Drugs, Doctors and Public Policy in South Asia

Pharmaceuticals, Physicians and Public Policy
How Wide is the 'Treatment Gap' for Anti-depressants?
Intrapartum Oxytocin (Mis)use in South Asia
Reforming Drug Regulation

Vaccines: Meeting Local Needs in Global Times
TB Control in Nepal and India: Are the Right Regimens Being Used?
Drug Promotion Practices: How Rational?
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From the Editor’s Desk

The pharmaceutical industry in India has a long and complex history. For the most part, while it has been regarded as an industry, it has been under the scrutiny of the health sector and its purveyors where its products are exclusively sold. This tension, between treating it as an industry to be nurtured, as an economic entity and as a producer of essential life saving good, has often put a bind on people oriented policy making for the sector.

An important actor in this scenario is the medical profession. It acts, or at least is commissioned by its professional mandate to act, in the interest of the patient and the welfare of people. On the other hand, it also takes on the role of promoter of medicines and becomes itself in a sense the first consumer of the products of the industry.

This makes for a complex of networks, pathways and ties among industry, the government, the consumer and the medical profession and health sector. It also determines the nature of policy especially mediated by interest groups which are made up largely of consumers and sections of health sector and government. Unravelling this web of relationships is not only a fascinating exercise but also brings into the foreground the nuances of drug manufacture, its monitoring and dimensions of the market which are not easily revealed otherwise.

This collection of papers has emerged from a research study ‘Tracing Pharmaceuticals in South Asia’, a collaborative project of the University of Edinburgh and the Centre for Health and Social Justice. Presented at a dissemination workshop in New Delhi, these papers provide a glimpse of a fascinating exploration that encompasses the day-to-day journey of pharmaceutical products viewed through an anthropological lens within a framework of pro-people policy making. We are grateful to Roger Jeffery and Abhijit Sen for making this issue possible, and to all the authors.

Also in this issue is an exploration of the demographic database on morbidity by Soumitra Ghosh and Arokiaswany in the section ‘Exploring Demography’, in which we hope to showcase research on demographic databases.

We are happy to announce a new website for this journal: www.jhs.co.in. We invite you to explore the ‘Knowledge Community on Health Studies’ and use the space to initiate discussion on topical issues---both those emerging from the articles in the issue and outside.
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When we take the ‘routine’ headache pill or a prescription medicine, little do we realise that there is a complex web of processes related to pharmaceutical production, distribution and marketing; diagnostic and therapeutic procedures and standards; global trends; as well as policy formulation, implementation and oversight related to government departments as diverse as health, chemicals, industry, labour, law, finance and others, that influence our decisions. It is well known that for the ‘patient’ the consumption of a medicine, unless it is a result of self medication, is not a matter of ‘choice’, but is determined both by the science of ‘medicine’ and by ‘market forces’ that define the relationship between the doctor and the medical representative (MR).

The series of papers in this issue demonstrate the relationship among pharma industry, physicians and public policy is not only complex, but often irrational, unethical, and ‘unscientific’. In times when accountability and transparency are becoming increasingly common ideas, it is important to unravel these relationships and introduce these complexities in scientific and public discourse. This is important because the Indian drug companies are often seen as the ‘David’ of the global pharmaceutical industry, ‘saviours’ for millions who can now access affordable anti-retrovirals, and leading the
economic charge from an industrial ‘underdog’ country in the era of globalised trade. At the same time the cost of healthcare, mostly that of medicines, continues to be a leading cause of impoverishment and indebtedness in the South Asian region.

Although the Indian market is growing fast, it currently accounts for no more than 2 per cent of world pharmaceutical sales by value (somewhat more by volume), with an estimated market of US$10.4 billion in 2007 at consumer prices, or around US$9 per capita. The Nepali market is far smaller, with one estimate placing its pharmaceuticals value at around NRs 6 billion (about US$85 million, or about US$3 per capita). India is attracting increasing attention from multinational drug companies as a market for their products, although the vast majority of pharmaceuticals available in India are already off patent and generics are likely to dominate the market for the foreseeable future [Piribo 2007].

Yet despite its size and sophistication, all South Asia’s drugs distribution systems can be described as ‘unregulated’. They meet the following criteria:

From a more technical perspective, an unregulated market for drugs can be considered to exist where: (a) Unlicensed individuals and/or entities trade in drugs that they are not authorized or entitled to deal with or in contravention of the applicable laws, regulations and norms; or (b) Licensed individuals and/or entities trade in drugs that they are not authorized or entitled to deal with or in contravention of the applicable laws, regulations and norms [International Narcotics Control Board 2007: 1-2].

One purpose of this collection, then, is to showcase recent research that tries to go behind some of these general descriptions, and to look at the implications for public health. We hope in this way to contribute to improving the available descriptions of how drugs are produced, distributed, marketed and consumed in South Asia. This collection of papers has been the result of the research and dissemination process associated with a collaborative research project ‘Tracing Pharmaceuticals in South Asia’, that was conducted across India and Nepal. The research focused on tracing three drugs - oxytocin, rifampicin and fluoxetine from production to prescription. These drugs belong to three different therapeutic domains – maternal health, tuberculosis and mental health -- and their usage regimens are vastly different. Their relevance in public health policy too is different. This variety has allowed the research team to uncover the complex web of production, distribution, regulation from different perspectives. Additional papers were invited from colleagues working on similar issues. In this Introduction we set out some of the context for these discussions, and provide an overview of each of the contributions.

**Pharmaceuticals Distribution Patterns**

We first describe the formal structure and processes involved in drug distribution in India, some of the problems with over-neat descriptions, and some of the challenges that these problems pose for the legal and regulatory framework relating to drug distribution.
We begin by setting out the broad-brush picture of the different agents in the system and the different procurement pathways. We then deal in more detail with the processes and significance of what seems to be emerging from our work so far. Certain themes remain under-specified in this collection, for example the implications of widespread parallel systems of distribution related to the so-called indigenous systems of medicine (also known as AYUSH, from Ayurvedic, Unani, Siddha and Homoeopathy).

In the simple models popular with industry analysts (see Diagram 1), the Indian drug distribution system has a small number of layers (four or five): the pharmaceutical manufacturers; clearing (or carrying) and forwarding agents (CFAs)/depots/super stockists; stockists; wholesalers; and retailers. The simple models also define only a small number of routes through which drugs flow. A similar picture (minus the CFAs) is sometimes presented in discussions of the situation in Nepal.

However, on closer analysis, this neat picture begins to break down. To begin with, the numbers within each of these categories turn out to be highly unreliable. Here we focus on India. At the top of the diagram – the number of production companies – estimates vary. An estimate of over 20,000 – though widely quoted – has been challenged: perhaps no more than 5,000 are active producers. There seem to be no viable estimates of the numbers of CFAs or super-stockists – and numbers seem likely to change quite quickly, since the roles reflect tax and licensing conditions rather than real economic need. Both Iyer (2000) and Ernst & Young (2006) estimate the number of stockists in India at 60,000. This seems to be a figure supplied by the All-India Organisation of Chemists and Druggists (AIOCD).

The number of small-scale suppliers, who often act as prescribers as well as retailers is subject to some considerable margins of error: the Ernst & Young report indicates that there are about 500,000 retailers or pharmacies in 2005, Ernst & Young 2005] whereas Iyer mentioned more than 550,000 retailers by 2000 [Iyer 2000] and Francis (2006) estimated 600,000 by 2006. Once again, these figures seem to be the same as the claimed membership of the AIOCD, and since it is not clear whether all retail outlets selling pharmaceuticals are in fact members, these figures should be used with care. Industry sources claim that retailers account for about 70-80 per cent of the pharmaceuticals sales in the country, with the remainder being sold directly through hospital pharmacies [Jayakumar 2007]. In rural and small-town India (probably accounting for 25-35 per cent of the market) 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 require patients to buy the drugs on the premises, whether they are in- or out-patients. Finally, the number of people who fill roles as prescribers – who earn at least a living through this means – are well in excess...
of the official figures of AIOCD

Diagram 2 is an attempt to move towards a more useful representation of the drug distribution system than is provided by Diagram 1. One example of additional complexity is the distinction we have made between large and small-scale producers. While the border between them may be uncertain, it is clear that the extremes operate in very different ways. The large companies should again be distinguished according to whether they produce the active pharmaceutical ingredients (API) or are merely in the business of formulations. A further distinction is to show that the CFA is to some extent part of the production company, even though if they represent more than one company that depiction is somewhat misleading. Large companies distribute their products through either company depots or CFAs, whereas the smaller companies use super-stockists.
But the boundary between the two kinds of companies is not clear-cut: small companies also often act as additional producers for the large companies. Small companies often formulate drugs and package them with the name of the large company, on what is called a ‘loan licence’: a license to manufacture a product in the factory premises owned by another party [Gross and Patel, 2002]. Alternatively, they may produce on contracts that grant the originator company more control over quality and output issues. But in both cases drugs are then sold in exactly the same way as the versions that have been produced in factories owned by the large producer. The use of loan-licensing or sub-contracting may be to avoid excise duty or sales tax, or to take advantage of the small-scale producer’s ability to pay lower wages, and smaller social welfare payments and other perquisites. The practice of loan-licensing also provides one of the channels by which ‘counterfeit’ medicines reach the market. In such cases, the small company produces more than the quantity contracted for, and then sells the remainder. In this case the term ‘counterfeit’ refers to the lack of approval from the company whose name

Diagram 2: Showing more complex relationships
appears on the package: the drug quality may or may not be acceptable, because the purpose here is to avoid the drugs appearing in the books of the wholesalers or retailers for taxation purposes.

Individuals also cross the boundaries between some of these categories, making them more fluid and permeable than they appear in this diagram. One example is the distinction between retailer/pharmacist and practitioner: it is common in much of the north Indian countryside (and also in smaller towns) for patients to approach a pharmacist and receive a diagnosis and prescription (often including powerful prescription drugs) without the intervention of any other kind of practitioner. Similarly, in most small towns and villages, the practitioner himself (and occasionally herself) also prescribes and dispenses the medicines they prescribe: indeed, there is rarely a consultation fee, but the practitioner makes his/her income from dispensing prescriptions. Finally, the ethnographic material suggests that it is also necessary to deconstruct the idea that drugs, once having reached a patient, are then consumed by that person. Rather, we have also to understand the life of drugs after this point, in which the portion unconsumed may be passed on, sold or traded with other patients; and prescriptions may have a life of their own, generating further drug purchases either for the original patient or for someone else entirely.

In this Issue
The papers in this issue develop different issues through more detailed consideration of their causes and consequences. Thus in second paper, Roger Jeffery and Santhosh M.R. discuss the range of regulatory issues considered by the major commissions charged with reforming the pharmaceuticals regulatory system in India since 1995, and show how detached they are from the everyday contexts of drug production and distribution that we have laid out above.

Patricia Jeffery, Gitanjali Priti Bhatia and Sakshi Khurana show in detail how the international guidelines for the use of oxytocin are systematically ignored by most prescribers of the drug – and how little urban policy-makers are aware of this. Oxytocin is an essential drug in emergency obstetric care, and essential obstetric care a matter of highest policy priority considering that the MDG 5 related to maternal mortality is one on which there has been the least progress, and one which is least likely to be met.

Ian Harper compares and contrasts the treatment regimens for the TB control programmes in India and Nepal (and the way rifampicin is used differently in the two countries). Each regimen has its supporters and critics: but one of the conclusions of this paper is the extent to which – once again – the control programme staff have little understanding or interest in how the programme is perceived in the outside world, and how those perceptions shape the ways in which public sector and private sector interact to produce actual patterns of use.
Mental health has emerged as an important public health issue over the last decade and there are serious concerns about the availability of treatment for conditions like depression. Stefan Ecks and Soumita Basu explore the use of the anti-depressant fluoxetine, in and around Kolkata, India, and discover interesting patterns of distribution and use which is almost entirely outside the knowledge or oversight of psychiatrists or others with psychiatric training. These findings have implications for WHO strategies for closing the Mental Health Treatment Gap.

Moving away from drugs to vaccines, Madhavi Yennapu explores the relationship between public and private sector in the context of vaccine production and its implications for the universal immunisation programmes in India. The paper explores the shortage of vaccines which are part of the Universal Immunisation Programme and the easy availability of new vaccines to understand the relationship between industry, physicians and policy making.

Amitava Guha describes key features of the promotion of medicines in India, focusing on the tactics used to confuse, or corrupt practitioners if medical representatives are unable to convince them of the value of their particular brand of medicine. While efforts to regulate such promotion have been missing in India, there have been some examples from the US which shows that such regulation is possible and can be made to work.

Finally, Suchitra Ramkumar looks at the dynamics of drug promotion in Chennai India. Her paper, based on a survey of doctors, medical representatives, laboratories and explores how far are prescribers aware of the pressures from producers and retailers.

Read together these papers offer an interesting perspective to observe and describe the interactions between patient, prescriber and the pharma industry. These observations also indicate the rules of engagement between the different parties. These rules or standards, by accepted norms of governance, should be determined by public interests, scientific validity, technical efficacy, economic efficiency and principles of equity. The papers indicate that such expectations are not being met both at the level of the interaction between individual elements of the web as well as overall. This consensus of conclusions has great implications for the rational practice of medicine and the overall health and well being of poor people.

Notes:
1. This paper emerged from the collaborative research project Tracing Pharmaceuticals in South Asia (2006-2009) that was jointly funded by the Economic and Social Research Council and the Department for International Development (RES-167-25-0110). The project team comprised: Soumita Basu, Gitanjali Priti Bhatia, Samita Bhattacharai, Petra Brhlikova, Erin Court, Abhijit Das, Stefan Ecks, Ian Harper, Patricia Jeffery, Roger Jeffery, Rachel Manners, Allyson Pollock, Santhosh M.R., Nabin Rawal, Liz Richardson, and Madhusudhan Subedi. Martin Chautari (Kathmandu) and the Centre for Health and Social Justice (New Delhi) provided resources drawn upon in writing this paper. Neither ESRC nor DFID is responsible for views advanced here.
Pratap Banu Mehta, social scientist, argued recently that governance reform is not so much about “implementing designs created by committees of technocrats. Rather, the first order of business is to restore credibility to the state itself” [Mehta, 2009]. But, in the sphere of pharmaceuticals, this task is not straightforward. Even in (or perhaps, especially in) developed industrial countries “the pharmaceutical industry influences the perspective of the regulatory agency-so it comes to adopt their interests over and above those of patients”, i.e. that “the agency could be said to be captured”. Regulatory capture matters because “the risk-benefit assessment of drugs has a high degree of technical uncertainty, which is inherent in toxicology, clinical trials, and epidemiology” and it therefore matters whether regulators “give the manufacturer the benefit of scientific doubt about safety and efficacy of their product” [Abraham, 2002: 1498]. Abraham
concludes that, in the case of the European and north American drug regulatory systems, there is insufficient public accountability (inadequate rights of access to regulatory information), a lack of independent tests and technical expertise, insufficiently clear and independent funding (some regulatory agencies are funded at least in part by user fees), and poor control over potential conflicts of interest for regulators.

But the debates that Abraham summarises are concerned largely with only one part of the field of pharmaceuticals regulation – relating to the approval of new drugs, and monitoring their effects. If one takes a ‘product-life’ approach to pharmaceuticals regulation, however, one needs to look at what happens to such approved drugs once they are formulated, distributed, marketed, prescribed and consumed. In Europe and north America, there tends to be an assumption – which may or may not be justified – that issues of prescriber and retailer regulation, ethical marketing and so on have been largely resolved. On the other hand, there is considerable concern about issues such as post-approval tracking and pharmacovigilance, to pick up adverse drug reactions (ADRs). But in the Indian system, these contextual issues have not been resolved; and ADRs are unlikely to be discovered nor acted upon. In India, and elsewhere, there are serious doubts over whether regulatory bodies are able to build public health concerns – especially those that affect the poor – into their deliberations.

In this paper we address these issues by using our research on ‘Tracing Pharmaceuticals in South Asia’ to consider issues of regulation and how far this constrains inappropriate use at all stages, from the sourcing of raw materials (bulk drugs) to the final consumption of the product. We consider the recent history of attempts to reform the Indian regulatory system, and suggest that they illuminate two key features of the situation. The first is that in contemporary India, issues of pharmaceutical regulation are rarely discussed in a ‘cradle-to-grave’ approach. The regulation of some parts of the process attracts far more attention than others, and the links between these parts are poorly co-ordinated. The second is that regulation takes place with two significant disconnects. The first is between the assumptions underpinning regulatory measures on the one hand and the everyday conditions of drug production, distribution and consumption on the other; and second, that the local regulation of production, distribution and consumption is inadequate to deal with the global context within which these processes take place.

