of ADHD medications and the per capita GDP of the OECD countries, given that income is a well-known predictor of health care spending.[19] Use of ADHD medications is positively related to per capita GDP, with a *p* value of less than 0.001 using a fixed-effects model.[20] Exhibit 3 illustrates the relationship between per capita (ages 5–19) use and per capita GDP. Data points on or near the diagonal line show countries using these medications at levels predicted by their per capita GDP. The United States uses them at a level that is about four times higher than would be predicted by income alone, holding

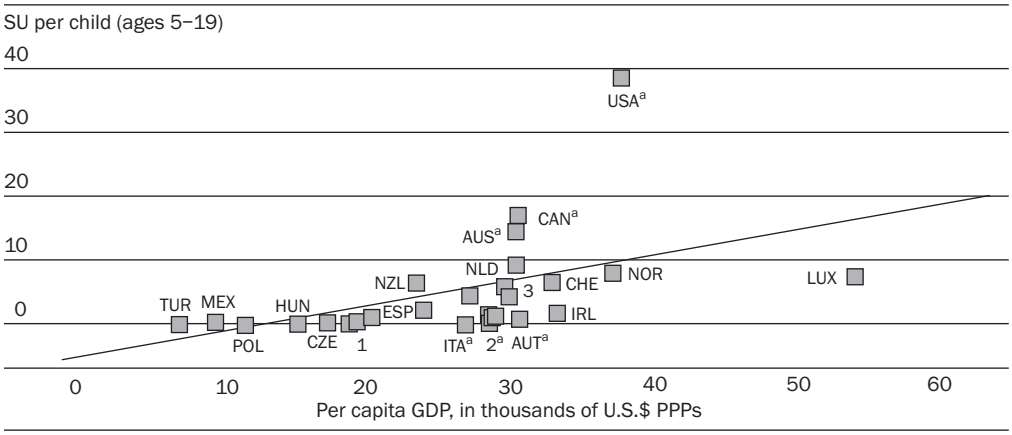
EXHIBIT 2
U.S. And Global Volume Of Attention Deficit Hyperactivity Disorder (ADHD) Medications, 1993–2003



SOURCE: MIDAS database, IMS Health, 1993–2003.

NOTES: Volume adjusted to generate dosage equivalence between short- and long-acting medications. Long-acting medications are weighted twofold over short-acting medications. SU is standard units.

EXHIBIT 3
Predicted And Actual Usage Of Attention Deficit Hyperactivity Disorder (ADHD) Medications In OECD Countries, By Income, 2003



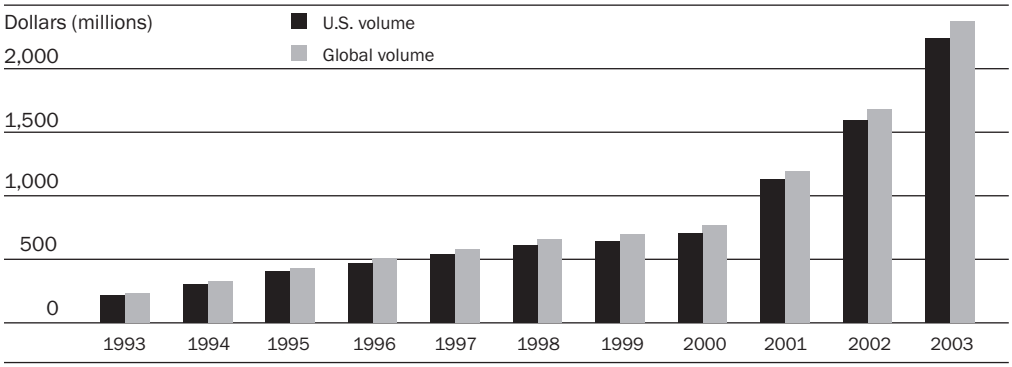
SOURCE: MIDAS database, IMS Health, 2003.
NOTES: Although the data are shown for a single year, other years look similar in overall patterns; 2003 is the most recent year for which data were available. Only twenty-seven of the thirty Organization for Economic Cooperation and Development (OECD) member states are represented; no data were available for Iceland, Denmark, or Slovakia.TUR is Turkey. MEX is Mexico. POL is Poland. HUN is Hungary. CZE is Czech Republic. PRT is Portugal. PRK is South Korea. GRC is Greece. NZL is New Zealand. ESP is Spain. ITA is Italy. DEU is Germany. JPN is Japan. FIN is Finland. FRA is France. SWE is Sweden. BEL is Belgium. GBR is United Kingdom. AUS is Australia. NLD is Netherlands. CAN is Canada. AUT is Austria. CHE is Switzerland. IRL is Ireland. NOR is Norway. USA is United States. LUX is Luxembourg. Where space prohibits labeling each point, abbreviations are as follows: 1 = PRT, GRC, PRK; 2 = FIN, SWE, FRA, JPN; 3 = GBR, BEL. SU is standard units. GDP is gross domestic product. PPP is purchasing power parity.
[a] Countries have significantly different usage than the predicted at the 95 percent confidence interval.

