Prozac on the loose: Rethinking the "treatment gap" for depression in South Asia

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Introduction

Antidepressants have ambiguous effects. More people are on them today than ever before. At the same time, the mental disorders they are supposed to treat also seem to be increasing steadily. Those who welcome the spread of these drugs praise their improved efficacy and safety. Others say they are no better than placebos or, even worse, that they can have extremely adverse side effects, among them a heightened risk of suicide. Hence, many critics of antidepressants allege that they do not benefit patients, but only pharmaceutical corporations. Patients' subjective experiences of them are also ambiguous. To some, it feels as if these drugs are giving them their lives back. Others find that the pills do not solve any of the social and economic problems that is causing them to suffer. Antidepressants make it hard to distinguish where the boundaries of the "thing" end and where the territory of the "self" begins, yet they are marketed as one more consumer commodity among others. This paper tries to unfold one more ambiguity of antidepressants: on the one hand, they are now advocated as essential medicines that must be provided by government health services even in poor countries such as India or Nepal. On the other, there is strong evidence that antidepressants are already rampantly used in these countries, and that the consequences of this situation are not properly recognized by policymakers.

This paper has four parts. We first analyze how depression and the alleged "treatment gap" in mental health between richer and poorer countries are presently seen in global health strategies. The second part describes the conceptual and methodological tools we developed in the research project *Tracing Pharmaceuticals in South Asia* to study the same set of questions in a wholly different way. The third part of the paper presents some of the key findings of our research on the production, distribution, prescription, and regulation of psychopharmaceuticals in India and Nepal. Here, we focus on a node in South Asian drug distribution networks that policy interventions for mental health systematically ignore: private medicine shops. We argue that there is not only a proliferation of generic drug manufacturers in South Asia, but also a proliferation of generic brands of psychopharmaceuticals, of private medicine shops, and of both licensed and unlicensed prescribers of these drugs. The fourth and concluding part of the paper highlights our main policy recommendation: any policy-oriented assessment of a "treatment gap" should start with research on actual availability of drugs in the private market.

1. Assessing the "treatment gap"

Since the 1990s, mental health has shifted from a marginal to a more central position within the policies advocated by the World Health Organization. This transformation culminated in the publication of the World Health Report 2001, which claimed that

depression will be the world's second leading health problem after heart disease by the year 2020, if calculated by disability adjusted life years (DALYs). To fight the rise of depression, the WHO embraced the extensive use of psychopharmaceuticals, among them the latest generation of antidepressants, the selective serotonin reuptake inhibitors (SSRIs). Even if SSRIs were often more expensive than older types, such as tricyclics, the greater expenditure was "offset by a reduced need for other care and treatment" (World Health Organization 2001: 61). According to the 2001 Report, SSRIs were a great success in countries of the global North. These new antidepressants were also an "attractive and affordable prescribing option in lower-income countries" (2001: 61). No patient in the world, whether rich or poor, should be "deprived, on economic grounds only, of the benefits of advances in psychopharmacology" (2001: 61).

Throughout, the report highlighted links between mental illness and economics. It argued that there is a "vicious cycle" of poverty, mental illness, and macroeconomic impacts. Poverty lead to a higher prevalence of mental disorders, which were not properly cared for and which, therefore, took a more severe course. In turn, higher prevalence, lack of care, and more severe course of disease had negative consequences on the economy as a whole: people could not work or were less productive, which lead to a decrease of economic performance. It also became more expensive to treat people properly, which further depressed gross economic income. For the United States, the report presents the staggering figure of a yearly cost of 2.5% of the gross national product (World Health Organization 2001: 27). To turn this situation into a *virtuous* cycle, the World Health Report advocated investments in psychiatric drugs as investments in global economic growth. Economic growth was, by suggestion, a cure against depression.

This link between poverty and mental illness was reiterated in many subsequent publications. For example, Patel & Kleinman (2003) argued in the *Bulletin of the World Health Organization* that there is a close relation between poverty and the risk of mental illness, with a low level of education as the most consistent association. They argued that "common mental disorders need to be placed alongside other diseases associated with poverty by policymakers and donors" (2003: 609). Development interventions for education and for the provision of microcredit were two key strategies to break the vicious circle of poverty and mental illness. At the same time, primary care services provided by national governments needed to be strengthened by the inclusion of psychiatric treatments.

This line of argument was given even more prominence the series on global mental health that appeared in six articles on 4 September 2007 in *The Lancet*. The third article in this series (Patel et al. 2007: 51) put exact price tags on various types of interventions against depression in primary health care. The highest economic benefit would come from a maintenance treatment with newer antidepressant drugs (i.e., SSRIs) in combination with psychosocial treatment: if money were invested in this way, up to US$2,459 per disability-adjusted life-year (DALY) would be saved for patients in low-income countries. Treatment with SSRIs alone would yield up to US$1,771 by averting lost productivity because of depression. In other words, spending a little money on antidepressants would give a big boost to economic productivity.