II

Regulation of Pharmaceuticals in Contemporary India

Pharmaceuticals regulation in India – with apparently strong regulations but weak implementation – is not a unique situation [Myrdal, 1968]. 1 Chibber has argued that state intervention in India was not per se a mistake, rather its state-led development problems must be put down to the poor quality of that intervention [Chibber, 2003]. In the rest of
this paper we assess how this situation has arisen with respect to pharmaceuticals and of attempts by the Government of India to prevent or ameliorate the inadequacies of its regulation in the country. In what follows, the term ‘pharmaceuticals’ regulation’ means the regulation of any aspect of the production, distribution, prescription or consumption of a pharmaceutical product or the raw materials that are used in its production.

Our research confirms the large gap between the regulations that exist on paper and the everyday practice of pharmaceutical use. At the level of the final consumer, there is considerable self-prescription of drugs: with or without a written prescription, ill people or their representatives can purchase virtually any medicines they can afford, without necessarily taking the advice of any kind of practitioner [Das and Das, 2007]. This is so despite classifications of medicines into categories that require the prescription of a qualified medical practitioner before they can be sold. Further, individuals can make a living through prescribing and selling medicines, despite regulations that restrict these activities to the holders of specified qualifications (medical degrees or pharmacy training): a situation of jugār medicine: medicine that is ‘make-do-and-mend.’ Even though the ideal and symbolic appeal of ‘real medicine (provided by government and nongovernment health institutions) remains strong, much everyday provision comes from “practitioners who are neither “quacks” nor legitimate doctors but who invent roles for themselves as medical authorities” [Pinto, 2004: 377].

Similar issues can be seen in terms of the licences needed to stock and distribute medicines, or to manufacture them. Although an Indian version of current WHO-Good Manufacturing Practice has been incorporated into the Drugs and Cosmetics Act (DCA) through the amendment of Schedule M, there is considerable doubt whether the rules are applied coherently or universally throughout the industry. Medicines cannot (in general) be introduced into the Indian market without approval by the Drugs Controller General of India (DGCI) whereas State Licensing Authorities (SLAs) issue manufacturing licences: but there inefficiencies and varying standards allow producers to get their new combinations of medicines approved for sale by the less strict SLAs (for a discussion of these relationships, see http://www.assocham.org/events/recent/event_278/_dr._surinder_singh.pdf). And, as we shall discuss later, the processes of removing dangerous or inefficacious medicines is very hard to implement. Few formal regulations affect marketing practices: although some of the producers’ associations have promulgated their own guidelines [see, e.g., OPPI, 2007] there is little evidence that such guidelines are followed, nor what action has been taken to discipline any infringements.

In independent India, pharmaceuticals regulation was divided between the Ministry of Chemicals and Fertilisers, now through a separate Department of Pharmaceuticals (for matters related to production quality and pricing) and the Ministry of Health (registration
of pharmacists entitled to stock and sell medicines and of practitioners entitled to prescribe them or to inject them). One mechanism to overcome these divisions has been through pharmaceuticals policies, for example the Drug Policies of 1978, 1986, 2002 and 2006. These have been contentious, however. The 2002 Policy was challenged in the Karnataka High Court through public interest litigation that claimed that, if implemented as framed, the new policy would ‘bring the control of prices entirely at the whims and fancies of manufacturers’ and would defeat ‘the very purpose of equitable distribution and availability of essential drugs at a fair price’ [The Hindu Business Line, 2002]. The Karnataka court ruled in their favour, but was over-ruled in the Supreme Court. Nonetheless essential and life saving drugs were ruled to remain under price control [Department of Chemicals and Petrochemicals, 2005: 2].

The global context affects pharmaceuticals regulation in contemporary India not just through the activities of WHO and other UN bodies, but also through the effects of policies adopted by globalised procurement agencies (such as The Global Fund to Fight AIDS, Tuberculosis and Malaria) and foreign regulators (see Diagram). The US Food and Drug Administration [FDA], for example, now investigates whether producers who wish to export either bulk drugs or formulations to the USA follow current Good Manufacturing Practice (cGMP) guidelines (US Food and Drug Administration,

Diagram: OOganisations in Pharmaceutical Regulation in Context (following Matsebula, Goudge and Gilson,2005)
It now plays crucial and detailed roles in setting production and record-keeping standards at Indian factories – roles that are likely to become more common since it established a New Delhi office (in January 2009) and will use it to monitor about 100 production plants in India (Shankar, 2009). Site visits of the scale and intensity mounted by the FDA probably far exceed those of the Government of India’s own regulators who are supposed to carry out the same tasks and to protect Indian consumers. In other words, perhaps without the general public being fully aware of what is going on, India is *de facto* accepting the idea that developing countries should not duplicate approval processes within country but should instead rely on the expertise of stringent foreign or global regulatory authorities.

**Commissions as a Means of Reform**

One means of integrating cross-ministry and inter-state concerns is through ad hoc commissions, committees and task forces. Here we describe only those established since 1995, when the Government of India began to grapple with the new form of globalisation ushered in by the Doha round of international trade negotiations and the creation of the World Trade Organisation, TRIPS and the extension of patent protection to pharmaceutical products in India. The issues considered by several of these reports go to the heart of the regulation problems and their characteristics shed light on the problems of moving towards a more effective regulatory regime.

In many of these committees, Dr R A Mashelkar played a central role. Those most relevant to pharmaceuticals are the Committee on Research and Development in Drugs and Pharmaceuticals (1999); the Expert Committee on a Comprehensive Examination of Drug Regulatory Issues, including the Problem of Spurious Drugs (2003); the Task Force on Recombinant Pharma (2005); and the Technical Expert Group on Patent Law Issues (2006).

Mashelkar had a distinguished career as a polymer scientist and manager of science. He was the Director General of Council of Scientific and Industrial Research (CSIR) from 1995-2006, a member of the Scientific Advisory Council to the Prime Minister and also of the Scientific Advisory Committee to the Cabinet. He came to public notice for his vigorous attack on American firms attempting to patent turmeric and basmati rice. He has a wide view of the role of science in Indian society, for example, seeing the need for child-centred education, woman-centred families, human-centred development, a knowledge-centred society and innovation-centred India [Mashelkar, 2000]. In the commissions he has chaired the interests that are always represented are civil servants from some (but not always all) of the Ministries of the Government of India that have an interest in the field: Health, Chemicals and Pharmaceuticals,
Home Affairs, Finance and Planning, for example (see Table). State governments – responsible for people such as drugs inspectors, or District Health Officers tasked with implementing regulations – are usually conspicuous by their absence, as are representatives of rural medical practitioners, pharmacists and drug wholesalers and consumers. Some committees, such as the Commission on Macroeconomics and Health, do draw on a wider set of constituencies, including (for example) the Voluntary Health Association of India, the Society for Education, Action and Research in Community Health, a journalist, economists and doctors from the private sector, as well as various Ministers and ex-Ministers. The 1999 Mashelkar Committee, however, leant heavily on industry representatives, especially large Indian multinationals, such as Ranbaxy’s and Dr Reddy’s. When new policy proposals are under consideration, the opinions of representatives of producer interests can be canvassed in other ways as well. Ram Vilas Paswan, as Minister for Chemicals and Fertilisers, called in 50 top executives from large Indian companies for consultation on his proposals for a new regulatory framework for clinical trials and the encouragement of innovation in research and development [Anon., 2009b].

The voices of others could also be provided by those invited to give evidence to the committees, or who came uninvited. For example, the deliberations of the 2003 Mashelkar Report had presentations by scientists, the Indian Medical Association (IMA), the Delhi Pharmaceutical Trust, Ahmedabad-based Consumer Education and Research Centre (CERC) as well as the Confederation of Indian Industry (CII). Four main topics have dominated the committees that have reported since 1995:
1. Drug price controls
2. Controlling spurious or counterfeit medicines
3. Improving the chances of inventing and patenting new chemical entities
4. Establishing a centralised National Drug Authority

Four other concerns have been noticeable by the lack of attention they have attracted [All-India Drugs Action Network, 2006: 1]:
5. Ethical promotion
6. Labelling and consumer information
7. Elimination of irrational drugs and combinations
8. Pharmacovigilance

We discuss these in turn, before considering the wider implications of these patterns for the quality of pharmaceuticals regulation in India.

**Drug Price Control**
A major concern of regulation has been of prices, and (not surprisingly), the main tussles have been between industry representatives (wanting to limit or remove price controls)
### Membership of Key Government Committees Reporting on Aspects of Pharmaceuticals Regulation in India, 1995-2006

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**Sources for Table:**

In 1970, almost all bulk drugs and their formulations were under price control, but the number was reduced to 347 bulk drugs in 1979, 142 in 1987 and then to 74 in 1995. A Drugs Price Control Review Committee (DPCRC) was set up in 1999: its recommendations led to the 2002 Pharmaceutical Policy, which proposed that, in order to reorient the domestic drugs and pharmaceuticals industry in the face of the challenges and opportunities from the liberalised economy, India’s accession to TRIPS and the impending advent of the product patent regime, the span of price control over drugs and pharmaceuticals should be reduced substantially [Department of Chemicals and Petrochemicals, 2002: section 11]. But in responding to the Supreme Court’s demands (see above) the Department of Chemicals had to ‘consider and formulate appropriate criteria for ensuring essential and life saving drugs not to fall out of price control and to review the drugs which are essential and life saving in nature’ [Department of Chemicals and Petrochemicals, 2005: 2]. In July, 2003, therefore, the Government prepared a ‘National List of Essential Medicines’ (NLEM) consisting of 354 drugs, of which only 50 were then under price control [Department of Chemicals and Petrochemicals, 2005: 3]. The relevant Lok Sabha Standing Committee in 2005 also strongly recommended bringing more NLEM Drugs under price control (citing the examples of Canada, Japan, and the UK) (Standing Committee on Chemicals & Fertilizers (2005-06), 2005: 49-50).

There are, thus, on-going pressures from civil society and political representatives to maintain or even strengthen price controls: and considerable dispute about whether the existing controls are successful. As elsewhere, of course, brand leaders are able to reduce price competition by enhancing the ‘reputation’ of their branded goods,
and by offering inducements to prescribers to use their products even though they are pharmacologically indistinct from those of their cheaper competitors. In some (but not all) market segments, the brand leaders show both the highest prices and the largest sales, suggesting that these strategies are successful. Such companies usually avoid the drugs that are under price control. The prices of most drugs in India are below international comparator prices [see, for example, Keayla, 1996; Lanjouw, 1997]. But some critics (including the Federation of Medical Representative Associations of India (FMRAI) point to the myriad ways in which the drug price control orders can be evaded [All-India Drugs Action Network, 2006; L. Taylor, 2007]. Certainly, the division of responsibilities between the body responsible for approving drugs for marketing (the Drug Controller General of India, attached to the health ministry) and that responsible for price regulation (National Pharmaceutical Pricing Authority, or NPPA, under the ministry of chemicals and fertilisers) does not help.

Around the time in 1995 when India signed up to TRIPS, many commentators predicted that this would lead to massive price increases in India [see Lanjouw, 1997 for a critical response]. Since then, commentators have been more cautious [see, for example, Grace, 2004]. The Ministry of Chemicals and Petrochemicals believes there are no upward price pressures in the pharmaceuticals market [Department of Chemicals and Petrochemicals, 2008: 17]. Nonetheless, the Ministry started a scheme in 2008 to provide all 350 essential drugs through Jan Aushadhi stores at a claimed level of around 75 per cent of the price of branded medicines available in the market: it is as yet too soon to see the impact of this scheme. Apart from this, following the recommendation of Pronab Sen Committee, the Government of India also constituted a ‘Committee on Price Negotiations for Patented Drugs and Medical Devices’ to explore the possibilities of introducing price negotiations before the grant of marketing approval of patented drugs.

The prices situation can be read in several different ways. On the one hand, price controls may have been successful; alternatively, the prices of drugs (and their availability for the poor) are set by a highly competitive market, and the drug price control orders play very little part in keeping prices low. In 2006, NIPER conducted a study on the Impact of TRIPS on pharmaceutical prices, with specific focus on generics in India which concluded that “fears pertaining to TRIPS related increase in drug prices in India are unfounded. Analysis of data on prices of selected drugs, following the TRIPS agreement shows that prices of drugs in India have been by and large stable ... No sudden changes in prices have occurred even after implementation of TRIPS (Post 1995) and are unlikely to occur even after introduction of the product patents” [NIPER, 2006].

Recently, NPPA has launched a grievance redressal cell (Complaint Submission and Redressal System, or CSRS) with a senior officer to hear grievances from the general
public on the issues of overcharging, shortages and sale of scheduled formulations without prior price approval of NPPA (http://nppaindia.nic.in/redressal.htm). However, as in the case of many other grievance-redressal mechanisms, the CSRS remains unknown to the general public.

**Controlling Spurious and Counterfeit Medicines**

The picture presented by mass media is one in which India is a major source of spurious and counterfeited medicines, both globally and within India itself. A BBC programme is often cited, as is an article in *The Lancet* [Chatterjee, 2001]. India is also listed by the Pharmaceuticals Security Institute [PSI] as one of the top five sources of counterfeit drugs [Taylor N., 2008b]. Accusations that the extent of counterfeiting in India is substantial, dangerous to the public and leading to large losses for legitimate producers are regularly put forward by representatives of multinational and large Indian companies. In 2002, a submission from the Confederation of Indian Industry (CII) to the 2003 Mashelkar Committee claimed that the WHO had estimated that 35% of fake drugs produced in the world come from India, which has a Rs. 4,000 Crore spurious drug market. About 20% of medicines in the country are fake or sub-standard. Of these, 60% do not contain any active ingredient, 19% contain wrong ingredients and 16% have harmful and inappropriate ingredients [Mashelkar, 2003: 76].

But the CII failed to provide the Mashelkar Committee with evidence to support its claims, and the WHO denied ever having produced a study with the results attributed to it [Mashelkar, 2003: 76-7]. In fact, Indian pharmaceutical companies’ unsubstantiated claims seem to be the sole source cited by the WHO [World Health Organisation, 2006]. In 2007, the OECD cited the 2005 European Commission data that 75 per cent of the cases of counterfeit medicines seized on the EU borders originated from India [Barnes, 2007]. By 2007, however, only 35 per cent of medicines seized by the EU and treated as counterfeit came from India, while medicines originating in Switzerland comprised 39 per cent of the total – but this statistic has not been widely cited [European Commission, 2008].

If we accept the existing data, according to the PSI the extent of counterfeiting varies dramatically by drug: ‘Over 60 per cent of drugs seized were for treatment of erectile dysfunction and … it seems likely Viagra (sildenafil citrate) accounts for a sizeable chunk of this’ [Taylor N., 2008b]. But there is no evidence for how far this applies in India. A former Drugs Controller General of India estimated that: “At present, about 5 per cent of the drugs available in India are counterfeit while 0.3 per cent are spurious” [Taylor N., 2008a]. His figures seem to derive from a report for WHO published in 2007 and based on an attempted random collection of 10,743 samples, of which 23 per cent were deemed *prima facie* suspect, but only 8 of these samples (0.3 per cent of the
original drugs collected) failed an assay test [Sheth et al, 2007].

Given the lack of reliable evidence in this area, unsubstantiated claims and rumour drive out harder sources of information. The CII agenda seems to be to separate the respectable, safe, large producers from the myriad of small and medium enterprises, and thus to establish trust in the big Indian companies and enhance their export potential. But perhaps, as Delhi’s then Deputy Drug Controller said in 2001, “Fake drugs are not Delhi’s problem” and “a lot of the times it is just old brand rivalry. The big fish cannot bear to find smaller chaps coming out with similar medicines so they say ‘spurious, duplicate, etc.” [Chatterjee, 2001].

**Improving Environment for Inventing and Patenting New Chemical Entities**

With the transformation of the international trade regimes, the Government of India is increasingly active in assisting Indian companies with export, new drug discovery and clinical research [Department of Chemicals and Petrochemicals, 2008: 16-7]. Figures showing the low level of R&D expenditure in the Indian industry, compared to its overall size, are quoted to show that such measures are necessary. The Government has introduced tax relief on research and development expenditures, loans on easy terms for drug discovery, and schemes to encourage collaborations between companies and public sector institutions.

In the run-up to the 2009 national elections, the Department of Chemicals and Petrochemicals announced eye-catching proposals to raise up to $2 billion annually through tax-free bonds to promote drug discovery and innovation-based pharmaceuticals industry in the country, in order to gain up to 20 percent of the world’s R&D business [Anon., 2009c]. Critics of these plans suggest that inadequate attention has been paid to the conditions in which drug discovery and testing is currently regulated. Specialists in medical ethics have accused some drug companies carrying out clinical trials in India of ‘compromising science and ethics in the pursuit of profit’ and that inadequacies in the oversight mechanisms allow clinical trials to recruit the ‘desperate’ and ‘most vulnerable’ members of Indian society [Taylor N., 2009].

Ensuring that these latter concerns are addressed is a task well beyond the competence of the regulatory agencies at present. Although they have been given some training by US and EU staff, the numbers of inspectors available to monitor even the 200 or so trials registered with the Clinical Trials Registry - India (CTRI) by March 2009, let alone the 850 or so registered with the US FDA as taking place in India, seems totally inadequate. The interests of the ‘industry’ and the lure of growth, foreign exchange earnings and increased employment seem to run well ahead of the ability to ensure that public health is not compromised.