all country-specific deviations constant. Canada and Australia also show higher-than-expected use. In contrast, Italy, Ireland, Austria, Japan, Sweden, and Finland use less than predicted by per capita GDP. A country-by-country analysis of the growth rate of use of ADHD medications over the past four years shows increases in both developed countries and developing countries.[21]

■ **Global expenditures.** Moving from use to spending, the global expenses regarding ADHD medications were U.S.$2.4 billion by 2003, representing a ninefold increase (adjusted for inflation) since 1993 (Exhibit 4). From 1993 to 2000, spending grew steadily (about 17.6 percent per year), but after 2000 the annual growth rate increased more steeply to 40.9 percent. This acceleration was largely driven by the U.S. market, where newer medications—primarily longer-acting formulations—became available. The United States dominates global spending on ADHD medications, making up approximately 92–95 percent of the total expenditures, with a 22.6 percent growth rate per year. Other countries showed a slightly slower spending growth rate than the United States—about 21.0 percent per year. A country-by-country analysis reveals that spending increases were much more pronounced in developed countries.[22]

■ **Medication mix.** There has been a clear change in the medications used to treat ADHD (Exhibit 5). The volume of short-acting medications plateaued and then steadily decreased after 1999, whereas the volume of long-acting formulations increased during the second half of the study period. The timing of this shift is related to FDA approval of Concerta (Johnson and Johnson), a controlled-release form of methylphenidate, in August 2000. Although the release of this and other relatively costly long-acting formulations such as Adderall XR (Shire) and Strattera (Lilly) help explain some of the increase in use, their presence is particularly related to the large spending increase. Using the same data set, we found that the increase in spending for ADHD medications in the U.S. market was attributable mostly to

EXHIBIT 4
U.S. And Global Spending On Attention Deficit Hyperactivity Disorder (ADHD) Medications, 1993–2003



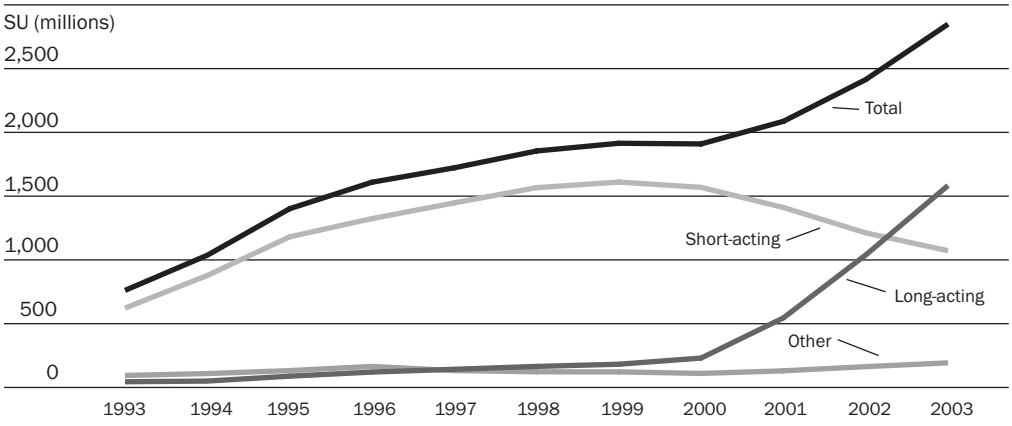
SOURCE: MIDAS database, IMS Health, 1993–2003.
NOTES: Spending is deflated to 2003 U.S. dollars using the U.S. Consumer Price Index. Cross-sectional variation from country to country was accounted for by IMS Health, which had converted all local currencies to U.S. dollars using purchasing power parity (PPP) methods. SU is standard units.

price increases.[23] From 1994 to 2003, U.S. sales volume increased 80 percent, while prices increased 285 percent in real dollars. In contrast, in OECD countries sales volumes increased 322 percent, while prices rose only 70 percent. A sampling of prices from *Consumer Reports Best Buy Drugs* reveals a large differential between short- and long-acting formulations.[24] Beyond the United States (data not shown), the use of short-acting formulations began to plateau in 2002, as long-acting formulations were introduced worldwide. These data suggest that the pattern in these countries lags behind that of the United States by several years.