	Treatment setting	Treatment coverage (target)	Intervention	Cost-effectiveness range (US$ per DALY averted)*
Schizophrenia	Hospital outpatient	80%	Older (neuroleptic) antipsychotic drug	$US 2499–7230
			Newer (atypical) antipsychotic drug	$US 16 174–20 583
			Older antipsychotic drug+psychosocial treatment	$US 1743–4847
			Newer antipsychotic drug+psychosocial treatment	$ US 10232–14481
Bipolar affective disorder	Hospital outpatient	50%	Older mood stabiliser drug	$US 1587–5295
			Newer mood stabiliser drug	$US 2943–6386
			Older mood stabiliser drug and psychosocial treatment	$US 1545–4928
			Newer mood stabiliser drug and psychosocial treatment	$US 2765–5908
Depression	Primary health care	50%	Episodic treatment with older (tricyclic) antidepressant drug (TCA)	$US 478–1288
			Episodic treatment with newer antidepressant drug (SSRI; generic)	$US 1003–1771
			Episodic psychosocial treatment	$US 537–1611
			Episodic treatment with older antidepressant drug+psychosocial treatment	$US 627–1586
			Episodic treatment with newer antidepressant drug+psychosocial treatment	$US 1140–2101
			Maintenance treatment with older antidepressant drug+psychosocial treatment	$US 749–1760
			Maintenance treatment with newer antidepressant drug+psychosocial treatment	$US 1449–2459
Panic disorder	Primary health care	50%	Benzodiazepines	$US 572–1075
			Older (tricyclic) antidepressant drug (TCA)	$US 305–619
			Newer antidepressant drug (SSRI; generic)	$US 567–865
			Psychosocial treatment	$US 338–927
			Older antidepressant drug and psychosocial treatment	$US 443–977
			Newer antidepressant drug and psychosocial treatment	$US 671–1188

DALY=Disability-adjusted life-year. *Range reported for six low-income and middle-income regions.[35]

Table 8: Interventions for reduction of mental disorders in low-income countries

Source: Patel et al. 2007

The argument pursued in the *Lancet* Series unfolds as follows: First, depression, alongside other mental disorders, is measured by the global burden of disease that it causes. Second, various kinds of interventions, above all pharmaceutical treatments, are shown to be both medically and economically effective. Third, calculations of how much money ***should*** be spent by national health systems on mental health treatments are contrasted with data on how much money is ***actually*** spent, and the difference between the two is found to be a huge "treatment gap." Fourth, various barriers to reform are identified and analyzed to show how they could be broken down. Fifth, a call for action summarizes the results and urges international organizations and national governments to change their mental health policies.

While our colleagues Petra Brhlikova, Allyson Pollock, and Rachel Manners evaluate the arguments on the global burden of disease and for the evidence of the therapeutic efficacy of antidepressants, we want to focus on the evidence for the so-called treatment gap.

A new WHO-sponsored initiative, the Mental Health Gap Action Programme (mhGAP), juxtaposes governmental investments for the treatment of mental, neurological, and substance use disorders (MNS) in low and lower-middle income countries with those in richer countries. It argues that national investments in these treatments show a vast treatment gap and urges an immediate increase in spending. A WHO report from 2008, called *Scaling Up Care For Mental, Neurological, And Substance Use Disorders*, puts exact figures on the magnitude of this treatment gap. It argues that the psychiatric treatment gap is "more than 75%". Divided by different types of mental disorders, the treatment gap was found to range from 32% for schizophrenia to 78% for alcohol use disorders. Depression treatments showed a gap of 56%. These percentages refer to a global average, not only to developing countries.

It is important to understand how these numbers are calculated. In the appendix of the report, a table classifies countries by the following criteria: World Bank income category,

gross national income per capita, population in thousands, MNS disorders DALYs, MNS disorders DALYs per 100,000 population, mental health professionals per 100,000 population, and health providers per 1,000 population. For India, the table argues the following: it is a low-income country with a gross national income per capita of only US$820 in the year 2006. The country's population was more than 1 billion people in 2002. Annually, MNS disorders are causing more than 27 million years of disability adjusted life years. This staggering figure means that 2625.3 disease-adjusted life-years per 100,000 population are lost. Juxtaposed to this is the scarcity of trained people who can help: there are only 1.87 health providers per 1,000 population and only 0.31 mental health professionals per 100,000 population (that is, 0.0031 per 1,000).

The situation in Nepal, another low-income country, is argued to be just as bleak, with only 0.32 mental health professionals per 100,000 and only 0.67 health providers per 1,000 population.

Countries with low and lower middle incomes by WHO region	World Bank income category	Gross national income per capita (US$ 2006)	Population in thousands (2002)	MNS disorders DALYs (in thousands)	MNS disorders DALYs per 100 000	Mental health professionals (per 100 000)	Health providers (per 1000)
South-East Asia Region							
Bangladesh	Low	480	143 809	3 472	2414.4	0.113	0.57
Bhutan	LM	1410	2 190	52	2393.6	0.46	0.27
Democratic People's Republic of Korea	Low	NA	22 541	446	1977.9	0	7.41
India	Low	820	1 049 550	27 554	2625.3	0.31	1.87
Indonesia	LM	1420	217 131	4 165	1918.4	2.91	0.95
Maldives	LM	2680	309	6	1977.6	1.56	3.62
Myanmar	Low	NA	48 852	1 010	2067.5	1.11	1.34
Nepal	Low	290	24 609	572	2324.1	0.32	0.67
Sri Lanka	LM	1300	18 910	468	2474.9	2.09	2.28
Thailand	LM	2990	62 193	1 493	2400.7	4.1	3.2
Timor-Leste	Low	840	739	3	429.4	0	2.29