**Establishing a Centralised National Drug Authority**

Under the Constitution of India, the regulation of ‘Drugs’ is a concurrent subject,
so the responsibility is divided between the Central Government and the State and Union Territories Governments. Unlike the movements to decentralise aspects of governance in India, since at least the 1970s the central Governments has tried to reduce states’ autonomy and centralise control in this field. The Hathi Committee of 1975 first proposed a national pharmaceuticals agency, to provide uniform standards and a single authority to register drugs, to ensure uniform standards across the country [Hathi, 1975: para. 33].

Although the 1978 National Drug Policy made no mention of this, the 1986 and 1994 Drug Policies proposed National Drug Authorities to monitor drug quality according to standard procedures. The 1999 Mashelkar Committee proposed establishing a Monitoring Authority to oversee Good Manufacturing, Good Laboratory and Good Clinical Practice – but this, too, was not implemented. The 2003 Mashelkar Committee proposed to strengthen the existing Central Drugs Standard Control Organisation (CDSCO) and the State Drug Controllers and create a Central Drug Authority (CDA) – a line also followed in the 2002 Drug Policy. Apparently, 15 state governments supported this idea [Ramachandran, 2003]. Nonetheless, in 2005 the Pronab Sen Committee returned to a centralising proposal, to ‘integrate the offices of the Drugs Controller General of India, the Central Drugs Standard Control Organisation (CDSCO) and the National Pharmaceutical Pricing Authority (NPPA), along with all the powers and functions of these bodies’ [Sen, 2005: 55-56]. A Bill was introduced in Parliament to establish a CDA, and Mashelkar’s views on this were regarded as so significant by the Parliamentary panel charged with investigating the Bill that it delayed its report until he had been consulted [Shankar, 2008]. The draft Bill was heavily criticised by the committee [Alexander, 2008b] and the need for redrafting led to its being abandoned before the Lok Sabha elections of 2009 [Alexander, 2008a].

Despite these repeated proposals, by 2009 the Government of India had made little progress towards creating a National Drug Authority, perhaps partly because, health being constitutionally on the concurrent list, centralisation of drug control may pose additional legal hurdles. Opposition was strongest in Maharashtra, where the state Drug Controllers’ Association opposed any dilution of the rights of state Drug Controllers. A test case for centralised versus local autonomy has been the struggle to ban 294 fixed dose combination drugs declared irrational by the then-DCG(I) Venkateshwarlu’s directive of October, 2007. Drug companies whose licences are still valid can continue to manufacture these fixed dose combinations, whereas the State Licensing Authorities (SLAs) were refusing, in early 2009, to renew the licenses that had expired [Anon., 2009a].

In general, however, it seems likely that the proposals for an NDA emerge from frustration at the inability to solve two problems. The first is varying procedures and
standards imposed by SLAs, a situation which has seen some producers apply for licenses from compliant SLAs if their own State is unwilling to grant a license quickly or on reasonable terms. Individual States have the right to refuse to licence production, but once a drug is approved in one State it can be sold throughout the country.

The second is the severe shortage of resources for testing drugs and licensing producers on the basis of the quality of facilities. Thus, despite repeated proposals from committees for the creation of new posts and investment in laboratory equipment, the current infrastructure is completely inadequate to cope with the numbers of drugs, producers, pharmacies and prescribers. According to Venkateshwarlu, DCG(I) (2006-08), “there is now a six to nine month backlog at each of the plants which results in less than 1 per cent of drugs being tested” [Taylor N., 2008a].

What is Left Out?
Among the issues that are not given the same degree of attention are the following.

**Ethical promotion and the restriction of incentives to prescribers and pharmacists**
Major issues arise with the possibility that drugs are prescribed or dispensed more for the financial interests of the prescribers and dispensers than the needs of the patient. One example is the substitution of drugs by the pharmacist: as Hazra, CDMU, told us in an interview “if you write the generic name the retailer interprets it like he has the license to give any medicines. So he gives that one that will fetch him the maximum commission” (December 29, 2006).

Evidence for the existence of undue pressures on prescribers in India is abundant. The Gujarat-based Torrent Pharmaceuticals openly announced in their website incentives for prescribing their medicines. The company then took hundreds of doctors on chartered flight to various tourist destinations such as Bali and Fuket. Though a formal complaint with evidences was made to IDMA on this, no punitive action has been taken so far [Nagarajan, 2008]. Medical representatives were willing to talk to us in some detail about the range of incentives they had available in return for substantial orders. They are under great pressure to extend the incentives given on the launch of a new drug, or to provide incentives to pharmacists if doctors are being given one. A medical representative described the process in small-town north India, “If I am promising a car to the doctor then the doctor has to commit to me. Then I will tell the doctor that … every month … suppose the cost of the car is Rs.2 lakh, then he has to give us the business of Rs. 50-60,000 or 70,000 per month in one or two years. He will have to write a lot of medicines. If the doctor is ready to commit then we don’t have any problem’ (Interview transcript, October, 27 2007, Bijnor)

Although there is a longstanding critique of these activities [Gulhati, 2004], then, there is little embarrassment amongst medical representatives in talking about them [see
also Roy et al, 2007]. Some doctors refuse to be seduced into prescribing on this basis, or check whether their patients have been given the drug they actually prescribed, rather than a substitute. It is hard to find any information about the effectiveness of the voluntary codes run by the larger pharmaceutical associations. In early 2009 Government officials hinted at the creation of legal restraints on unethical promotion, but this seems to have been pre-election posturing rather than a serious proposal [Alexander, 2009].

**Local-language labelling and information sheets**

We know that many prescribers and most patients in India are not literate in the English that is used in drug information packs. Add to this that – as in many other countries – drug information varies from brand to brand, leading to the possibility of misleading patients and prescribers about appropriate use, co-occurring effects and drug interactions. A WHO study called for “further training and continued education aimed at drug regulatory officials” to “provide the necessary knowledge and enable national authorities to meet the need for drug information that is independent of commercial interests” [Reggi et al., 2003] but no substantive moves have been made in this direction in India.

A particular issue in India is the labelling of Ayurvedic medicines: after complaints that some ingredients turn out to be heavy metals or even steroids, Ayurvedic medicines for export now need to be labelled with their ingredients; no equivalent regulations apply for drugs sold within India [Chandy and Mathew, 2006: 59]. Many pills are sold in small numbers, cut off from the full strip and without any information on co-occurring-effects or advice about co-consumption with other medicines. In the absence of effective information, the Indian Medical Association’s call to be allowed rights to prescribe “off-label”, activists noted “the western example of off-label use being cited by the IMA cannot be applied to India because Indian patients often have poor levels of literacy and education” [Sharma, 2004: 1372]. Obtaining informed consent is so hard, some argue, that off-label uses would be equivalent to treating patients like guinea-pigs. Despite these concerns, few efforts have been made to change the situation.

**Eliminating harmful, ineffective and irrational combinations of drugs**

Activists have been involved in trying to reduce the number of drugs for sale in the Indian market, and particularly combinations of drugs, since the early 1980s. The Government of India introduced a ban, using the generic name of the drugs involved, but manufacturers have avoided the ban by saying that their drug name was not on the list. In pharmacology the number of drugs that should be used for therapeutic reasons is around 7000 but the Indian market contains almost 70,000 drugs, and 151 dubious combinations of drugs that are not approved in developed countries [MIMS, March 2009]. Although irrational combinations was an issue taken up with some zeal by Dr Venkateshwarlu, his successor has taken what some see as a ‘softer’ stand, for example allowing these dubious fixed dose combinations to stay on the market as long as they are
checked for harmful effects [Anon., 2008].

An additional issue in India is the possibility of registering a drug as Ayurvedic, and thereby avoiding both licensing and price controls. Most of the evidence about the significance of these processes, however, is little better than anecdotal. While Drug activist groups (such as AIDAN, the All-India Drugs Action Network, and the FMRAI, Federation of Medical Representative Associations of India) are actively engaged in campaigning against these practices, progress is very slow. The magnitude of the task is reflected in the fact that the single best-selling formulation in India – Corex, an expectorant, sold by Pfizer – is regarded by many as one of the key examples of ineffective combinations.

Pharmacovigilance
Pharmacovigilance, which includes post-marketing surveillance or Phase IV trials, involves issues of safety and ongoing technical support of a drug after it receives permission to be sold. Clinical trials rarely involve enough patients to be sure that less common side effects and Adverse Drug Reactions (ADRs) are picked up by the time a drug enters the market. In addition, in everyday use, a drug is used in combination with many others, and drug interactions may only be picked up some time after the drug has been introduced. Pharmacovigilance is gaining importance in developed countries and can lead to drugs being recalled. But record-keeping by Indian doctors is completely inadequate to contribute substantially to these processes [Anon., 2007]. With WHO support, a National Pharmacovigilance Programme was launched in India in 2005 [Patvardhan, 2005] but its effectiveness remains unknown. This might not be a problem, were the populations covered in developed countries similar (in body mass, for example), disease patterns alike, and the kinds of multi-drug prescribing akin to those in south Asia. None of these is likely to be true, however, there are unknown numbers of safety issues that are not being picked up.

Effective pharmacovigilance systems would take not only a greater investment in testing laboratories to eliminate the possibilities of spurious drugs being implicated in adverse reactions, but also some system of tracing patients and being able to record which drugs they had taken. Such a system might be possible within the urban middle class market (where body mass and disease patterns may not be very dissimilar from those of developed countries. But in urban slums and the rural areas, especially where the public health system has collapsed, the chances of any ADRs being picked up are slight. Furthermore, given the drug consumption patterns we have described for India, there can be no guarantee that drugs approved for limited populations (e.g. sub-sets of sufferers from a particular condition for whom possible risks are outweighed by benefits) will not be consumed by many others for whom
the balance of risks, costs and benefits are very different. Once again, no serious attention has been given to these issues within any of the documents we have been able to access.

Significantly, in our view, two things are missing from these Commissions. The first is a frank acknowledgement of how little effect the current regulations have: how far they are flouted in practice, however well they have been crafted. There seems to be a wilful blindness towards the everyday circumstances in which most drugs in India are produced, distributed and consumed – and the conditions within which substantial numbers of people get such limited access that these concerns seem illusory. The second, and linked to this, is the absence of a clear strategy to change that situation. The end state – a ‘modern’ society where rational considerations hold sway, preferably through the activities of small numbers of producers and marketing firms, with an honest and efficient, technically qualified regulatory agency to keep an eye on them – is imagined, with no defined steps that might lead to that situation, except for more laws or regulations added onto the existing ones. In other words, policy debate proceeds to ignore institutionalised corrupt practices and vested interests and relies on “a conceptualisation of policy that is technical and depoliticised” [Harriss-White, 1996: 85].

The image of society, industry and politics is dual: an existing modern sector that is assumed to be distinct from a non-modern one, and it is assumed that the modern sector will – within a finite period – swallow the non-modern sector up. The liberalisation of the Indian economy since 1991 might be thought to hasten such a process. But it is clear that deregulation of pharmaceuticals is not a defensible option in India, at least not in the ways that are being tried out in other industries. No alternative strategy has been set out. Furthermore, the modern sector is in fact interlinked with the non-modern one. Small-scale manufacturers, for example, make many of the drugs sold by the large companies under loan licences, and the expansion of sales outlets is heavily linked to the unlicensed practitioners and quasi-legal pharmacies, for example. In this sector of the economy, the mirage of ‘India Shining’ seems to have completely eclipsed that part of the ‘Republic of Hunger’ that, in part, makes the former possible.

III
Conclusion
The regulation of pharmaceuticals in India is a particular example of how the industry is modernising: the government rationalises, tries to apply scientific knowledge to controlling this area of social life, and in this way extends its reach, in order to reduce the risks to which its citizens are subject. In the specific field of pharmaceuticals, such interventions are justified both by the relative ignorance of patients about their medical needs and by the potential for unfree competition posed by very large companies in
oligopolistic markets. Not unreasonably, when India ‘models its pharmaceutical regulations’ it, draws on a range of international examples – including Canada, the UK, and the USA – because these countries face many similar challenges. But despite the rising strength of Indian manufacturing capacity, India’s system of pharmaceutical regulation remains partial and ineffective. One reason for this is that the expertise mobilised in attempts to reform the current system is curiously “detached from local contexts” [Jansen and Roquas, 2005: 142, 143]. The national commissions, committees, task forces and expert groups, whether set up by the Health Ministry, the Department of Chemicals and Pharmaceuticals, or the Planning Commission, focus on only a subset of the significant issues and rarely draw on knowledge of everyday practices of the distribution, prescribing and consumption of pharmaceuticals.

It could be argued that there is merely a problem of timing: that it is only a matter of time before the realities of a modernising India catch up with the framework of regulation that has been established. But this seems unlikely. Pinto, for example, suggests that jugār practitioners are ‘representatives of development, not aberrations from it’ (Pinto, 2004: 337). In many parts of rural India, and in some parts of urban India as well, the state has failed to provide adequate numbers of properly trained ‘legitimate’ health workers. As a result, ‘equality for all is precluded and what remains is equality for some’. Targeting the ‘inventive quasi-institutional practitioners’ misses the point: these people survive in the spaces left vacant by the state. Yet they are not outside local power relations, nor is their presence just a sign of the temporary, as-yet-inadequate spread of cosmopolitan medicine. Rather, their activities provide evidence of how development, as a global project of myth-making, gains its local character [Pinto, 2004: 355-56, 358].

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Notes:

1 More research is needed into which regulations are implemented, however.

2 In some cases, branded generic products are more expensive than those produced by innovator brands.

3 In India, a drug is defined as spurious “a. if it is manufactured under a name which belongs to another drug; or b. if it is an imitation of, or is a substitute for, another drug or resembles another drug in a manner likely to deceive, or bears upon it or upon its label or container the name of another drug, unless it is plainly and conspicuously marked so as to reveal its true character and its lack of identity with such other drug; or c. if the label or container bears the name of an individual or company purporting to be the manufacture of the drug, which individual or company is fictitious or does not exist; or d. if it has been substituted wholly or in part by another drug or substance; or e. if it purports to be the product of a manufacturer of whom it is not truly a product.” (Drugs and Cosmetics Act, Amendment Act of 1982. Section 17-B)

4 The Pharmaceuticals Security Institute [PSI] is closely linked to the International Federation of Pharmaceutical Manufacturers & Associations (IFPMA). The IFPMA Director-General serves as the PSI President.

5 This study used flawed methods of collecting samples, and therefore cannot be relied on, but the contrast with the industry estimates is too large to be ignored. A new study on similar lines was started in late 2008, involving the collection of 24,000 samples.

6 The Government is also addressing the complications generated by the rise of technologies such as biogenetics (See Anon., 2005 for discussion of the 2003 Mashelkar Task Force report).

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Two Day Seminar

“Socio-Economic and Educational Status of Muslims in Maharashtra”
on 21st & 22nd December, 2009, organised by Tata Institute of Social Sciences

The present seminar is being organised to discuss the ‘socio-economic and educational status of the Muslim community in Maharashtra’. The discussion will be organised around the following sub-themes:

- Economic Status, Employment, and Institutional Credit
- Educational and Health Status
- Demography, Urbanisation and Ghettoisation
- Access to Public Infrastructure, Housing, and Public Programmes
- Status of Muslim Women
- Identity Stereotyping and Politics of violence
- Crime and Punishment
- Political Participation and Representation
- The Muslim OBCs: The Status and Way Forward

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Intrapartum Oxytocin (Mis)use in South Asia

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Abstract: Oxytocin is a natural hormone with uterine stimulant properties that plays a prominent role in obstetric practice. Clinical guidelines for oxytocin use intrapartum emphasise that injudicious use has serious potential for adverse outcomes for mother and baby. Oxytocin is readily available in South Asia and widely used in ways that flout these guidelines. Yet recommendations for active management of third stage of labour (AMTSL) include the administration of oxytocin to prevent post-partum haemorrhage (PPH). Troublingly, these proposals seem to ignore oxytocin’s already extensive life independent of policy interventions. Taking oxytocin as an example, the paper argues that policy-makers urgently need to engage with the everyday realities of drug availability and use in South Asia.

I
Introduction

Oxytocin is a natural hormone with uterine stimulant properties that plays a prominent role in obstetric practice. It was first synthesised by Du Vigneaud in 1953 [Mousa and Alfirevic, 2007]. In the late 1960s O’Driscoll advocated oxytocin use intrapartum as a component of active management of labour (AML i.e. first and second stage of labour, before the baby is born), a package aimed at limiting the length of labour in nulliparous women [O’Driscoll and Meagher, 1980]. Later, oxytocin was found to be effective in preventing and controlling post-partum haemorrhage (PPH) in the third
stage of labour [Prendiville, Elbourne, and McDonald, 2000]. PPH is regarded as a key cause of maternal mortality throughout the Global South—estimates for India suggest that between 31 per cent and 38 per cent of maternal deaths are due to haemorrhage [Registrar-General India, 2006: 17,15]. Proposals for the active management of the third stage of labour (AMTSL) include administration by local-level government health workers, such as nurse-midwives, of either oxytocin (by intramuscular injection) or misoprostol (administered by pill).