Discussion

The use of stimulant medications in the United States has greatly increased during the past twenty years.[25] Although the increase might be leveling off for children, much concern has been raised regarding the potential

EXHIBIT 5
Global Volume Of Attention Deficit Hyperactivity Disorder (ADHD) Medications, By Category, 1993–2003



SOURCE: MIDAS database, IMS Health, 1993–2003.
NOTE: SU is standard units.

for overdiagnosis of the disorder, the potential for overuse of these medications, and the possibility of diversion and abuse, weighed against their important clinical benefits under conditions of careful diagnosis and treatment monitoring.[26] This study has confirmed that the United States is by far the world's largest consumer of ADHD medications. Why other countries have lagged behind is not well understood. Advertising in the United States is clearly an important factor; the number of U.S. medical specialists who are able to diagnose and treat ADHD is also crucial. Clearly, national policies about the purchase of medications by the health system—as well as the very nature of different national health care systems—are essential factors. It appears that little difference exists in the rates of the disorder between the United States and other countries, although rates of "diagnostic prevalence" (that is, cases actually diagnosed by clinicians) lag well behind true prevalence outside the United States.[27]

Other countries, however, are beginning to follow U.S. trends. Over the past decade, use of ADHD medications in non-U.S. OECD countries has increased at rates even greater than those in the United States. Furthermore, countries using the most ADHD medications per capita are those with the highest incomes. Over the past five years, many developing countries have had yearly growth rates in use and spending that exceed 20 percent.[28]

Although the use of ADHD medications is increasing globally, the cost of these medications is escalating even more rapidly. With the advent of longer-acting stimulants and nonstimulant agents, spending for ADHD medications has risen dramatically. Note that a month's supply of generic methylphenidate taken two or three times per day costs around U.S.$25, whereas the cost of one month's supply of Concerta 18 mg, taken once a day, is U.S.$109.[29] The change to long-acting agents began in the United States in 2000; other countries are following the same trend but with a lag of several years. We can expect that the already burgeoning global costs for medication treatment for ADHD will rise even more sharply over the next decade.

Our analysis of ADHD medication use as a function of per capita GDP showed that despite robust predictions of use from this indicator of national income, other factors might explain variation in use. For example, U.S. clinicians tend to recognize ADHD as a debilitating disorder.[30] Furthermore, changes in the federal special education law (the Individuals with Disabilities Education Act [IDEA]) enacted in 1991 opened up special education services for children with ADHD, prompting greater diagnosis.[31] Other factors include widespread third-party medication coverage, marketing efforts by pharmaceutical firms, and a general increase in the use of all psychotropic medications for children.[32] Finally, the United States has the highest overall drug spending per capita among the OECD countries.[33]

Despite major differences from the U.S. health care system and considerable regulation of pharmaceutical prices, Canada also exhibits high usage of ADHD medications.[34] This pattern might be a function of its proximity to the United States, with exposure to U.S. advertisements and cultural norms. Within other countries (such as Sweden and France), strict governmental regulation against the prescription of ADHD medications might also explain some of the variation in use.[35] For example, in France, use of methylphenidate, the only approved ADHD medication, requires a hospital-initiated prescription from a neurology, psychiatry, or pediatric specialist.[36] In the Netherlands, there are lower rates of prescription than in the United States, but major increases of stimulant use became evident in the late 1990s.[37] Other potential factors related to differential use rates include differing diagnostic criteria for ADHD, the professional training of physicians and mental health care providers with respect to ADHD, differences in national health care systems, rates of overall pharmaceutical spending, perceptions of ADHD by parents and teachers, and variation in educational systems.[38]

Understanding determinants of the use of ADHD medications, their costs, and their po-

tential risks and benefits is now a global issue. ADHD clearly involves biological, behavioral, and environmental factors.[39] Economic and cultural differences among countries are likely to be salient for adoption and usage of medication treatments. Given the global diffusion of ADHD medications as well as the prevalence of this condition, ADHD could become the leading childhood disorder treated with medications across the globe. Clear priorities are (1) determining long-term benefits of pharmacologic treatments and (2) ascertaining economic, professional training, and cultural factors that promote optimal prescription and monitoring.[40]

We recommend that countries actively compare data on use and spending, to adjust overuse or underuse, and that they weigh carefully the potential benefits versus the potential liabilities (side effects, addiction, diversion) of medication treatment for ADHD. During this era of global rises in medication use and expenditure, the stakes are high.

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