Source: WHO 2008

One publication that the 2008 mhGAP Report refers to, a paper in the Bulletin of the WHO (Kohn et al. 2004), calculates a treatment gap of 56% for major depression for *all* countries, not only for low/lower-income ones. In Kohn et al.'s paper, the "56%" gap refers to the percentage difference between number of people *needing* treatment for mental illness and number of people *actually receiving* treatment, found in 59 studies of service utilization rates for selected psychiatric disorders in community-based surveys in different countries. That means that "56.3%" refers to the "median rate untreated," which is the difference between those found in need of depression treatments in community-based surveys and those who receive medical help. Among the 59 studies analyzed by Kohn et al. 2004, a 56% gap in service utilization was calculated in a study on "psychiatric morbidity among adults living in private households" in the UK in 2000 (Singleton et al. 2001) and in two studies on service utilization among Mexican Americans in the United States from 1998 and 1999 (Vega et al. 1998; Vega et al. 1999). Hence the evidence for the claims made in the mhGAP Report of 2008 is scarce and not up-to-date. The "56%" treatment gap presented in the 2008 document is *not* about treatment gaps between poorer and richer countries today, but about service utilization gaps in a handful of countries, both rich and poor, over the past 25 years. The data on which claims about treatment gaps are far from exact, yet the exactness of numbers suggests that exact numbers can be given (also see Brhlikova, Pollock & Manners' paper).

It is also important to highlight what "service utilization" in the WHO statistics means. Kohn et al. (2004: 859) define service utilization as "seeking assistance from any medical or professional service provider, specialized or not, public or private." Excluded from this category were, however, "traditional healers and non-professional providers." Kohn et al. (2004: 859) also point out that the 59 studies they drew on "did not report utilization by treatment modality," which means that one can neither distinguish between pharmacological and non-pharmacological treatments, nor between providers who openly declare that they are prescribing psychopharmaceuticals and those who do so invisibly. As we argue in this paper, such a definition of service providers and treatments provided creates major blind spots in the assessment of how large the "treatment gap" might be.

2. Why "tracing" pharmaceuticals?

Our initial research proposal responded to a call from a joint initiative of ESRC and DFID to fund social science research that had the potential to show new ways of understanding global poverty. Research should contribute to poverty-reduction strategies such as the Millennium Development Goals (MDGs) by providing governments and international organizations with a new *methodology* of studying the causes and consequences of poverty. Our team proposed to find new ways of studying economic inequality in relation to pharmaceutical practices in India and Nepal.

We started with a range of hypotheses about the relations between pharmaceuticals and poverty in South Asia: (1) because of a crumbling governmental health system, private health care is the first port of call for most patients; (2) because of the absence of comprehensive health coverage even among middle and upper-class people, health expenses have to be paid out of pocket by patients; (3) the greatest share of private health expenditures are on pharmaceuticals; (4) despite the high costs of obtaining competent medical treatment, many medicines are inappropriately prescribed; (5) despite the high costs of privately bought drugs, many of them are of substandard quality or even outright fakes; (6) the costs of obtaining high-quality and appropriate drugs for a sick family member are a major reason why South Asian households fall into poverty.

Both in India and in Nepal, there are various governmental regulations in place that aim to keep drugs affordable, to minimize the inappropriate use of prescription drugs, and to stamp out substandard drugs, but these rules assume very high levels of public sector competence and an adequate infrastructure. We further reasoned that much policy-making ignores the existence of private and informal systems of medicine distribution that bypass regulatory structures.

Other than any research carried out to date, we decided to do an in-depth study of three selected molecules: oxytocin, rifampicin, and fluoxetine. Among these three, we expected that fluoxetine—and psychopharmaceuticals in general—would be predominately used only in the private sector. Fluoxetine only recently entered the essential drugs lists in South Asian government hospitals, e.g. in West Bengal it appeared only in 2007. Mental health is not included in the MDGs set forth by the United Nations, and it has also never been a priority of government policy in India. To be sure, there has been a National Mental Health Program (NMHP) in place since 1983. Budget allocations for the NMHP have been growing rapidly: the programme's 10th Five Year Plan (2003-2008) had a budget allocation of US$ 42 million, which was seven times more than the budget for the

9th Five Year Plan (US$ 6 million). The budget for the 11th NMHP, to run from 2009 to 2014, is predicted to increase exponentially, to US$ 200 million (Sinha 2009). The NMHP contains a number of psychosocial and public education components (Agarwal 2004), but in practice it focuses on making psychopharmaceuticals more available in state hospitals and health posts (Jain & Jadhav 2009). The role of the state in the provision of antidepressant treatments still seems small in comparison what is available privately. Our choice of fluoxetine, instead of older antidepressants such as amitriptyline that are much more entrenched in government drug supplies, was meant to highlight the private sector further.