Yet oxytocin is widely available and used in the formal health care system in South Asia, even in apparently remote rural areas. Moreover, the clinical guidelines for intrapartum oxytocin use are often flouted, whether in urban nursing homes and hospitals or in rural home births. Injudicious intrapartum use of oxytocin has serious potential for adverse outcomes, including uterine rupture and foetal asphyxia. This understanding motivated us to include oxytocin in the Tracing Pharmaceuticals project and our concerns have subsequently been enhanced by the proposals for AMTSL that would extend its availability even further.

II

Clinical Guidelines for the Use of Oxytocin

We begin by outlining the clinical evidence and guidelines related to oxytocin use to augment labour (in first and second stages) and to prevent and treat PPH in the third stage of labour. Oxytocin is also used to “abort the fetus in cases of incomplete abortion or miscarriage” [www.drugs.com accessed 25/09/07], but we shall not discuss this use here.

Oxytocin in the intrapartum period

Augmentation of labour increases the frequency, duration and strength of contractions. In the first stage, the intention is to cause the cervix to dilate and in the second stage, to cause the head to descend. The clinical guidelines formulated by O’Driscoll and Meagher for oxytocin use in AML were based on their 14 years of practice in the National Maternity Hospital in Dublin [O’Driscoll and Meagher, 1980]. Apart from oxytocin, the AML package includes a strict definition of labour, amniotomy and continuous support during labour in order to avoid the potential risks associated with oxytocin use. Table 1 summarises the conditions under which they and others recommend that oxytocin be used intrapartum.
Table 1: Intrapartum Oxytocin Use: Clinical Guidelines*

<table>
<thead>
<tr>
<th>Exclusion of at-risk women</th>
<th>Contra-indications include: hypertonic uterine contractions, foetal distress, any condition where spontaneous labour or vaginal delivery are inadvisable, prolonged administration in oxytocin-resistant uterine inertia, severe pre-eclamptic toxaemia, severe cardiovascular disease, impaired placental function which might lead to hypoxia.</th>
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<tr>
<td>Parity</td>
<td>Recommended only for nulliparous women. In multiparas, inefficient uterine action is rare and slow progress of labour is more likely to be associated with other causes (e.g. foetal malpresentation or malformation). Multiparas are prone to uterine rupture and oxytocin stimulation increases the risk of rupture, so oxytocin should be used in multiparas only in exceptional cases determined by the obstetrician.</td>
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<tr>
<td>Examination prior to oxytocin administration</td>
<td>A strict definition of labour to admit only women in labour. Oxytocin use is conditional on there being a single foetus in vertex presentation.</td>
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<td>Mode of administration</td>
<td>Artificial rupture of membranes is the first intervention offered in the case of slow progress of labour (less than 1cm dilatation per hour): this is often sufficient to augment labour. Moreover, oxytocin is often ineffective with intact membranes and can increase the risk of infusion of amniotic fluid into maternal circulation. Oxytocin may cause hyperstimulation of the uterine muscles and the effective dose varies across women. To ensure optimal contractions, oxytocin should be administered cautiously by intravenous infusion and stopped immediately if hyperstimulation or foetal distress occurs.</td>
</tr>
<tr>
<td>Monitoring the woman &amp; foetus during oxytocin administration</td>
<td>All labouring women should be assigned a personal nurse who is present from admission until the baby is born. After amniotomy, vaginal examinations should be performed hourly. To detect uterine hyperstimulation or foetal distress, the progress of labour and interventions should be detailed on a partograph, recording contractions, mother’s blood pressure &amp; foetal heart rate (the latter by direct auscultation for one minute every 15 minutes during the first stage and after each contraction during the second stage).</td>
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<tr>
<td>Setting/availability of emergency facilities:</td>
<td>AML recommended only for institutional deliveries in facilities with adequate equipment to deal with obstetric emergencies (e.g. Caesarean section or resuscitation of the infant).</td>
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Since AML was first proposed in the 1960s, the practice with or without modifications “has been widely adopted across the world” [WHO, 1996]. The recent literature suggests that oxytocin is used intrapartum in the majority of deliveries in the US “with augmentation being more the rule than the exception” [Freeman and Nageotte, 2007: 445]. A review of studies on the use of oxytocin and misoprostol in seven low-income countries showed that up to 50 per cent of deliveries in public hospitals were induced or augmented (up to 20 per cent in Ethiopia and Tanzania, and 40-50 per cent in the other five countries) [Lovold, Stanton, and Armbruster, 2008]. Such high percentages of induced and augmented labours are worrying in the context of developing countries where “current evidence-based guidelines are rare, care is less regulated, and staffing and monitoring capabilities are limited … [o]xytocin is often administered without the aid of a precise dose/time regulatory infusion pump, external fetal monitor […] or one-on-one care” [Lovold et al., 2008: 277].

The concerns over the frequent use of oxytocin intrapartum, however, extend to developed countries. Oxytocin as a drug associated with ‘a heightened risk of harm’ and one that may ‘require special safeguards to reduce the risk of error’ was recently included in the list of high-alert medications [Clark, Simpson, Knox, and Garite, 2009: 35.e1]. Clark et al. point out that recommendations on oxytocin administration currently used in practice are vague and that ‘in many instances, the apparent efficacy and safety of the various anecdotally derived means of administration (“the way we have always done it”) owe their success primarily to the resiliency of maternal-fetal biology rather than carefully considered scientific evidence’ [Clark et al., 2009: 35.e1]. Guidelines for oxytocin use in augmentation of labour are often based on and reflect various practices across institutions and countries.

Recent evidence found oxytocin to be effective in shortening labour [Wei, Wo, Xu, Roy, Turcot and Fraser, 2007], but data from clinical trials did not support the belief that oxytocin reduces the rate of Caesarean sections [NICE National Collaborating Centre for Women’s and Children’s Health, 2007]. Although more evidence from clinical trials is currently available, systematic evidence for oxytocin use is still lacking [Bugg, Siddiqui, and Thornton, 2008]. Clinical trials are often small, exclude at-risk women, look at varied practices and report only selected maternal and neonatal outcomes. The problem also lies with the definition of ‘delay’ in the first and second stage of labour and, in practice, various criteria have been used [NICE National Collaborating Centre for Women’s and Children’s Health, 2007], as well as various oxytocin dosage regimens [Bugg et al., 2008; NICE National Collaborating Centre for Women’s and Children’s Health, 2007].

A summary of the evidence relating to augmentation of the first stage of labour suggests no differences in outcomes, other than shortening its duration [NICE [National
There was no evidence of abnormal foetal heart rate or of changes in the Caesarean section rate. Nevertheless, the NICE guidelines emphasise the need to monitor the foetal heart rate continuously when oxytocin is used for augmentation. The evidence comparing low-dose regimens (starting dose and an increment of up to 2mU/min) and high-dose regimens (starting dose and an increment of 4mU/min or more) shows that high-dose regimens result in shorter labours, lower Caesarean section rate and higher chance of vaginal delivery but more hyperstimulation of the uterine muscles. The data on neonatal outcomes were insufficient to draw any conclusions on neonatal morbidity and mortality. Current specific recommendations on oxytocin augmentation in the first stage include a consultation with the obstetrician about whether oxytocin should be considered. For multiparas, a full assessment, including an abdominal palpation and vaginal examination, is required. When oxytocin is used, the foetus needs to be continuously monitored; the time between dose increments should be at least 30 minutes and the dose should be increased until there are 4-5 contractions in 10 minutes. Women should also be advised to have a vaginal examination four hours after oxytocin is started. No evidence for oxytocin augmentation in the second stage of labour was identified. Moreover, since there is a risk of uterine rupture NICE guidelines do not recommend oxytocin use in this stage.

The WHO recommendations, however, do not distinguish between augmentation in the first and second stages of labour [WHO, 2003a]. They suggest a starting dose of 2.5 units in 500ml of dextrose (or normal saline). The dose should be increased until 3 contractions lasting 40 seconds in 10 minutes are attained with maximum infusion rate of 60 drops per minute. If satisfactory contractions are not established, the concentration of oxytocin should be increased to 5 units in 500ml dextrose (or normal saline) with the same rate of infusion and increments as above. Women should be carefully observed throughout, and their pulse, blood pressure and contractions monitored; the foetal heart should be monitored every 30 minutes and the IV infusion should be stopped in the event of abnormal foetal heart rate or of uterine hyperstimulation. Apart from these differences, the guidelines provided by NICE and by WHO are alike in requiring oxytocin to be administered by IV infusion and the continuous monitoring of contractions and foetal heart rate.

Although the NICE guidelines summarise some high-quality evidence on oxytocin use in the first stage of labour, their conclusion emphasizes the importance of further research into the start dose and increments of oxytocin infusion. The data on neonatal outcomes were also insufficient. To provide clear recommendations for practice, the Cochrane Collaboration Group proposed two systematic reviews in 2008. These will aim to evaluate the available evidence on the effect of oxytocin administered because of
slow progress in the first stage of labour with respect to uterine hyperstimulation and its impact on changes in foetal heart rate, Caesarean section rate, and incidence of serious neonatal morbidity or perinatal death (e.g. birth asphyxia, neonatal encephalopathy, childhood disability), and maternal death or serious morbidity [Bugg et al., 2008]. A comparison will also be made between various dose regimes of oxytocin (i.e. starting doses and the increments in oxytocin infusion) [Mori, Ullman, Pledge, and Walkinshaw, 2008].

Although the clinical evidence is not always completely clear-cut, then, guidelines suggest that oxytocin should be administered intrapartum very cautiously and only under specific conditions because of the risks to the mother and her baby. The WHO practical guide from 1996, for instance, explicitly warned against the intramuscular administration of oxytocin because it is harmful for the foetus and increases the risk of uterine rupture. The guide also recommended that oxytocin augmentation should be restricted to labours supervised by obstetricians and to facilities that provide surgical services and (whenever possible) foetal surveillance by electronic monitoring [WHO, 1996]. More recent WHO guidelines recommend either oxytocin IV infusion for labour augmentation, with the precautions outlined above [WHO, 2003a], or that oxytocin only be used for the prevention of PPH in the third stage of labour [WHO, 2003b].

Oxytocin in Active Management of Third Stage of Labour (AMTSL)

A Cochrane systematic review has found active management of the third stage superior to expectant management in terms of blood loss, PPH, and shortened labour [Prendiville et al., 2000]. AMTSL is a package of interventions including early cord clamping and cutting, controlled cord traction to deliver the placenta, and the routine administration of a prophylactic uterotonic drug just before, with, or immediately after, the birth of the baby [Begley, Devane, Murphy, Gyte, McDonald, and McGuire, 2008]. Clinical evidence suggests that oxytocin and syntometrine are the drugs of choice for preventing PPH. Meta-analyses of clinical trials showed that prophylactic oxytocin is effective in reducing both blood loss greater than 500ml (RR 0.50; 95 per cent CI 0.43 to 0.59; 7 trials, more than 3000 women) and the need for therapeutic oxytocics (RR 0.50; 95 per cent CI 0.39 to 0.64) [Cotter, Ness, & Tolosa, 2001]. When compared to oxytocin alone, syntometrine (a combination of oxytocin and ergometrine) is associated with a small but significant reduction in the risk of blood loss between 500 and 1000ml (RR 0.82; 95 per cent CI 0.71 to 0.95); side-side effects such as nausea, vomiting and elevated blood pressure are, however, more common due to ergometrine [Su, Chong, & Samuel, 2007]. Syntometrine should therefore not be administered to women with pre-eclampsia or cardiac conditions. More data on the side-effects, optimal dose and route of administration of oxytocin are needed, however [Cotter et al., 2001]. In addition, the
question of optimal timing remains open: timing might affect the blood perfusion to the baby and the loss of maternal blood during the delivery, whilst uterotonics administered before the delivery of the baby may cause acute perinatal asphyxia [Begley et al., 2008]. The main recommendation is to administer the relevant drugs at the delivery of the anterior shoulder, but this might require additional staff to be present at the labour. Typically, it is more common to administer uterotonics intramuscularly or by IV infusion immediately after the birth of the baby. Oxytocics are, however, sometimes administered at the crowning of the head or even after the delivery of the placenta [Cotter et al., 2001].

On the other hand, oxytocin and ergot preparations are not stable in tropical climates: according to the product information for Syntocinon (a leading brand of synthetic oxytocin), it should be kept below 25°C and should not be frozen. In much of the Global South, especially in rural areas, health facilities are unlikely to have reliable electricity supplies or refrigeration facilities; heat-stable oxytocin is being developed, however. In addition, oxytocin and ergot preparations require syringe technologies and sterilisation equipment (although the “Uniject™” device might circumvent this). Thus, whilst oxytocin is very effective in preventing and controlling PPH, several recent clinical trials have studied the effectiveness of prostaglandins and particularly misoprostol, which is cheap, can be administered in pill form and is not heat labile.

Other recent studies evaluated the impact of the various interventions entailed in AMTSL and showed some adverse neonatal outcomes, including an increased risk of acute perinatal asphyxia if uterotonics are administered before the baby’s delivery, and lower haematocrit levels and haemoglobin concentration up to six months after birth due to early cord clamping [McDonald and Middleton, 2008]. Little is known about the effects of particular components of AMTSL. Based on this, a new systematic review on ‘active versus expectant management in the third stage of labour’ has been proposed [Begley et al., 2008]. Currently, only a protocol is available.

AMTSL, then, is associated with some adverse effects (e.g. nausea, vomiting and hypertension when ergometrine was used as a part of the routine care) as well as having effects on the baby. Nevertheless, organisations such as International Confederation of Midwives (ICM), International Federation of Gynaecology and Obstetrics (FIGO) and WHO have accepted the proposal in Prendiville et al [2000] that AMTSL should be applied routinely in maternity hospitals. There are still some question-marks over the evidence about exactly how and when oxytocin should and should not be used. Some good quality clinical trials have been conducted but often they were small, based on different practices, and often reporting only selected maternal and neonatal outcomes. Therefore it is hard to compare them and to draw any conclusions and recommendations for best practice. Evidence on adverse neonatal outcomes is lacking. It is not known if
Intrapartum interventions involving uterotonic drugs (such as oxytocin) enhance the risk of PPH [McDonald, Abbott, and Higgins, 2004], because intrapartum interventions have been studied separately from third stage interventions and little is known about how they impact on the need for further interventions postpartum.

**Oxytocin Availability in South Asia**

With these considerations this in mind, we now shift our focus from the guidelines for oxytocin use to its availability and use in South Asia. During the Tracing Pharmaceuticals project, we interviewed medical representatives, in urban and rural settings alike. They said that they do not actively promote oxytocin—mainly because oxytocin sales are sufficiently buoyant for producing companies not to perceive any need for high-profile and energetic marketing strategies these days. Our interviews with wholesale stockists and retailers endorse this interpretation.

<table>
<thead>
<tr>
<th>Table 2: Oxytocin Brands Available in India</th>
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<tr>
<td><strong>Evatocin</strong></td>
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<tr>
<td>Foetocin</td>
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<td>Gynotocin</td>
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<tr>
<td>Indox</td>
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<td>Oxybro Inj</td>
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<td>Oxystar</td>
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<td>Oxytocin Inj</td>
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<tr>
<td>Oxyton-5</td>
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<td>Pitocin</td>
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<tr>
<td>Syntocinon</td>
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<td>Syntocinon</td>
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Source: CIMS India July-Oct 2006

Note: The dosage varies across products, with the majority containing 5iu/ml; Oxybro Inj contains 5iu/5ml, and Pitocin is available in the two dosages (5iu/ml and 5iu/5ml) at the same price. The dose is not known for Oxytocin Inj by Prem Pharma. Recommendations for the intramuscular injection of oxytocin in AMT-SL are for 10iu and pharmaceutical companies might market oxytocin in such dosages in the future: this would provide room for confusion and quite possibly for even more dangerous use of intrapartum oxytocin such as we outline in this paper.

We could not do a comprehensive study of oxytocin availability, but it can be readily obtained in disparate places, whether retail outlets near urban nursing homes and hospitals offering delivery facilities or small pharmacies in towns remote from large towns. Our interviews and some spot checks on stocks in retail outlets, also indicated that oxytocin is well known, routinely kept in stock by wholesalers and retailers, and relatively cheap. Moreover, oxytocin can easily be purchased over-the-counter (as our research assistants did several times), despite being a prescription-only drug. Table 2
lists the brands of oxytocin marketed in India, their producers and prices: all are locally manufactured.

**Urban Obstetricians and Intrapartum Oxytocin Use**

Active management of labour is high profile in obstetrics circles in contemporary India. For instance, Daftary and colleagues have produced “an indigenously developed protocol of labour management” [2003], whilst Shyam Desai, in his presidential address to the Federation of Obstetric and Gynaecological Societies of India (FOGSI), placed AML—including labour acceleration using oxytocics—at the heart of Safe Motherhood initiatives in India [Desai, 2005]. The use of oxytocics for augmentation is part of ‘programmed labour’ discussed in several sources [e.g. Meena, Singhal, and Choudhary, 2006; Yuel, Kaur, and Kaur, 2008].

Systematic evidence about intrapartum oxytocin usage in institutional deliveries in South Asia is hard to come by, however. Nevertheless, the urban obstetricians we interviewed during the Tracing Pharmaceuticals project strongly advocated AML. They took intrapartum oxytocin use for granted as routine, normal and appropriate in their repertoire of interventions, the drug of choice for augmenting labour. One described oxytocin as ‘the spinal cord of our speciality’ (Interview, October 24, 2007 Bijnor, western Uttar Pradesh). Obstetricians, including those nearing retirement, said that they had been told during their medical training that oxytocin use intrapartum was appropriate and that such use had been widespread throughout their working lives. Several obstetricians provided off-the-cuff estimates of intrapartum oxytocin usage in their institutions—sometimes upwards of 70 per cent. Some of this apparently high usage might be because a high proportion of institutional deliveries are difficult labours.

Nevertheless, oxytocin was also being used in pre-booked deliveries, which suggests a more routinised use, even when labours are progressing normally. A senior midwifery lecturer in Delhi described her arguments with staff at the Safdarjang Hospital—the government hospital where her trainee midwives received their practical training—when she wanted her students to experience ‘normal deliveries’. The hospital staff said they routinely administered oxytocin to all women in the labour wards because of pressure of numbers: women’s labours could not be protracted, because of bed shortages and a rapid through-put needed to be maintained (Interview, March 10, 2007 Delhi). Our own observational data (e.g. from two sessions of several hours each observing the labour room of a large teaching hospital in Kolkata), also suggest that oxytocin is used in a large proportion of institutional deliveries. We cannot adjudicate on whether such usage is over and above what might be classed as ‘medical need’, although the clinical guidelines suggest that oxytocin use should be exceptional rather than routine.

Intrapartum oxytocin use, then, seems to be very common and highly valued in institutional deliveries in the region. Why this might be remains uncertain. Oxytocin use
may be a form of ‘crowd control’ to ensure that labour room beds are vacated quickly [cf. Van Hollen’s discussion of busy hospitals in Chennai city: Van Hollen, 2003a, b]. A government obstetrician suggested that intrapartum oxytocin use enables private doctors to regulate the time when women deliver: “Because everything is money-oriented exactly. They want to work in day, take rest in night.” (October 24, 2007 Bijnor). And in other research in Bijnor in 2002-4, lay people frequently (and cynically) suggested that the financial interests of non-government health care providers lead them to administer drugs (or conduct even more lucrative Caesarean sections). Perhaps for several reasons, intrapartum oxytocin use seems to be normalised in institutional deliveries in the region.

Moreover, the clinical guidelines for intrapartum oxytocin use are not necessarily being followed in institutional deliveries. Writing about Karnataka, Matthews et al. comment: “[m]ore than 90 per cent of all women, and more than 75 per cent of women with no complications, were given repeated injections or intravenous infusions of oxytocics to hasten labour. Women in private and mission hospitals were more likely to have a doctor present during the delivery, but even here most women received repeated injections of oxytocics to speedup labour”[Matthews, Ramakrishna, Mahendra, Kilaru, and Ganapathy, 2005: 399; our emphasis]. An unpublished study in Jamshedpur also found that oxytocin use was routine in two hospitals (one government, one run by Tata), administered by different grades of staffs, sometimes IV but sometimes IM. In the government hospital, women received very little attention or monitoring, whereas monitoring was routine in the Tata hospital (Judith Sim, personal communication, 12 March 2009). During our observations in a Kolkata teaching hospital, women admitted to the labour ward were examined (to assess cervical dilatation and the baby’s presentation) and most were straightaway attached to IV saline drips containing oxytocin. Thereafter, checking of the drip, internal examinations, foetal heart monitoring, etc. were done infrequently and irregularly and there was no continuity of care. Labouring women were left to their own devices, often two to a bed, whilst staff spent much of their time congregated at a desk at one end of the ward. Discussing institutional deliveries and the incidence of neonatal encephalopathy in Kathmandu, Ellis comments that “the most striking potentially preventable risk factor for adverse outcome” was ‘induction of delivery’ using oxytocin infusion [Ellis, 1999: 167; see also Ellis, Manandhar, Manandhar, and Costello, 2000]. Similarly, although the evidence is sparse and unsystematic, intrapartum oxytocin use in hospital deliveries in low-income countries more generally seems to be associated with enhanced risks of stillbirth, neonatal resuscitation, neonatal deaths and uterine rupture [Lovold et al., 2008]. In brief, institutional deliveries are no guarantee either of quality of care or of safety.

**Intrapartum Use of Oxytocin in Rural Home Deliveries**

Many studies in South Asia have shown that the bulk of health care, especially in rural
areas, is provided by private practitioners of various kinds—trained in various medical traditions or none—operating outwith the formal government health care system. Given the government sector’s lack of capacity, perhaps the private sector plugs an important gap in provision. In this case, though, oxytocin is being administered in circumstances that raise serious disquiet. Table 3 summarises how oxytocin is being used intrapartum in rural home deliveries in South Asia. In itself, of course, using oxytocin during home deliveries flouts the clinical guidelines because the recommended monitoring and emergency facilities are absent. Moreover, oxytocin is usually administered by intramuscular injection. A few studies indicate how frequently oxytocin is used, whilst others merely indicate that its use is commonplace and well-known.

A study conducted in 12 Uttar Pradesh districts found that oxytocin was administered

<table>
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<tr>
<th>Table 3: Intrapartum Oxytocin Use: Practice in Rural Home Deliveries in South Asia</th>
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<td><strong>Exclusion of at-risk women</strong></td>
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<td><strong>Setting/availability of emergency facilities</strong></td>
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Note: This table should be compared with Table 1, which outlines the clinical guidelines for intrapartum oxytocin use. The points listed in Table 3 are probably widely applicable in South Asia although few of the studies cited in the text explicitly mention them. This listing draws mainly on the research on childbearing in Bijnor district (western Uttar Pradesh) conducted by Patricia Jeffery and Roger Jeffery.
in 48.2 per cent of home deliveries (n=2,992) across the state (ranging from 74.7 per cent in Muzaffarnagar to 16.7 per cent in Chitrakoot). Almost two-thirds of the women reporting injections had had more than one. Traditional birth attendants (TBAs) and auxiliary nurse-midwives (ANMs) were the primary decision-makers for using the injection (29.8 per cent and 29.6 per cent respectively) and informal private practitioners and ANMs were the primary injection service providers (48.2 per cent and 32.8 per cent respectively) [Das, Agarwal, Tripathi, and Parveen, 2005]. A study in rural Kanpur reported similar patterns of use, although absolute levels were lower (23 per cent, n=527), and there was a statistically significant relationship between injection use and the presence of a provider (trained or otherwise) [Sharan, Strobino, & Ahmed, 2005]. Research in two villages in Bijnor district, western Uttar Pradesh, indicates that between 1983 and 1987, oxytocin was being administered in about 15 per cent of deliveries (n=237) by the government pharmacist as part of his (illegal) private practice [Jeffery, Jeffery, & Lyon, 1989:111-112]. In 1998–2002, oxytocin injections were administered by untrained private rural medical practitioners (male) in 48 per cent of deliveries (n=346) [Jeffery and Jeffery, 2008: 72]. In the early 2000s, these practitioners charged between Rs100 and Rs150 per injection, a considerable mark-up on the retail price of around Rs20 for a phial of 5iu of oxytocin, but not prohibitively expensive even for poor families. A Karnataka study reports that ‘injections to increase pains’ (probably oxytocics) were injected in 21 per cent of all home deliveries, including 51 per cent of those attended by government auxiliary nurse-midwives [Matthews et al., 2005:397; Ramakrishna, Ganapathy, Matthews, Mahendra, and Kilaru, 2008: 96; see also George, Iyer, and Sen, 2005 for a report on elsewhere in rural Karnataka]. Similarly, writing about rural Rajasthan, Iyengar notes that intramuscular oxytocin injections are ‘widely used’ intrapartum [Iyengar, Iyengar, Martines, Dashora, & Deora, 2008: S27], whilst Van Hollen describes its use by the local multi-purpose health worker as ‘almost routine’ during home deliveries in Tamilnadu [Van Hollen, 2003a, b]. Bang, Bang, Baitule, Reddy, and Dashmukh [2005] report that in rural Maharashtra oxytocin injections were administered by unqualified private practitioners) in between 21.2 per cent and 23.1 per cent of the cases they studied and that they raised the risk of birth asphyxia and stillbirth threefold. Similar usage was acknowledged in personal communications from colleagues in Bangladesh and Pakistan [Jeffery, Das, Dasgupta, and Jeffery, 2007]. During the Tracing Pharmaceuticals project, our interviews with rural practitioners (mostly untrained and working in a private capacity) also indicated that they are very familiar with oxytocin and that some routinely administered it by IM injection to augment labour. A few talked about the dangers of using oxytocin in home deliveries, but many administered oxytocin in circumstances comparable to those outlined above, generally at the behest of the labouring woman and/or her female attendants, or because the TBA
recommended its use. Oxytocin may also be used intrapartum in urban home deliveries: a study in a poor area of Delhi reported oxytocin use in 68.9 per cent of home deliveries, administered by private ‘doctors’ in 86.8 per cent of cases [Caleb, 1995]. Similar use has also been documented in Sudan and Guatemala [Lovold et al., 2008].

An additional feature of oxytocin is its cultural acceptability. In the local understanding of pregnancy, a woman’s body becomes increasingly ‘hot’ (in the humoral sense) until uterine contractions are sparked off. According to the Bijnor study, desi [folk] methods of ‘heating’ a woman’s labour—‘heating’ drinks such as tea containing unrefined sugar, loosening her plaits, unlocking padlocks, etc.—were still common in the early 1980s [Jeffery et al., 1989: 103ff.]. They had almost disappeared by the early 2000s and village women and their attendants regarded intrapartum oxytocin injections as the most effective method of speeding labour, especially in labours perceived to be lengthy and in which the contractions had ‘cooled’ (become infrequent or less intense). They were popular with women wanting their labour to end quickly and many women had several injections within a few hours. They called these injections dard barhāne kā tikkā [pain/contraction enhancing injection]. Other sources talk of garmī ri huī [Iyengar et al., 2008: S27] or garmī ki suī (heating injection), and other variants on the theme are widespread in the region. Further, as many sources suggest, hyperdermic needles are powerful icons of ‘modernity’. Based on her study in rural Sitapur (UP), Pinto argues that injections enable local practitioners to re-assert their quasi-institutional authority through association with modern biomedicine [Pinto, 2004, 2008]. In line with this, Das et al. found that intrapartum oxytocin use was greatest among women of higher socio-economic status and the relatively more educated, suggesting that it was used less because of need and more because of ability to pay and an association with ‘modernity’ [Das et al., 2005].

Many rural medical practitioners have no formal medical qualifications. Others have training in ayurveda, unani or homeopathy, but their practice usually includes, or is even dominated by, cosmopolitan remedies. Rural practitioners, however, have often had previous urban employment as compounders (pharmacists), ward boys, etc. in urban facilities. One explanation for how oxytocin use might have become widespread in the rural areas was proposed by several interviewees: that rural practitioners learn their trade primarily by observing clinical practices in urban facilities and adopt them in their rural practices. Interviews with rural practitioners also indicate that they maintain relationships with urban facilities, often accompanying labouring women whom they refer there (in the 2002-4 Bijnor study, villagers alleged that they take a commission for doing so). There are, then, many opportunities for them to observe oxytocin use in urban facilities.

If urban usage fails to follow clinical guidelines, rural practitioners are unlikely to
appreciate the dangers of administering oxytocin injection in situations where they cannot adequately monitor the labour or provide emergency care if matters go awry. Indeed, even if urban practices do follow clinical guidelines, rural practitioners might not emulate them if they are unaware of the rationales behind them. In sum, the enthusiasm of obstetricians for using (and sometimes misusing) oxytocin intrapartum in urban nursing homes and hospitals probably leads directly and indirectly to its use and misuse in the rural areas—a series of unintended consequences that the urban practitioners we interviewed were generally unwilling to acknowledge.

**Conclusions**

This paper has focused on intrapartum use of oxytocin in South Asia. More work is required to establish how commonplace intrapartum oxytocin use is in South Asia, whether in rural home deliveries or in urban institutions. We also do not know how much of that use departs from the clinical guidelines for its use and there are no data providing systematic information on the impact of such use on maternal mortality and morbidity, stillbirths and neonatal mortality and morbidity. The National Family Health Survey (NFHS)—the main source of national-level information about pregnancy, delivery and post-partum care in India—has collected nothing on intrapartum oxytocin use in its 1992-1993, 1998-1999, and 2005-2006 rounds, for instance.

Nevertheless, advocacy of AMTSL includes proposals to issue local-level health workers with oxytocin to avert and (if necessary) arrest post-partum haemorrhage. Policy documents, however, tend to present government programmes as if they are hermetically sealed from the wider world in which they are embedded. With respect to the use of oxytocin in AMTSL, they are silent about its significant life out with the realm of government policy and provision—indeed, a life that is also beyond its purview. The lack of concern about oxytocin misuse that has emanated from the professional and policy circles involved with issues of reproductive and child health is troubling. Our interviews with policy-makers and employees of NGOs in Delhi and Kathmandu, for instance, indicate that they are often aware of the kinds of oxytocin usage we have described, that they consider PPH a more significant issue than oxytocin misuse (despite the lack of evidence base) and that they are naively complacent about the prospects of retaining control over the oxytocin issued for AMTSL purposes.

The policy recommendations have no robust mechanisms to prevent oxytocin designated for PPH prevention from being used intrapartum, whether in local-level facilities by government staff themselves or by seepage into the private sector. The health care market is huge, diverse and, of course, inflected with market incentives and the imperative to make money: its implications for Safe Motherhood initiatives must be addressed. To be realistic, women in South Asia (in many areas, the vast majority of
women) will continue to deliver their babies outside the government sector—and much greater attention must be paid to these ground realities if policy interventions are to have their hoped-for impact (and not to be undermined by their undesirable unintended consequences). Of course, intrapartum oxytocin (mis)use is not the only serious issue at stake for Safe Motherhood. But tracing how pharmaceuticals such as oxytocin are being used “on the ground” and understanding how they are embedded in wider social and economic contexts provides crucial support for our view that policy-makers urgently need to engage with the everyday realities of drug availability and use in the Global South.

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Notes:
1 This paper emerged from the collaborative research project Tracing Pharmaceuticals in South Asia (2006-2009) that was jointly funded by the Economic and Social Research Council and the Department for International Development (RES-167-25-0110). The project team comprised: Soumita Basu, Gitanjali Priti Bhatia, Samita Bhattacharai, Petra Brhlíková, Erin Court, Abhijit Das, Stefan Ecks, Ian Harper, Patricia Jeffery, Roger Jeffery, Sakshi Khurana, Rachel Manners, Allyson Pollock, Santhosh M.R., Nabin Rawal, Liz Richardson, and Madhusudhan Subedi. Martin Chautari (Kathmandu) and the Centre for Health and Social Justice (New Delhi) provided resources drawn upon in writing this paper. Neither ESRC nor DFID is responsible for views advanced here.

2 The ‘medicalisation’ of childbirth has not been uncritically accepted within professional circles, as well as beyond, but we cannot address this issue here.

3 There are many possible variations of these three interventions. First, several uterotonic agents are available, with variations in timing, dose and route of administration (e.g. oxytocin can be administered as IV infusion or intramuscularly, syntometrine as an IM injection, and ergometrine IV or IM). Secondly, there are also possible variations in the timing of cord clamping and cutting and in the initiation of controlled cord traction. Variations in practice across health centres and countries mean that some women receive mixed management, a combination of expectant and active management that does not include all the components of either (Begley et al., 2008). For a discussion of the disparities in standards for AMTSL and in their implementation in practice of hospitals in developing countries, see Stanton, Armbruster, Knight, Ariawan, Gbangbade, Getachew et al. (2009).