The approach that we took in the project *Tracing Pharmaceuticals in South Asia* was entirely different from the methods that had been used so far. A conceptual starting point for our research was the realization that disease categories are co-constituted by the available diagnostic procedures and treatments. Today it is hardly controversial to say that biomedicine, despite its best efforts to portray itself as a universal and objective science, has seen its diagnostics and therapies change drastically over time. What remains controversial is the question of what drives these changes. According to standard biomedical explanations, it is continual scientific progress and an ever-closer grip on the biology of health and disease that bring these changes. A different view comes from critical science studies, which argues that the availability of treatments, especially of pharmaceuticals, transforms the way that diseases are described and categorized. Indeed, the transformative powers of pharmaceuticals are not even limited to health and healing, but they also have a much broader impact on society: "As medical technology, pharmaceuticals are not only products of human culture, but producers of it" (Van der Geest, Whyte & Hardon 1996: 155).

Applied to mental health, this means that one should *first* look at what kinds of drugs are actually available and who is using them. Such an approach advocates a reversal of commonsense ideas in both public health research and medical anthropology. In both fields, it seemed obvious that mental health problems needed to be studied as a causal and temporal sequence. It was commonsensical to ask first how mental symptoms are perceived by patients, then to ask what causes the symptoms, and then to ask what kind of treatment would be best to cure sickness. This model presupposes that sickness episodes truly *start* with a patient's perception of symptoms, which are then given diagnostic meaning by a doctor, and which are then treated with the best available medicines. But if one starts with evidence from what pharmaceuticals are prescribed and only then how depressive symptoms are perceived and its causes explained, a different picture emerges.

To start with drugs rather than with symptoms has great advantages, with all the three fields of research that we chose: rifampicin and infectious diseases; oxytocin and childbirth; fluoxetine and mental health. In relation to mental health, this new methodology seemed particularly promising, because it allowed us to bypass the thorny problem of the transcultural validity of psychiatric disease classifications. In the case of tuberculosis, there is no question about biomedicine being able to diagnose a patient as infected with Mycobacterium tuberculosis. In the case of childbirth, it is beyond dispute that oxytocin augments uterine contractions during labour. But in the case of depression, there is no pathogen that can be identified, and there is not even a conclusive theory about the pharmacological action of antidepressants. How to measure "depression" and other mental illnesses without imposing a Euro-American set of categories upon other cultures remains one of psychiatry's greatest problems (e.g., Kleinman & Good 1985;

Dawson & Tylee 2001). Continuing attempts to make the American Psychiatric Association's *Diagnostic and Statistical Manual* more sensitive to cross-cultural variations is a working example.

We reasoned that questions of mental health in South Asia could be approached in an entirely new way if we gave medicines, as easily traceable, observable and stable referents, would take precedence over psychiatric diagnostics and controversial epidemiological calculations. The social importance of material things has often been observed by anthropologists (e.g., Appadurai 1986). Applying a notion of "social biographies of things" to the anthropology of pharmaceuticals, Van der Geest, Whyte & Hardon (1996: 153) observe the same power of concreteness in medicines: "By applying a 'thing', we transform the state of dysphoria into something concrete, into some thing to which the patient and others can address their efforts". The materiality of medicines is particularly pronounced in the domain of psychopharmacology where, as many critics claim, "it is actually the drug, rather than the depressed patient, that serves as stable reference point" (Lakoff 2002: 72). The "thinginess" of drugs allows an anthropologist to study "depression" with a crosscultural perspective even if there is no consensus about the symptoms of "depression." Even if psychiatry has persistent problems in finding physical referents for its categories and in measuring their severity, the drugs that are used are concrete enough to be compared. Hence it looked especially fruitful to us to start crosscultural research on depression with observable treatments rather than with symptoms and causes. In the research project *Tracing Pharmaceuticals*, we did not start with epidemiological assumptions about burdens of disease, nor with evidence-based claims about the efficacy of various drugs, nor with comparisons of how much money is spent on mental health treatments in South Asia as opposed to Europe or North America. Instead, we decided focus on the molecule fluoxetine and to discover its actual availability and spread in South Asia.

3. Following fluoxetine around

In the initial phases of our research, we wanted to collect the existing evidence of how widely fluoxetine is available. One excellent starting point was the product listings in the ready drug reckoners used in India. These are book-shaped registers of pharmaceutical products according to therapeutic segments. For each active ingredient, a short description of indications, side effects, and similar drug information is given, followed by an alphabetical listing of existing brands by name, with details about dose, packaging, and recommended retail prices. The figure below (###) is a copy from one of these drug manuals, called *Drug Today*, with listings of fluoxetine products. CIMS India, which is the market leader in this type of publication, is owned by a London-based corporation, CMPMedia. CIMS India has an online directory designed to look like a Google search page. A CIMS search in March 2009 showed that there are sixty-six different brands of fluoxetine available in the Indian market, many of them in three to four different doses (ranging from 10mg to 80mg) and form of packaging (tablets, capsules, suspensions). Among these, 23 products were combinations of fluoxetine and alprazolam, and three products combined fluoxetine with olanzapine. When we first looked up various drug reckoners in the winter of 2006, the number of brands listed was roughly similar to what they are today.