4 When misoprostol was used there was a higher risk of severe PPH (RR 1.32, 95 per cent CI 1.16 to 1.51; 16 trials, 29042 women) and greater use of additional uterotonic but fewer blood transfusions (RR 0.81, 95 per cent CI 0.64 to 1.02; 15 trials, 27858 women) than when injectable uterotonic (oxytocin IM or IV, ergometrine, ergometrine plus oxytocin) were used. Oral misoprostol (600mcg) was associated with higher rates of side-effects, such as nausea, vomiting, diarrhoea, shivering and pyrexia (greater than 38°C) when compared with injectable uterotonic as well as placebo. Results from a small number of trials suggest that side-effects associated with misoprostol use are dose related and that rectal misoprostol resulted in less pyrexia and shivering than oral misoprostol (Gulmezoglu, Forna, Villar, & Hofmeyr, 2007). Although less effective in preventing PPH than oxytocin, misoprostol showed promising results when compared to placebo and for its easier administration was tested in home-deliveries in developing countries (Derman, Kodkany, Goudar, Geller, Naik, Bellad et al., 2006; Miller, Lester, & Hensleigh, 2004). More research on the optimal dose and mode of administration is needed if misoprostol is to be recommended for resource-poor settings.
5 Definitions of AMSTL differ slightly. FIGO-ICM prefer 10iu oxytocin administered by IM injection, or IV injection, drip or push after induction or augmentation within one minute of foetal delivery, with 0.2 mg ergometrine administered in the same way as oxytocin or 600mcg misoprostol (oral tablet) or other prostaglandins as second line drugs. WHO prefer 10iu by IM injection oxytocin within one minute of the baby’s delivery, and if oxytocin is not available they recommend 0.2 mg IM ergometrine or prostaglandins; they also specify that a check is made before giving these medications that there are no additional baby(s): for more details, see http://www.who.int/reproductive-health/impac/Clinical_Principles/Normal_labour_C57_C76.html#C73 per cent20Active per cent20management per cent20of per cent20the per cent20third per cent20stage

6 We have been unable trace data that provide overall information for South Asia on oxytocin sales over time, so we cannot comment on these assessments.

7 We could not conduct a systematic study of drug transport and storage. This aspect merits further work for heat-labile drugs such as oxytocin, since turnover and seasonality may impact on drug efficacy.

8 Research on childbearing in Bijnor district (western Uttar Pradesh) was conducted by Patricia Jeffery and Roger Jeffery and funded by Social Science Research Council [now Economic and Social Research Council] in 1982-3 and 1985 and by Wellcome Trust in 2002-4).
I

Introduction

With the advent of streptomycin in the 1940s, the management and treatment of tuberculosis has been primarily focused on drug interventions. As therapeutic agents have been developed for TB treatment, the history of research and development into how best to treat the condition has focused primarily on two sets of issues: what combination of drugs taken over what period of time can achieve the best chance of cure, and how can the emergence and prevention of drug resistance be managed [Toman 2004a]. Currently, there is a range of anti-tubercular pharmaceutical agents available on the markets. ‘First line drugs’ are used for the treatment of non-drug resistant tuberculosis, and ‘second line drugs’ for the treatment of drug resistant tuberculosis (MDR-TB). Unfortunately the so-called ‘short-course regimens’ – developed after rifampicin entered the market after the late 1960s - still require at least six months of treatment. Existing understanding and best practice is that therapy is divided into two phases: An initial ‘intensive phase’
– lasting usually 2-3 months, and involving combinations of three to four drugs – and a ‘continuation phase’, in which two drugs are given for a further 4-6 months [Toman 2004b]. Trials have shown that at least two so-called ‘bactericidal’ drugs are required in the initial phase (either rifampicin and isoniazid, or streptomycin and isoniazid), and that the combination with pyrazinamide in this phase shortens treatment from 9 to 6 months. The intensive phase is said to kill the ‘actively growing and semi-dormant bacilli’, and ‘the continuation phase eliminates most residual bacilli and reduces failures and relapses’ [Harries 2004: 124]

Since the 1990s, both India and Nepal have adopted the WHO-advocated TB control strategy, Directly Observed Therapy, short-course (DOTS). This strategy emphasises case-finding activities using smear microscopy of suspects, and then the administration of a short course therapy regimen under ‘direct observation’ by those responsible to the health system. In the context of Nepal and India, however, the short-course regimen chosen for the DOTS programme differed: India introduced an intermittent regimen (one administered three times per week, rather than daily); and Nepal has a longer continuation phase of treatment but without rifampicin. While these technical decisions were made by small groups of national and international experts, they were controversial. In both cases widespread resistance to the choice of the regimen hindered the uptake of the DOTS programme.

In this paper we examine and compare these regimens and the reactions to them in the context of Nepal and India. We do so from the perspective of an attempt to understand the market and other forces driving the sales of TB drugs, which we address in the first section. The majority of TB patients receive their treatment outside the public sector. We argue that while the scientific evidence may be equivocal over the efficacy of the national DOTS regimens, policy decisions should be made in the light of this local context. Secondly, we examine the reaction to the prescribed national regimens from practitioners in the private sector in Nepal and India. Although the regimen decisions were made in part because of cost implications, the very choice of the regimens themselves has hampered efforts to ‘integrate’ the non-public sector into an overall attempt to control tuberculosis.

The data for this article comes from the project ‘Tracing Pharmaceuticals in South Asia’. In this we mapped patterns of production, distribution, marketing and retail of three key generic drugs (oxytocin, rifampicin and fluoxetine) in three regions of South Asia (Nepal, West Bengal [WB] and Uttar Pradesh [UP]). We drew on qualitative data using semi-structured interviews, in particular with producers, medical representatives, pharmacists (including distributors and retailers), and providers (including qualified and unqualified prescribers). Topics included questions about the everyday working practices of the interviewees, with specific questions about our focus drugs, here rifampicin and
other associated TB drugs. We asked about sub-standard and counterfeit medicines; patterns of supply; prescriptions by certified and non-certified medical practitioners; and over-the-counter sales by pharmacists. Since each of the drugs is inserted in different ways into national and international health programmes, and drug procurement procedures differ widely, we also interviewed donor agencies and health activists about how they saw the problems posed by the supply chains, distribution and consumption patterns of each of the three drugs. Over 80 percent of the interviews were recorded, transcribed and (where necessary) translated into English by the research assistants. In each site we also took whatever opportunities were presented to observe interactions among key members of the field: providers with clients and medical representatives, for example. All unrecorded interviews, and any observation material, were noted down (either at the time or immediately after) and typed up in as much detail as possible as soon as we were able to reach a computer. Because of the roles played by global donors in TB control, we made special studies of the documents on the national TB programmes in India and Nepal in order to investigate linkages between international organisations and donors, and national governments and health systems, as well as how these national programmes interact with the pharmaceutical commodity chains we identified.

II

Understanding TB drug Markets in India and Nepal

A recent evaluation of the current drug market in India values the Indian TB drug market at USD 94m, with 74 per cent contained within the private sector. The report suggests that this market is mainly for first line drugs, with only 9 per cent for second line, and that the value of this market was driven mainly by the availability of Fixed Dose Combinations (FDCs). For example, a review of CIMS in March 2007 revealed 36 companies in India producing Rifampicin products; 19 in uncombined form and with the range of combined drugs as follows; 34 in combination with isoniazid; 12 with isoniazid and ethambutol; 19 with isoniazid and pyrazinamide; and 19 with the four drugs combined. When we combined the data from CIMS, IDR and MedCLIK the total number of producers marketing a range of single and combined drugs went up to 52 (though in several cases, a single firm – such as Cadila and Wockhardt – markets drugs under two or even three names). The seven companies listed by IMS with the highest sales figures in 2006 were: Lupin Labs. (45.4 per cent) Macleods Pharma (19.7 per cent), Novartis (6.5 per cent), Shreya Lifescience (4.9 per cent), Cadila Pharma (4.7 per cent), Concept Pharma (4.5 per cent), Wockhardt (2.5 per cent). Each produces a different range of FDCs that feed into this intensely competitive local market. Characterized as ‘therapeutic anarchy’ by one WHO official we interviewed, this wide range of therapeutic combinations from such an array of companies – many of unknown quality – is one of
the major obstacles to controlling TB as a public health problem, and is a major concern for the rise of MDR-TB.

The quality of drugs, and particularly FDCs, is a problem. One survey (including drugs from India) showed that 10 per cent of samples contained less than 85 per cent of their stated content, with more FDCs than single formulations being substandard [Laserson et. al 2001]. It has also been reported in India that only 55 per cent of doctors in one survey prescribed regimens that conformed to the NTP/WHO recommendations (Prasad et. al 2002). In 1998 this had been even fewer at 29.4 per cent, and that ‘as many as 102 different drug regimens were being prescribed by 187 PPs’ [Singla et al 1998: 387]. Faults in the duration of treatment and drug dosage were also reported (Uplekar et al 1991; Singla et al 1998). In addition, faulty dosages of rifampicin prescribed by practitioners did not take into account weight variations of patients [Prasad et al 2002]. Cost is also important, with patients frequently being over-treated and spending up to five or six times the costs required to achieve cure [Arora et al 2003]. Delays in the recognition of TB also increase costs with delays of referral into the public system (Rajeswari et al 2002). Most of these studies pre-date the WHO recommendation that FDCs should be used routinely in TB treatment, and so this might have shifted in the intervening years. Several RMPs and private doctors interviewed in our project said that they prescribe the brands – AKT (Lupin) and Forecox (MacLeods), for example – and thus it seems not unreasonable to assume that they are less likely to make a mistake with the regimen combination itself.

Almost everyone involved in the provision of DOTS and public TB services we interviewed saw the uncontrolled availability of TB drugs and the ‘private sector’ as a major, perhaps even the major, difficulty in the control of tuberculosis. A DOTS Programme Officer in Uttar Pradesh assumed that 60-70 per cent of resistance was due to ‘barefoot doctors’ or quacks, and their misuse of rifampicin, and the giving of incorrect combinations. While he reckoned that some of the bigger companies (like Ranbaxy, Lupin, Macleods, Cadila) behave ‘ethically’ by visiting only doctors, it is the bare foot doctors that ‘know the public pulse’. A local chest physician and RNTCP supervisor also agreed that most treatment of TB patients went on in the private sector and that there were multiple different regimens prescribed, many very poor. Both men linked this directly with the promotion practices of the company Medical Representatives (MRs), feeling strongly that the only way to deal with this was to centralise treatment policies and regimens. In their opinion, the commercial interests of the doctors remain the biggest problem.

In Lucknow, a chest specialist also perceived village doctors and their ‘cocktail regimens’ that clients stop after a few weeks as an issue. A Lucknow pulmonologist also pointed to the poor quality of rifampicin on the market, arguing that smaller, less well
known companies have bioavailability problems with their combinations. He himself writes the brand names of the bigger companies – Lupin, Macleods, Cadila – to avoid these problems. Similarly the superintendent of a TB Hospital in Delhi, who worked as a State TB Officer in the past, felt that (along with poorly run TB programmes), private physicians and the poor regimens they prescribe were most important cause of the rise of MDR-TB. Third on his list were the patients, as they can be irregular in taking drugs and side effects are an issue as well, he explained. In Kolkata, we were told by the director of a State TB control centre that the private practitioners see the DOTS programme as competition.

The forces that drive this growth in the market in its current form – the increased use of numerous and varied combinations – is linked to several factors from the international, national and more local arenas. Interviews conducted with marketers working with Lupin and other TB drug producing companies allowed us to begin to paint a picture of the forces at work in the production of this ‘anarchy’. It is to this we turn to next.

Firstly, the WHO and the International Union Against Tuberculosis and Lung Disease (IUATLD) currently promote the use of FDCs as a means of reducing monotherapy and decreasing the risks of developing drug resistance. This they have been doing since 1994, and with renewed vigour since 1998 (WHO 2002b). The 4-dose FDC was added to the WHO essential drug list in 2002 (WHO 2002c). WHO suggests that their use also decreases the risk of mal-prescribing and means that fewer tablets have to be taken at one time by the patients. This advocating for the use of FDCs has accompanied the increasing use of the Global Drug Facility (GDF) for many countries procuring their DOTS programme drugs. Companies such as Lupin and Macleods strive for these lucrative GDF contracts, and this has had an effect on the promotion of FDCs over and above single dose drugs.

Secondly, a more local explanation for the rise of FDCs is that rifampicin and the single first line drugs are price-controlled by the Government of India. Changing the various drug combinations is a mechanism for avoiding this.

Thirdly, companies also respond to pragmatic prescriber forces. One Medical Representative (MR) working for Lupin explained that the range of TB products they produce was a direct response to the changing patterns of how medical practitioners prescribe. He went on to explain the different dosages in tablets and how these are prescribed as per the weight of the patient. Further, he explained how different combinations of single tablets are prescribed for differing ‘sets of patients’ based on their capacity to understand the importance of the length of treatment, and their awareness of the issues and thus to prevent the growth of MDR. Part of the MR’s job is to survey the prescribing habits of the doctors. The availability of a range of combinations and dosages is rationalized as a factor of the difference between individual patients, and the doctors needs to respond to these:
“Suppose, a person comes from the village, he will not have the awareness as to how he is supposed to take all the four medicines. For him, the doctor will write in fixed dose combination. It will be easier, just two tablets daily he has to take. If a patient goes who is well aware and informed, he will be given AKT4. So it differs from patient to patient. So every doctor writes all the drugs. So a big doctor of chest TB will write all the drugs, individual drugs, fixed dose, AKT4.”

An MR can meet up to 200 doctors per month, and the prescribing habits of these doctors are fed up the Lupin chain of command, to the area managers, and then to the product management team who has oversight of the trends across the whole country and abroad. The MR explained that Lupin must be reactive. Promotion of these products responds to what the doctors do, and this is monitored through the chemists’ surveys.

The larger companies also have a concern for patient convenience, linked to a concern for the vexed question of patient adherence to treatment. Thus a marketing manager from West Bengal told us why AKT4 is in strips, and how these are created so the patient has to buy all the drugs necessary for treatment and not just single drugs that they can afford. He emphasised the importance of the strip: it is cheap, and the patient can carry all the drugs ‘in his pocket’. Another MR suggested that their marketing is always conducted within the parameters set by the WHO. They encourage this in the doctors he meets, he said, but within this the product promotion depends on the individual prescribing behaviour of that doctor, and the company decides what gifts can be presented. From a pragmatic perspective, then, the wider the range of products and combinations that you have then the more likely that you are able to dominate the market.

In Nepal, too, interviews indicated how markets were conceived of in this way. So an employee of Concept in Nepal explained that their Rifa-i-6 product is unique because it has pyridoxine (vitamin B6) added to the rifampicin and isoniazid, unlike other companies’ products. A Lupin MR in Kathmandu will try to talk the doctors out of using Macleods’ FDC products. As AKT4 comes in a combi-pack, and each tablet can be removed separately, then this allows the rifampicin to be taken before breakfast. He claimed that the bioavailability of the Macleods’ rifampicin is reduced in their FDCs.

An ex-State TB officer in Delhi explained that FDCs are good for compliance, and different combinations are made to reflect the different weights and needs of patients. Companies, he suggested, are concerned with patient management issues and responsive to these, and to the question of compliance, but just the sheer numbers make it so complicated. A WHO advisor in India also reckoned that the number of FDCs on the market was an issue of different dosages for different weights of patients, although he too was confused about the reasons for the huge numbers available on the market. For him, the remaining problem was one of quality assurance and this is why the RNTCP needs to procure drugs centrally. A private doctor in Kolkata said that the problem with 50 or so companies pushing their combinations in the private marketplace is that it is very difficult to know if the information that the companies give is valid or not. His advice was to stick with the well-known brands, those of Novartis, Lupin and Macleods.

Now we can begin to understand why there are so many FDCs on the market, as companies respond to the prescribing habits of the doctors, keep an eye on the WHO recommendations, and advertise their differences. But the national programmes and the
regimen prescribed through the DOTS programmes in India and in Nepal also have their effects. We begin with the case of India.

The Indian Scenario: Intermittent vs Daily Regimens and the Issue of Direct Observation

India launched its Revised National TB Control Programme (RNTCP) from 1997. The DOTS programme was rolled out between 1997 and 2005; latterly the expanded STOP TB programme was adopted. The regimen for the national programme is currently divided into three categories, each one intermittent.

1216:0:.1. Category One, for those with smear positive disease, and serious patients, involves Isoniazid (H), Rifampicin (R), Ethambutol (E), Pyrazinamide (Z) three times a week for two months, followed by Isoniazid (H) & Rifampicin (R) three times a week for a further four months.

1432:0:.2. Category Two, for treatment ‘failures’, ‘relapse’ and treatment after ‘default’, has Streptomycin (S) added for the first two months, then the 4 drugs for a month followed by HRE for a further five months.

1648:0:.3. Category Three (less serious non-infectious disease), has HRZ for two months and then HR for four months.

These are provided in ‘patient-wise boxes’, not as FDCs. These sturdy boxes are marked with the patient’s name, and have bags in them (coloured differently for each category of treatment), which contain the blister packs for an entire course for one patient, the intensive phase and the continuation phase separately. For both phases pyridoxine has been added as ‘filler’ for the days when the TB drugs are not taken. Direct observation has also been decreased to once per week for the continuation phase rather than daily when the TB drugs have to be taken in the IP.

The rationale for intermittent therapy is linked to the presupposition that direct observation is mandatory, and that it is easier to be observed three times a week than on a daily basis. In the Q & A section on the RNTCP website we find:

‘What is the basis for supervised, intermittent therapy? Various studies have shown that during domiciliary treatment, when patients have to take drugs for a prolonged period, there are a large amount of concealed irregularities. Regular clinic attendance does not translate into regular treatment. Non adherence to treatment is a universal human trait and can only be overcome by establishing a human bond between the patient and provider. Daily supervision of treatment is not logistically feasible in India. In vitro experiments have demonstrated that after a culture of mycobacterium tuberculosis is exposed to anti tuberculosis drugs for a period of time, it takes several days (the LAG PERIOD) before renewed growth of bacteria occurs. Other than thiacetazone, all other drugs exhibit this lag phenomenon and can be used for intermittent therapy’. 11

One WHO advisor argued that the Indian TB programme had attained 86 per cent success using intermittent therapy. The Indian programme had been against the idea
of FDCs, he said, and anyway they have as good treatment success as those that use FDCs. He saw the reasons with ‘defaulters’ as much more complex than problems with ensuring patient compliance – these problems might include cultural issues or operational issues, he argued, rather than the regimen itself. In other words, the failure levels in the intermittent regimen were not worse than in the daily regimen. He remained unconvinced by the trials that suggest that intermittent therapy has worse outcomes. Similarly an ex-State TB Officer for Delhi argued that the outcomes are good for the IR, although it is even more important to observe the patient directly. Although FDCs are not used in the programme, he stated that their packs are dose-related, and have a longer shelf life. As they are singly swallowed, there is less of a problem about the absorption of rifampicin. The director of the state TB control centre and a WHO advisor in Kolkata assured us that the IR is based on ‘science’ and that it is very important to persuade others of this fact. The problem lies with default, but surely, they rationalized, it is better to be directly observed three times per week rather than daily? Another government doctor agreed, and said that the choice of the IR was a local Indian concern, and based on the direct observation issue. They added pyridoxine, he said, so that patients can say ‘I am taking TB drugs every day of the week’, and this is what they think. He feels that supervisors who give patients their medicines for a month at a time should be punished.

What evidence is there for this use of IR as the national regimen? In a review of the existing evidence Tom Freiden, the WHO TB officer in India when it was introduced, and a passionate defender of DOTS, justifies its use scientifically (Freiden 2004). He suggests that experiments in animal models even show an increase in efficacy using intermittent HRZ, and – speculatively – that it is ‘perhaps slightly more effective than the daily regimen’ (ibid. 132). A 2005 Cochrane review is more circumspect, arguing that there is no evidence to support assertions that intermittent regimens are better than daily ones, and calling for more research. A recent review of the evidence suggests that the relapse rate for IR in India is not known, as the data are not systematically followed up (Bhargava & Jain 2008). These authors argue that further evidence, since the publication of the Cochrane review, points to a significant advantage to daily therapy over IR. Our point here, however, is not to argue over the evidence base for its use – which remains equivocal - but to point to broader, local and pragmatic issues which may be more important than the ‘science’.

Firstly, the use of intermittent therapy has increased the anxiety over direct observation of treatment. As a Lupin representative we interviewed argued, effectiveness is not at stake should every dose be taken, but if a dose is missed with the intermittent regimen you are in effect missing three doses. This fact of the intermittent dosage schedule explains why the government regimen needs to be observed, contra to the daily regimen for which observation is not necessary, he said. For this reason he – as did others –
saw the regimen as less effective. In his opinion, the rationale for the choice of the intermittent regimen was cost, decided by certain ‘agencies’. The problem lies solely in the programme itself and its rigid structures of observation. How is it possible, he said, to have volunteers across India observing all these TB patients take their drugs? Not unreasonably, he asks:

‘Because you are not getting your entire medicine in one go, you will have to go to the DOT centre, take your medicine, take your medicine there and come back... And you cannot get DOT treatment other than your centre. Suppose I am going for a marriage in some other city, I will not get the medicine and you are not giving medicine for those periods to carry on with this. What will happen then?

He also sees it as a problem of the psychology of the patient, who would rather be taking daily doses of the drug. Intermittent therapy is ‘not tuned in their mind,’ he said. However, he also explained that he has talked to many doctors who are not prepared to get involved in the DOTS programme, because of staffing and resource issues and that it increases their administration loads through the stringent recording and reporting formalities.

Perceptions of the local understandings and meanings attributed to intermittent therapy and the DOTS programme are thus a particular problem for the Indian Revised National Tuberculosis Control Programme. Several chest physicians noted that by recommending the addition of streptomycin to a regimen that is failing, as in the case of category two, the WHO is contradicting one of its cardinal rules: that you never add a single drug to a failing regimen, as to do so could well be the equivalent of monotherapy (cf Bhargava & Jain 2008). Those in the RNTCP acknowledged this, but asked what else they could do (given the lack of laboratory ability to diagnose MDR and such limited resources).

Further interviews with chest physicians revealed these perceptions and difficulties with the current DOTS programme and its regime. A chest physician in UP, and a visiting RNTCP supervisor, highlighted that in their experience, private doctors exploit the perception that DOTS is intermittent therapy, as most patients would rather have the daily therapy. Again, they argued this meant that direct observation was even more essential. In Lucknow, the doctor in one DOTS centre acknowledged that many private doctors say that the government medicines are no good, and that they write prescriptions for their own benefit. Another senior chest specialist in Kolkata said that the DOTS programme will not work: that DOT is not implemented strictly enough; that Category 2 and 3 are both wrong; that the programme doesn’t take the issue of side effects seriously enough; that they haven’t worked out what to do with migrants;12 that there is far too much MDR-TB that they have no idea about because of the lack of laboratory backup. There is no way that they will ‘contain’ the TB issue by 2015, he claimed. He was also disappointed that the WHO recommendations are not ‘evidence based’.

A Kolkata pulmonologist also stated that middle class patients would avoid the
government clinics because they are dirty, crowded, and they don’t trust the free medicines. Another senior and influential senior chest physician in Kolkata quoted the book *Timebomb*, and a recent piece of research suggesting that in a survey of 100 doctors, 85 different regimens were prescribed! However he was highly critical of the DOTS programme for several reasons: the criteria were too rigid, people had to wait too long to get their medicines, and the whole programme was too ‘cumbersome’; it failed migrants; he regularly sees patients under the DOTS programme who are not having their issues addressed, and most people are suspicious of, and don’t like, the government services. Yet another Kolkata private physician explained that he doesn’t like the DOTS regimen because it is too short, and that he only refers the poor to the DOTS clinic, stating that ‘if a patient can afford the medicine I don’t send them’. Many find the direct observation too inconvenient and lose too much potential income. Another Kolkata chest physician, himself responsible for supervising a DOTS clinic, admitted that he doesn’t send TB patients there if they would like to see him privately. The government programme is overly bureaucratic and the drug supply often poor, he said. The patients don’t understand why they take drugs on alternate days. For him, the question of trust is primary, but in the government clinics they ‘force compliance’. The times are inconvenient, and whereas he gives his private cell number to patients to call should they want to, patients just don’t feel close to the clinic staff. He admitted that the issue with his private patients is keeping track of them. Again, another private practitioner who does not refer anyone to the DOTS programme sees the issue with lack of flexibility of direct observation and patients losing work; and that no-one takes the free drugs seriously. Yet another private practitioner, after complaining about the irrationality of category two, focused on the question of trust, in this case trust in companies, and so she prescribes Lupin’s products. She likes the idea and theory of the government service, but in practice it is different, and the profile of the government services needs to improve. The most high profile and vocal anti-DOTS advocate, and secretary of the Bengal Tuberculosis Association, is mainly concerned that the drugs are given on alternate days, whereas it should be daily: It looks to him as if ‘ours is a poor country, we cannot afford it’. He also has a problem with the lack of flexibility with weight schedules, and that therefore too many patients get the wrong dosages.

These practitioners involved in treating TB patients raise many criticisms of the programme. These range from broader perceptions of the quality of government services, to questions of trust and accountability. But central, too, were the criticisms – some reflecting on the evidence debates, others perhaps from personal prejudice – on the use of IT in the DOTS regimen. No one we spoke to used it in their private practices. At the least this adds fuel to their criticism of the government services, and makes the flexibility that many patients require more difficult. How do these issues play out in Nepal, where the technical issues are somewhat different?
III

DOTS and the Rregimen in Nepal

The regimen chosen for the DOTS programme in Nepal is administered daily, has to be supervised institutionally as DOT in the intensive phase and was until late in 2008 as follows:¹³

- Category One: 2HRZE/6HE
- Category Two: 2SHRZE/1HRZE/5HRE
- Category Three: 2HRZ/6HE

This eight month regimen, administered daily, lacks rifampicin in the continuation phase. One senior advisor to the TB programme in Nepal acknowledged that the WHO does not like using rifampicin through the whole regimen. This would mean that DOT is necessary for the whole six months rather than just in the intensive phase he argued. He also suggested that it was too expensive for Nepal. As in the Indian situation, the decision or at least justification for the regime came from the absolute need to observe directly any combination of drugs administered to patients that contains rifampicin.

The criticisms and issues related to this regimen in Nepal differed from those in India. Here there was widespread criticism of the continuation phase drugs, rather than the dosage schedule. For example, a senior and well known TB specialist in Nepal explained that he uses a six month regimen, as he prefers the continuation phase with rifampicin in it. For this reason, he said, he only referred those who could not afford it into the DOTS programme. He was concerned with the ‘slightly higher’ relapse rates when the CP contained INH instead of rifampicin. He had talked the issue of rifampicin in the CP over with many of his colleagues and that they shared his concern, although the patients themselves are not aware of these issues. Another senior Kathmandu chest physician stated that he was somewhat suspicious of the cure rates claimed by the DOTS programme. He also gives rifampicin to all his patients throughout the full regimen, and as he was responsible for the treatment of army personnel with tuberculosis he had not adopted the DOTS regimen for this reason. He saw the DOTS regimen in Nepal as an inferior regimen, and was surprised that the patients themselves were not shouting for the better regimen. He is unable to accept that they have 90 per cent cure rates with the ethambutol-based regimens. He also treats patients privately because many have difficulties and ‘hassles’ going to the DOTS clinic every day, and taking the time off work can be expensive.

Outside Kathmandu, the concerns were the same. A senior physician in Lumbini, in the Western Region, also complained that the Category 1 regimen was not good, and that he did not like HE in the regimen at all. Since the combination of HE was ‘bacteriostatic’ he explained, they should have HR in the continuation phase as this is ‘bactericidal’. As
he said: ‘From my experience, by giving HE in the continuation phase there is a high chance of relapse.’ So he does not refer to the DOTS programme, but prescribes the HR regimen. He also had a problem with the quality of the government drugs, and with the lack of accountability in the DOTS system: ‘one person does the check up, another person does the test and then another person gives the medicine’, so no one cares. At the nearby DOTS clinic, the young man working there said there were some problems with several doctors in the local government hospital: they ignore DOTS and treat all their patients privately. They complain that the regimen is no good, he told us, and they asked him why they should give poor quality drugs when they have their own. He was sceptical of this claim, and thought it more likely related to their business interests: they own or had shares in private clinics. Many patients who arrive late to the clinic have not even heard that the TB medications are free, he said.

However, despite these claims of not liking the current regimen the market for rifampicin and TB drugs has changed since the DOTS programme started, certainly in Kathmandu. It was widely represented during our interviews in Kathmandu that sales in the private sector for TB drugs had decreased after the success of the DOTS programme. A Macleods’ MR explained that the market had fallen out of their TB sales, including second line drugs since the implementation of the country wide DOTS-plus programme (for cycloserine, ethionamide, and PAS). He said that prior to this in Nepal they had no competitors for these three drugs. He reckoned that the numbers of patients not availing themselves to free TB drugs was small, and limited to a few with ‘high social status’ and those who wanted to keep their disease secret. This marketer said that he had not been able to break into the market of the few high profile TB specialists who remain loyal to certain other companies. He also highlighted how the products launched in the country are dependent on existing trends and sales of other companies.

The Sales Manager for a Nepali company explained that a combination of the emergence of the government DOTS programme and companies like Lupin diversifying into combination strips had reduced their own sales. He argued that while they would produce rifampicin for the government, this market is too vulnerable for them: there is no guarantee that the government would purchase from them. Although he did not mention this, now that the DOTS programme in Nepal procures all their drugs from the GDF there is no opportunity at all for local Nepali companies to sell to the government.

In a brief survey of TB drugs’ sales outside a major public hospital in Kathmandu, six retailers each said that their sales of TB drugs had decreased, and that the available drugs were now mainly combined drugs from the major Indian producers. All stocked Lupin’s products, but Macleods, Concept and Cadila were also represented. Outside another large teaching hospital with a well-functioning DOTS clinic run by a very enthusiastic community physician, not one of five retailers admitted to stocking any
TB drugs. One paediatric Kathmandu physician complained that it was very hard to get any uncombined rifampicin since the DOTS programme had gained momentum. Another physician suggested that companies like Lupin now barely needed to market their drugs, as the brand names are now so well known: ‘everyone knows AKT4, you ask any layman, he will know about AKT4’.

However, despite this a technical subcommittee of the National Tuberculosis Centre decided on the six month regimen and the main issue was really only the cost of the rifampicin. A senior representative at this meeting acknowledged this regimen had lower ‘relapse rates’ and less ‘treatment failure’, and it is more acceptable because of the decreased time it has to be taken. Adherence should increase, despite the need for increased observation. In autumn 2008 the new regimen was rolled out across Nepal.

In Nepal, several issues emerge from these research observations. Firstly, in the wake of a well run DOTS programme, sales of certain single and combination drugs can decrease. Nepal is dependent on TB drug imports from India, and the evidence points to the possibility that more FDCs from reputable Indian companies are on the market now as a consequence. From a public health perspective, this is surely better than the Indian situation: The chances of mal-prescribing and consumption ought to decrease as a consequence. Secondly, the decision to change the national regimen from an eight-month to a six-month one will also allow even greater harmony between the national regimen and those prescribed in the private sector.

IV Discussion

Critiques of the DOTS policy are wide ranging and suggest, for example, that it doesn’t address poverty, with which TB is ultimately associated, and that prevention campaigns based on case management have never eliminated a disease (Enarson D & N Billo 2007); or that the DOTS strategy is unlikely to overcome the massive social, cultural and economic barriers that feed tuberculosis (Gandy & Zumla 2002); or that the uncritical application of DOTS regimens in areas where TB, as a complex bio-social issue where levels of MDR-TB are not known, may deny patients the drugs they really require for MDR-TB (Farmer 2003). This latter point is also true in India, and is a particular problem for the category 2 treatment protocol (Bhargava & Jain 2008). However, much of the debate around DOTS has focused on direct observation. WHO pushed the direct observation angle very hard, to the bewilderment of many involved in and researching TB control issues. For example, in the WHO publication Toman’s Tuberculosis, amongst the operational requirements in the key to cure is that treatment should be directly observed, by a ‘trained, accountable individual’ and that this is particularly important when rifampicin is included in the regimen (Toman 2004c). Ultimately, the argument
goes, ‘the only means of ensuring that treatment is taken as prescribed is by direct observation’ (Bock 2004: 265). Ian Smith, the first WHO MO for Tuberculosis Control in Nepal, and a pioneering DOTS advocate, phrased it thus:

There are several ways by which we protect Rifampicin. The most effective and important is to observe every dose taken by the patient. Other ways include combining tablets of Rifampicin with Isoniazid to prevent monotherapy in fixed dose combination tablets (but quality and bioavailability must be ensured), use of blister packs, training health workers, using ‘balanced’ regimens, restricting use of Rifampicin to mycobacterial diseases only, and preventing misuse of medicines by ordering supplies on the basis of reported cases (Smith 2004)

By insisting that this observer of treatment is accountable to the health service the WHO and other DOT advocates have stimulated heated debates that have ranged across the sciences and social sciences, and been the focus of many editorials, perspectives and opinion pieces in major medical journals and elsewhere. This focus on ‘observation’ has tended to be at the expense of other aspects of the overall policy. However, baffling to many of us researching and commenting on this direct observation component of DOTS has been the ideology underlying the policy, that of the lack of trust towards either the patient (Bakhish 2006) or to the patient’s family members (Nichter 2008). A Cochrane review of direct observation studies for randomised and quasi-randomised controlled trials comparing health worker, family member and community member observation with self administration at home found no evidence of difference for DOT compared with self-administered treatment (Volmink & Garner 2007). When more qualitative studies were also reviewed, more richness was added to the critique including: the importance of socio-economic circumstances and individual agency; the importance of stigma; differing explanatory models of TB; that punitive sanctions are a barrier to the uptake of services; and that services need to fit more easily into the patterns of patients lives rather than vice versa (Noyes and Popay 2007). Only recently has the WHO released its insistence on DOT publicly – partly in response to these criticisms – as a component of TB control, but this may take a long time to filter down in practice across the diverse locales where DOTS programmes come to ground.