The drug reckoners do not give any indication of what the market share of each of these brands is. This information is collected by an international market research company called IMS-ORG. To obtain the latest data from this company is so costly that only

larger pharmaceutical companies can afford to pay for it; our budget did not stretch that far. In India, then, the situation is the same as in other countries, where there is a "private life of numbers" (Lakoff 2005) on which drugs are sold in what quantities. It is a "private" life because neither government agencies nor international organizations such as the WHO actually have this information. We tried to approach a few of our key informants in companies who are regularly buying the market statistics and would not mind passing them on to us. As it turned out, it took a long time until we finally obtained data on fluoxetine from contacts in Delhi.

This proliferation of fluoxetine brands can be partly explained with reference to the drug patent laws that were in place from the 1970s until 2005. Unlike many other pharmaceuticals markets in developing countries, the Indian market is dominated by domestic generic manufacturers, not by Euro-American giants. This situation emerged from 1972 onwards, when the then Indian government under Indira Gandhi introduced a new patent law that only acknowledged process patents but not product patents. When new molecules were introduced in Northern markets, these could be reverse-engineered in India and be sold at a much lower price than the branded original. This patent regime was in place until India's full accession to the Agreements on Trade-Related Intellectual Property Rights (TRIPS) under the World Trade Organization (WTO) till 2005. It allowed Indian firms to outdo multinationals and to turn India into the world's leading producer of generic medicines by volume. Non-Indian drugs firms capture less than 25% of the Indian market, with the rest divided up by thousands of national and regional generics manufacturers.

This applies also to the psychopharmaceuticals market, where almost all the dominant firms are Indian. And it applies particularly to Fluoxetine: Eli Lilly's branded Prozac was never even introduced in India. Lilly never bothered to bring Prozac to India because it could not hope to make any serious profits there. In the US in 2009, Eli Lilly's Prozac 20mg sells for around US$ 40 per 10 capsules. In India, where the market is completely dominated by generics, the typical price charged for 10 capsules of fluoxetine 20mg is less than US$ 1. Other multinationals that took their products to the Indian market had to do so at a heavily reduced price. For example, Pfizer India sells sertraline under the brand name Daxid at a vastly lower price than its Zoloft brand in the US. In 2009, more than thirty rival versions of sertraline were available. Faced with such competition, Pfizer sells Daxid at a price that is even lower than some of its generic competitors (for example, Torrent's Serenata and Ranbaxy's Serlift). Fierce competition between generic manufacturers is the first reason fluoxetine is relatively affordable to Indian patients.

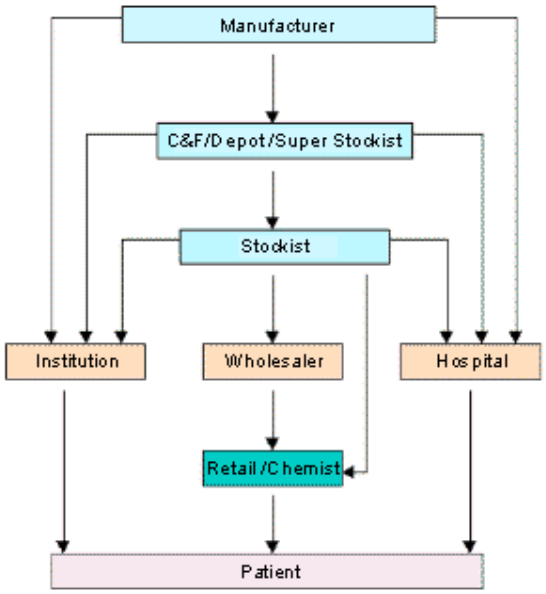
In the early stages of fieldwork we focused on interviews with acknowledged experts on pharmaceutical availability and affordability. In Kolkata, we made contacts to several NGOs, among them the Community Development Medicinal Unit (CDMU), which is a partner of many other Indian health action groups. The main goal of the CDMU is to supply its member-partners with quality-tested essential drugs at the lowest possible price. The CDMU does so by going directly to drug manufacturers, which allows them to bypass for-profit distributors and retailers. The organization also publishes the *Rational Drug Bulletin* and organizes seminars, workshops and training programmes for the rational use of medicines. With funding from the World Health Organization and Health Action International, CDMU carried out a study on drug prices and affordability in West Bengal (Tripathi, Dey & Hazra, 2005), which found that generic fluoxetine is highly available and affordable across all districts and cities of West Bengal. In 2005, the most-sold generic of fluoxetine, Cadila's Fludac, was on sale in 74% of medicine shops. At

least one brand of generic fluoxetine was sold in 77% of all shops. The study included the startling observation that fluoxetine is more widely available even than vital drugs such as Ibuprofen or Ciprofloxacin. The CDMU study also found that it was easier to buy fluoxetine than amitriptyline, which had long been the most commonly available type of antidepressant in West Bengal and, most likely, South Asia as a whole.

If the affordability of fluoxetine is initially an outcome of patent regulation, this is not enough to explain its widespread availability. Nor, indeed, is it enough to explain the competition at the level of the manufacturers only by reference to the absence of product patent protection until 2005. There must be a wider network of players to make the wide availability and affordability of a drug like fluoxetine possible. What our research brought out clearly is that it is not enough to look at only one level, e.g. at government drug supplies or at pharmaceutical manufacturers, but one needs to look at all nodes in the network to find out how widely psychopharmaceuticals are actually used.

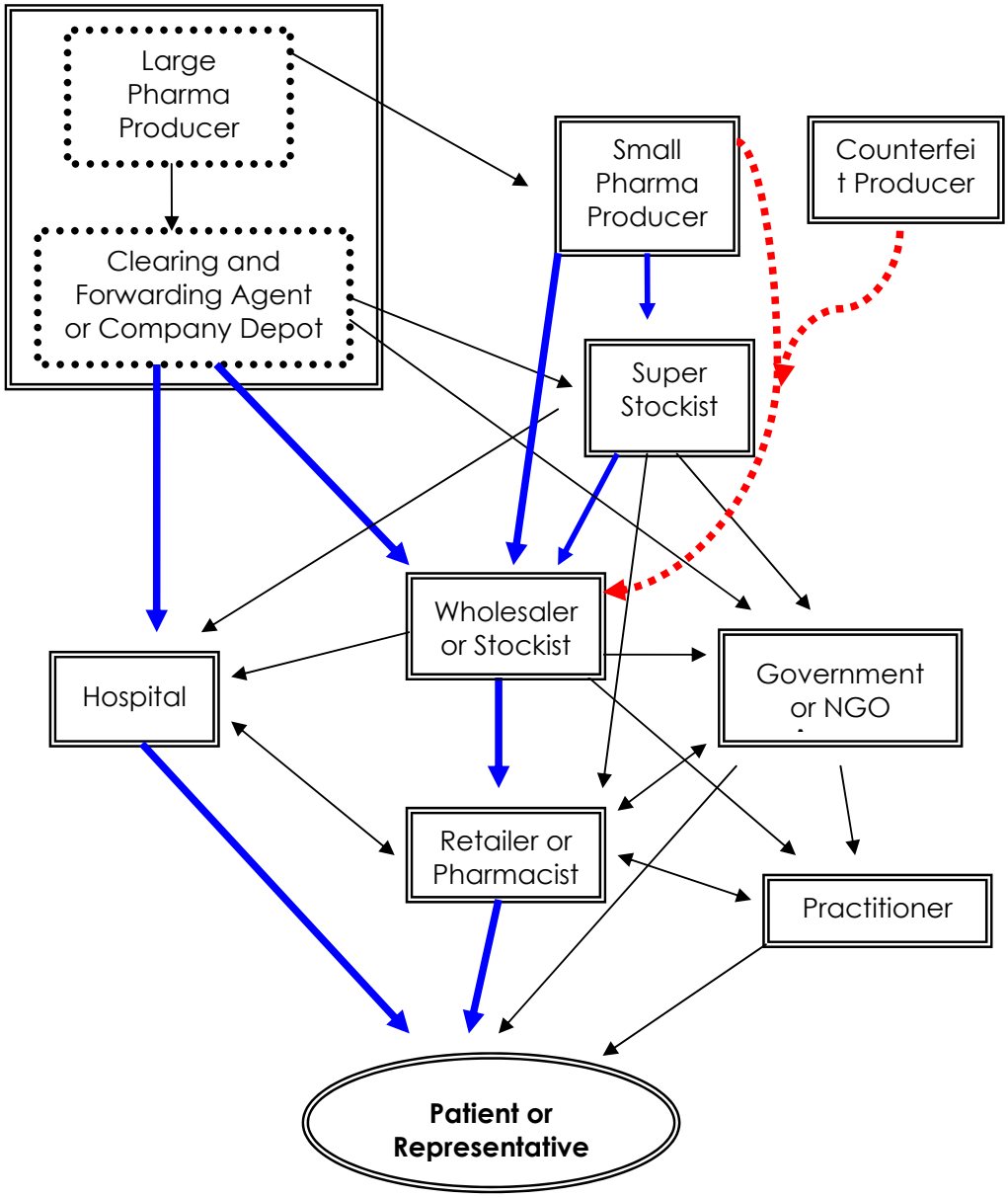
When we started to trace fluoxetine, oxytocin and rifampicin, we gradually built a far more complex map of the agents involved with drugs than is usually available even to experts. Simplistic models of "distribution" in South Asia, such as the following diagram, which is taken from an industry publication:

Diagram 1: Channels of drug distribution



Drug distribution in South Asia is, however, more complicated. A working version of the model that Roger Jeffery built from our data looks like this:

Diagram 2: Tracing Pharmaceuticals in South Asia



The assemblage of players involved comprises clearing (or carrying) and forwarding agents (CFAs), depots, superstockists, stockists, wholesalers and retailers. This model does not even mention various types of regulating agencies. Between 2006 and 2008, we conducted dozens of interviews with people in all nodes represented here (except producers of fake drugs, which was too dangerous!).

While building a more fine-grained picture of drug distribution, we realized how much gets overlooked by the methods used by the WHO in regards to the "treatment gap." The most glaring oversight is the existence of a multitude of generic manufacturers. But there are many other agents who are usually not given any attention, among them are private retailers.

There is a direct co-constitution between the rise of generic manufacturers in South Asia and the proliferation of private medicine shops. Since drugs are affordable, it makes sense for medicine shops even in remoter areas of rural India to stock fluoxetine and other drugs, because the local markets have enough potential users. In turn, since there are so many actual and potential users of fluoxetine, the market for the drug is growing and more drugs are manufactured.

The formal regulations concerning pharmacies require a degree in pharmacy, a medical qualification, a science degree and two to three years' experience in prescribing, or matriculation with science subjects and five years of experience. However, the majority of all pharmacies does not have someone trained in pharmacy or pharmacology looking after the day-to-day business. A common practice is to open a shop in the name of a pharmacist, who may be named on several other licenses as well, and may rarely if ever attend the pharmacy. The boom in drug retailing across India is triggered by the laxity of regulations, which produce low thresholds to set up a business in this area.

The retailers comprise a wide variety of operations, ranging from small shops to retail chains. In most cases they are family firms, with a single owner or a set of brothers, sometimes continuing a longer family tradition. They will normally have a small number of employees, who often turn over quite quickly: these ex-employees can often be found in rural areas or in small towns having set up businesses as drug retailers themselves, or having set up a medical practice of their own. Across South Asia, the first point of medical contact is often a pharmacist or other unlicensed prescribers, such as the so-called Rural Medical Practitioners (RMP). It is common for patients, especially in the countryside and also in smaller towns, approach a medicine shop and receive a diagnosis and prescription (often including powerful prescription drugs) without the intervention of any other kind of practitioner. Similarly, the prescriber also dispenses the medicines prescribed: indeed, there might not even be a consultation fee, but the practitioner makes his income from dispensing prescriptions. That is why it is hard—if not impossible—to draw clear lines between them.

Retailers need several different licences for their shops, and the range and complexity of the rules offer plenty of opportunities for retailers to fall short of the requirements (Narayanan 2007). So it is not necessarily the lack of regulations but the question of enforcement.

Industry sources claim that retailers account for about 70-80 percent of the pharmaceuticals sales in the country, with the remainder being dispensed through hospitals (Jayakumar 2007). In rural and small-town India and Nepal, private medical

practitioners (whether formally trained or not) usually keep stocks of most of the medicines they expect to prescribe. Most small hospitals and nursing homes also have in-house pharmacies and may require patients to buy the drugs on the premises, whether they are in- or out-patients. Pharmacists' recommendations to customers on which drugs to buy are based primarily on profit calculations. As in any business, these calculations are complex: the retailers cannot simply try to sell as many expensive drugs as they can. Successful retailers strike a balance between expensive and cheap products. They also try to capitalize on good relations with other players in the distribution system.

For example, manufacturers, stockists, distributors and sometimes medical representatives offer price reductions to the retailers to move drugs more quickly or to increase the margin that can be earned by the retailer in order to get him to stock a particular product. Linked to company bonuses is the widespread practice of substitution, in which the pharmacist replaces the prescribed drug with another (usually, but not always equivalent pharmacologically). A more profitable brand, for the pharmacy, is one for which the most bonuses are given. The companies have to keep an eye on the retailers while the retailers have little to lose if they do not sell a particular product. The proliferation of medicine shops in India can, therefore, be partly explained by the way in which profits are shared between several players in the distribution network. Again, this is a systemic effect that is not easily visible. In order to see it, one needs to look at several levels simultaneously.

The openness of retail shops allows for a key phenomenon of South Asian pharmaceutical markets: the "floating prescription". For drug manufacturers, psychiatrists have enough expertise to set a prescription trend, whereas non-specialists only want to prescribe drugs that are firmly established. According to the psychiatrists and marketing specialists we interviewed, the route through which the non-specialists learn about the most common antidepressant treatments was not through medical marketing, but through prescriptions that patients carried around with them, from one prescriber to another. A psychiatrist interviewed in Lucknow in 2007 explained the phenomenon of the floating prescription as follows:

> "…depending on how much we [psychiatrists] use it, those [fluoxetine] prescriptions generally go to the suburban and rural areas, or to the general physicians in the cities also. Because the patient who has come to see me, who is on fluoxetine, and he has some gastric problem tomorrow, and goes and sees some gastroenterologist, or his family physician. He gets to know that a product called fluoxetine is there in the market, and is being used by the psychiatrists. … So the next time when he gets a similar kind of patient, he experiments and prescribes fluoxetine to him."

A Kolkatan marketing director for psychopharmaceuticals described the link established between psychiatric and general prescription habits as follows: "Once the consultant prescription is done, it floats in the market and immediately it reaches the GP … When a consultant shows faith in a particular product, it is immediately picked up by the GP."

There are different situations in which a psychiatrist's prescription might travel with the patient to a non-specialist. A patient could regularly see a psychiatrist but also seek treatment from a GP for illnesses that do not require specialist attention. In another common scenario, a patient may pay several visits to a psychiatrist and then stop consulting him, perhaps because access is too cumbersome, or because his fees are too

high: "They continue with the drug by the consultant and then, if they face any problems, they go to the GP. The GP learns about the prescriptions and he will immediately ask what the actual problem was," said one of the marketing managers we interviewed. One important reason why GPs and other non-specialists try to imitate the prescription style of psychiatrists could be their fear that the patient might go back to the psychiatrist and reveal the GP's ignorance about diagnosis and treatment. Copying prescriptions and forming a consensus about a "good drug" from a "good company" avoids loss of face among doctors.

Floating prescriptions are possible because prescription drugs are easily available over the counter. Theoretically, if a drug has a legal classification as a "Schedule H" drug, it cannot be sold over the counter. Many packets are stamped with messages such as: "SCHEDULE H DRUG: Warning: To be sold by retail on prescription of a Registered Medical Practitioner only". In reality, such drugs are easily available from any medicine shop. It does not matter if a prescription is old or was written for another person, because almost any drug can be bought without any prescription whatever.

The retailers whom we interviewed excuse this illegal practice with reference to India being a poor country: why should anyone be forced to waste money on doctors' fees if the required medicine can be obtained directly from the shop? For the retailers, this is not just about making money, but also about maintaining good relations with customers. Making a fuss about prescriptions or even turning down a customer's request to buy a drug is bad business.

What is striking about floating prescriptions is how long they can linger: some seem to drift through a series of doctor-patient encounters for up to 10 years. Marketing managers told us that they often can only guess at where demand for a product is generated, since floating prescriptions widened the gap between active promotion to doctors and actual sales in shops.

Floating prescriptions not only bring fluoxetine from psychiatrists to the GPs; they also carry the drug from licensed to unlicensed prescribers. Here again, floating prescriptions both establish fluoxetine as a trusted molecule in the treatment of depression, and particular brands as trusted products that can be safely prescribed even by people without formal training. Drug companies never officially endorse unlicensed prescribers, such as the RMPs. However, in practice they have begun targeting them individually, almost as if they were licensed GPs.

The floating prescription is another link in a much wider chain of people and processes that together account for the widespread use of antidepressants in South Asia over the past decade.

The side-effects of this situation are ambiguous. In some ways, the semi-legality, or even illegality, of retailers helps to make drugs widely available and also relatively affordable. Indeed, it seems that the state tolerates illegality because it takes some pressure off its own crumbling state health services. *If* the state authorities were to enforce the laws strictly, there would be far fewer shops, and those that existed would probably be more expensive (not least because they would have to recoup the costs of properly trained personnel). But the shady legality of many retail practices produces high "collateral" costs, and customers have to bear the risks of getting the wrong drugs from the hands of

untrained retailers or untrained prescribers. Fluoxetine and other psychopharmaceuticals are among the drugs that are both underused and overused in this way.

4. A new approach for research on global mental health

The current WHO mental health strategy on closing the treatment gap between richer and poorer countries is based on an outdated research methodology. In this paper, we bracketed the question if antidepressants are pharmacologically as effective as the WHO claims them to be. We also left aside the debatable issue of how DALYs and macroeconomic costs of depression are calculated for countries like India and Nepal. Here, we only focused on how the WHO methodology starts with epidemiological assessments of disease prevalence, and argued that in the case of depression, there is no specific pathogen (as for TB/rifampicin) or clinical situation (as for delayed labour/oxytocin) that could vouch for these findings to be valid independent of a complex web of cultural, economic, and historical circumstances. That the WHO studies have to draw on epidemiological studies that are up to 25 years old and that do not consider the immense changes in the recognition and treatment of depression that have taken place since the late 1980s is, we think, a grave weakness of its methodology. Even more seriously, the exclusive focus on licensed prescribers and a lack of data on what treatments are actually provided makes it impossible to put exact figures on any "treatment gap." Above all, a failure to notice of how widely antidepressants are used in South Asia's private health markets renders its claims about the treatment gap undependable. The lack of proper evidence motivates a misplaced effort to make antidepressants more widely available through government health services. If there is a problem, it seems to be neither the scarcity nor the price of antidepressants, but their overuse and wrong prescription.

It might seem easy to dismiss the findings on medicine shops and the wide circulation of fluoxetine in South Asia as merely anecdotal. It might seem that an ethnographic study of a limited number of people who deal with one particular drug molecule cannot be representative of what happens in depression treatments in South Asia as a whole. We would counter this argument by saying that, in the case of depression and its treatments in South Asia, it is more truthful to work with less exact numbers than with misleadingly precise ones.

We would also hold that an ethnographic study of only a few strategic nodes in drug distribution networks can shed far more light on what is happening today "on the ground" than any attempt to produce ahistorical pictures of disease prevalence and treatment gaps. That there are more than sixty generic versions of fluoxetine available, that even untrained Rural Medical Practitioners are using the drug, that prescriptions are "floating" in the market thanks to doctor-shopping patients and the easy over-the-counter availability cannot be anecdotal evidence, because for any of these findings to be possible, they *must* reveal large-scale relations of production and distribution in South Asia. If, for example, ten shops in Kolkata, ten shops in Kathmandu, and ten shops in Delhi all name the same handful of brands as their best-selling products; and if all of them say that patients often come with "floating prescriptions" (be it old prescriptions or emptied packets), then this will hold true, in all reasonable likeliness, for these regional markets in general.

The main policy recommendation that this paper developed is that any strategy for better mental health treatments in South Asia must take into account how much

antidepressants are already used in the region. A round of interviews in a number of local medicine shops on what brands of antidepressants are on sale and who the main prescribers are of these drugs yields far more useful information far more quickly than any of the data sets used by the WHO to date.

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