However, few of these studies have taken into account the specifics of the regimens themselves, as we have here. In short, we argue that it is important to take the local context of drug availability and practitioners’ understandings and perceptions into account when planning services. The absolute insistence on DOT, in that it remains the rationale for the intermittent therapy in India, is a serious policy error. Intermittent therapy may well have higher relapse rates than daily therapy, although there may not be enough supportive evidence to support this claim. More importantly, however, in a context where most of the TB treatment services still lie in the private sector, and given such widespread resistance, why add to excuses that private practitioners may provide for not referring into the system? It is hard enough to implement public services
as it is. The same issue applied in Nepal, but for a different technical reason: Here, and despite the apparent success of the DOTS programme, a major problem was that rifampicin was not used in the continuation phase. Given that market forces, and the success of the DOTS programme, has resulted in the wider availability of a few well-known and trusted companies’ FDCs being available on the market, it seems to make sense that policy should further this thrust, rather than struggle against it. In short, while the science is important, so too are the local market conditions and local practitioner perceptions when considering national policy. National programmes should be more pragmatic when considering regimen choice.

References:


Note:

1 This paper draws from the collaborative research project Tracing Pharmaceuticals in South Asia (2006-2009) that was jointly funded by the Economic and Social Research Council and the Department for International Development (RES-167-25-0110). The project team comprised: Soumita Basu, Gitanjali Priti Bhatia, Samita Bhattachari, Petra Brhlikova, Erin Court, Abhijit Das, Stefan Ecks, Ian Harper, Patricia Jeffery, Roger Jeffer, Rachel Manners, Allyson Pollock, Santhosh M.R., Nabin Rawal, Liz Richardson, and Madhusudhan Subedi.
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2 The ‘First line drugs’ are as follows: Isoniazid (H), Rifampicin (R), Ethambutol (E), Pyrazinamide (Z), and Streptomycin (S). ‘Second line drugs’ include Kanamycin (KM), Amikacin (AMK), Capreomycin (CM), the Quinolones (FQ) – Cipro, Ofx, Gfz, Mfx - the thiamides (Ethionamide or Prothionamid), Cycloserine (CS), and Para-aminosalicylic Acid (PAS)

3 The DOTS policy includes five core elements; political commitment to increasing resources and including TB as an activity integral to national health systems; sputum microscopy services so that the disease can be correctly identified; short-course chemotherapy, including the direct observation of treatment; uninterrupted supply of drugs and finally, recording and reporting systems (WHO 2002).


6 Lupin’s full list of products available on the market, for example, includes first line drugs and those for the treatment of MDR-TB. In short, the first line drugs are available as single tablets, in strips as single tablets and in Fixed Dose Combinations (FDCs), all with branded names. The branded AKT range – AKT2, 3 & 4 – are ‘kits’, or strips, of rifampicin and isoniazid; rifampicin, isoniazid, and ethambutol; and rifampicin, isoniazid, ethambutol and pyrazinamide respectively. Akukit is the two dose combination, and Akurit 3 and 4 the 3 and 4 dose FDC, all combined in the one tablet. There are also different dose tablets for the individual drugs, including a paediatric range and combinations. Lupin’s are the most popular brands on the market in India and Nepal.

7 This paragraph of the paper is taken from a review of the existing data prepared by Ricks: ‘The Role of Private Practitioners and Pharmacists in Tuberculosis Control in India’. August 2008. Dissertation prepared for the Centre for International Public Health Policy.

8 On the rationale for FDCs see Blomberg et. al 2001, who highlight that the bioavailability of rifampicin in FDCs is a particular issue, one that is easily compromised if manufacturing norms are not strictly adhered to.

9 The GDF is run by a group from the Stop TB partnership secretariat and housed in the WHO. Announced in 1998, a business model for it was developed through 2000, and it was launched in 2001. It acts as a mechanism whereby countries running DOTS programmes can procure their drugs (see http://www.stoptb.org/gdf/).


12 Currently policy in India states that all patients have to register an address and prove it before they can enter into the programme. For many migrants this is a real problem. One private doctor in Delhi we spoke too, and who had signed up to act as a private DOTS provider, had been struck off the programme because recognizing this as an issue she had falsified some of the addresses, then promptly lost them to follow-up.

13 In the Autumn of 2008, after the data collection for the research finished, the Nepal NTP started the process of changing its regimen to a six month one. However, an in-depth review of the programme in 2007 advised that one of the disadvantages of this shift was that – as in India – DOT for any rifampicin based product would result in greater demands on patient time, increasing the direct observation from 2 to 6 months.

14 In a review of the Nepal TB programme in which Ian Harper participated in Autumn 2007, this issue was a key concern raised with the team in an open discussion about the regimen with respiratory physicians.

15 For a summary of the 2003 BMJ debates see Harper (2006). Here the issues were framed as the questions of ‘science’ and evidence, contra the WHO’s dependence on ‘faith’.
How Wide is the ‘Treatment Gap’ for Antidepressants in India?

Ethnographic Insights on Marketing Strategies

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Abstract: This article aims to show that current estimates of treatment gaps for antidepressants in India do not take sufficient notice of the actual availability and affordability of antidepressant drugs. Specifically, the authors try to show that antidepressants are widely given without prescription and that uses are often beyond the control of licensed service providers. Overprescription and misuse of antidepressants might be just as problematic as a lack of drugs and treatments. The driving force in the proliferation of psychotropic drugs even in developing countries like India is private industry pharmaceutical marketing.

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I

Introduction

During the 1990s, mental health moved from a marginal to a central position within global health policies. This shift 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, WHO and other organizations 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).

Once there were unambiguous guidelines in favour of antidepressants in place,
the next step was to assess the gaps in the provision of these drugs worldwide, and it emerged instantly that there is a wide “treatment gap” for depression between developing and developed countries. Closing these treatment gaps is the objective of several high-profile campaigns. For example, the WHO-sponsored 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 states that national investments in these treatments show a vast treatment gap and urges an immediate increase in spending. mhGAP (WHO 2008) argues that the psychiatric treatment gap is “more than 75 per cent” worldwide, that is, only 25 per cent of people who need treatment receive it. Divided by different types of mental disorders, the treatment gap was found to range from 32 per cent for schizophrenia to 78 per cent for alcohol use disorders. Depression treatments showed a gap of 56 per cent. These numbers were only about the global situation, so the treatment gaps had to be deeper in developing countries.

There can be little doubt that the overall assessment of a psychiatric “treatment gap” is correct, if one accepts the premises of DALYs, the efficacy of drugs, and the lack of government spending in this area. Yet what we aim to show in this article is that the “gap” has so far been calculated on a very tenuous base of data. We suggest here that current estimates of treatment gaps do not take sufficient notice of the actual availability and affordability of antidepressant drugs in India. Specifically, we try to show that antidepressants are widely given without prescription and that uses are often beyond the control of licensed service providers. We conclude that overprescription and misuse of antidepressants might be just as problematic as a lack of drugs and treatments. The driving force behind the proliferation of psychotropic drugs even in developing countries like India is private industry pharmaceutical marketing.

II

Concepts and Methodology

The data presented here are drawn from the ESRC/DFID-funded project ‘Tracing Pharmaceuticals in South Asia’. 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 the causes and consequences of global poverty. Research should contribute to poverty-reduction strategies (especially the Millennium Development Goals) by designing and testing new methodological approaches. Our team proposed to find novel ways of studying economic inequality in India and Nepal in relation to pharmaceutical production, distribution, prescription, and regulation. For this we proposed to study the social life
of three drugs in depth: oxytocin, rifampicin and fluoxetine. The three drugs belong to three different therapeutic segments, namely, reproductive health, tuberculosis, and mental health.

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. For example, fluoxetine was only made available in West Bengal government hospitals since 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 in India 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). But the role of the state in the provision of antidepressant treatments still seems small in comparison to what is available privately. Our choice of fluoxetine, instead of older antidepressants—such as amitriptyline, which is long used in government facilities—was meant to highlight the private sector further.

We started our research by following each of the three drugs and visited almost everyone the drug who knew about the drug. This took us to doctors, manufacturers, medical representatives, wholesaler, and retailers.

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. An alternative 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 can 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 is commonsensical to ask, firstly, 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 on what pharmaceuticals are used and only then asks how “depression” is recognized and treated, a different picture emerges.

The social importance of material things has long been studied by anthropologists (e.g., Appadurai 1986; Latour 2005; Henare, Holbraad & Wastell 2007). 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 is especially fruitful to start crosscultural research on depression with observable treatments rather than with symptoms and causes. In our research, 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.

II

Proliferation of Brands

In the initial phases of our research, we collected 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 registers of pharmaceutical products according to therapeutic segments. Printed as cheap paperbacks, such drug reckoners are sold widely, to such an extent that urban street hawkers sell them alongside popular magazines and pirated bestsellers. 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. CIMS India, which is the market leader in this type of publication, is owned by a London-based corporation, CMPMedia. CIMS India also 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 primarily collected by IMS-ORG, an international market research company (http://www.orgims.co.in/). 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.

This proliferation of fluoxetine brands can be partly explained by 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 per cent 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.

Many analyses of the Indian pharmaceutical market stop at manufacturing and the drug patent laws. We found, however, that the patent regime is not enough to explain the wide circulation of antidepressant drugs in India. R&D and patent monopolies are not what distinguish drug companies from one another, but above all their marketing strategies. What approaches are there to the marketing of antidepressants?

III
Marketing Antidepressants Directly to Prescribers

Prescription pharmaceuticals present a unique challenge for marketing, because the ‘target customer’ is the prescribing doctor and not the patient who is buying and consuming the drugs. It is the prescriber who diagnoses the disease and arrives at the conclusion of what kind of medicine the patient should take. In South Asia, prescriptions are written using brand names of the medicines, rather than the generic names. For example, doctors write ‘Fludac 20mg’ instead of ‘fluoxetine 20mg’. The Medical Council of India actually asks licensed doctors to prescribe by generic names as far as possible. Many state ministries of health in India, such as those of Rajasthan and Kerala, have tried to make it mandatory for doctors to prescribe in generic name, but have generally failed to enforce it. When a doctor not only chooses the generic molecule but also a company’s brand, he or she becomes even more important for the pharmaceutical marketing efforts.

A key factor that makes it even more interesting for marketing antidepressants is the absence of a strict measure for depression. There is no pathogen that can be identified in the patient suffering from, and there is not even a conclusive theory about the pharmacological action of antidepressants (Moncrieff 2008). Lack of reliable measures allows prescribers to interpret depression in more than one way, and the clinical uses of “antidepressant” drugs are constantly expanding beyond symptoms of “depression,” and now include social phobia, premature ejaculation, or insomnia. As Kalman Applbaum (2006: 107) points out, the effects of SSRIs on the body are so ambiguous that there is great scope for marketing-drive reinterpretations and diagnostic expansions.

Most psycho-pharmaceutical companies not only visit psychiatrists but also doctors
not specialized in this field. In fact, GPs are seen as the main source of prescriptions for SSRI antidepressants such as fluoxetine. As soon as a drug is securely lodged with psychiatrists, GPs come into marketing focus. According to a Zonal Sales Manager, sales of fluoxetine are not anymore at the centre of his attention, and that his campaigns concentrate on launching newer antidepressants. During an interview with us in early 2007 he explained:

Things like [Fluoxetine] are cash cows. It is productive. We have to build brands now to build our future. .... [Fluoxetine] was one of the brands giving very good dividends. Kolkata and all the suburbs starting selling fluoxetine. We started promoting to GP segment, not psychiatric. We are not focusing on psychiatry, we are focusing on GP segment. And we also got the results. Suddenly there was the increase in the sales..... This tremendous sales we got but not from psychiatry, but from physicians but from diabeto, cardio and all.

A senior MR of an MNC showed us a visual chart he uses during doctor visits. The promotional material contains colourful diagrams of the stomach and the brain. At the bottom of the chart was a picture of a sad-looking man looking down his body, towards his belly. The ad text suggested a connection between depression and gastroenterological problems. A marketing director explained such promotional strategies as follows:

I can tell you that people with stomach problem, [or] arthritis, go to the GPs. Patients normally complain to doctors that ‘I am taking this medicine such a long time still I am not cured. Gas is still there (sir aapne kya dawayi diya hai ke pet ka dard thik nahi ho raha hai... gas to ho raha hai).’ The doctor gets confused about what kind of problem it is.... It is generally seen all over the world now that if the treatment of the physiological disease is not accompanied with psychological treatment then the overall management of the disease is not there. This is one message we give to GPs. And we also have a programme for educating doctors, and we are doing that quite successfully. We are explaining it to the doctors, ‘Sir, this is very important. If you don’t do this, then the patient will not get better.’ This concept was not there with the doctors earlier.

Marketing antidepressants aims at displacing non-pharmacological interventions, such as counselling, as much as possible. Depression “management” might need interventions that include both medication and other alternative means, but pharmaceutical producers try to convince doctors that drugs must always be prescribed. Still now, doctors are often engaged in counselling the patient and trying to unearth the “cause” of depression is important to them. One of the GPs interviewed in a poorer area of Kolkata explains that as a GP, he also plays the role of a family counsellor. At the same time, many GPs try to avoid medication for mild symptoms of depression. A gastroenterologist from Kolkata found it useful to keep his patients away from antidepressants altogether, as he is worried that the patient may get hooked on to it and in the long run it may prove to be more harmful than useful:
I was never fond of prescribing medicines that I was not specialized in. [Q: Others are saying that lots of gastric troubles are psychosomatic] Yes, that is true. But my way of dealing with them is: look, you don’t have to take anything, get lost! [Laughs] I really don’t use psychotropic medicines … once they have taken a prescription for tranquilizers, and maybe they got some temporary relief, what they start doing is, they ignore your advice and keep on taking it without your advice. And eventually they will become dependent on that.

The above case again illustrates how the doctor is the first and foremost agent that pharmaceutical marketing needs to convince of the absolute necessity of drug prescribing. In this case, patients of the gastroenterologist do not buy psychotropics because he thinks that they can cope without it.

Doctors always strive to be seen as “up-to-date” with the latest medical developments, and it is primarily the pharmaceutical industry which tries to be the supplier of know-how. Continuing Medical Education (CME) is an important form of drug marketing. CME events are organised and sponsored by drug manufacturing companies. These usually take place in small conference rooms. GPs and other non-specialists are invited by pharmaceutical companies along with a specialist ‘opinion formers’ who elaborates on the latest drugs and disease management. Within the pharmaceutical industry, doctors are usually categorised into categories of ‘opinion formers’ and ‘followers’. The ‘opinion formers’ are specialists who can influence the prescribing habits of doctors who are in other therapeutic sectors. The marketing executives also classify doctors into ‘core’ and ‘non-core’ group based on their ‘potential’ as measured by the number of patients he sees per day. An MR told us, “We visit the core doctors at least twice a month and for the non-core doctors, we usually schedule a single visit a month.”

### III

**Marketing Antidepressants Indirectly: ‘Floating Prescriptions’**

Prescription pharmaceuticals present a unique challenge for marketing, because the ‘target customer’ is the prescribing doctor and not the patient who is buying and consuming the drugs. It is the prescriber who diagnoses the disease and arrives at the conclusion of what kind of medicine the patient should take. In South Asia, prescriptions are written using brand names of the medicines, rather than the generic names. For example, doctors write ‘Fludac 20mg’ instead of ‘fluoxetine 20mg’. The Medical Council of India actually asks licensed doctors to prescribe by generic names as far as possible. Many state ministries of health in India, such as those of Rajasthan and Kerala, have tried to make it mandatory for doctors to prescribe in generic name, but have generally failed to enforce it. When a doctor not only chooses the generic molecule but also a company’s brand, he or she becomes even more important for the pharmaceutical marketing efforts.
Another very important route through which non-psychiatrists learn about psychotropics is through ‘floating prescriptions’. 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 both 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.

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

Unlicensed allopathic prescribers, usually called Rural Medical Practitioners (RMPs), are also important players in the social life of antidepressants. They have been able to survive in the interstices of legality and illegality, not least because their toleration takes some pressure off the state’s own crumbling health services. According to many of our respondents, patients in the rural and suburban India will be the first victims if the laws of licensed prescribing were to be strictly enforced. But the shady legality of many retail practices also produces high “collateral” costs, and customers have to bear the risks of getting the wrong drugs from the hands of untrained prescribers.

Most of the RMPs get into this profession as a form of self-employment with a very low threshold of entry. The RMPs call themselves “friend of the poor” and say that this profession gives them a sense of “serving the society.” Their backgrounds are similar: they belong to the poorer section of the society themselves; they have had some contact with a licensed prescriber as their assistant, relative, hospital or pharmacy staff.

Being the first point of contact for many patients in the rural areas, the RMP also sees a regular turnover of medical representatives (MR) at their doorstep. Once we accompanied an MR of fluoxetine producing company to an RMP sitting in bustling central Kolkata. His small chamber in the middle of a slum was crowded by patients of all ages. We had to wait outside for a few patients to leave before we could step in. Our MR was ready with his visual flipchart to remind the doctor of his brands. He started with his brand of fluoxetine, telling him about the anti-depressants in one sentence and requesting him repeatedly to write it. The MR later told us that he has been promoting fluoxetine to RMPs quite some time and with ‘good results’.

Pressure of the high sales targets on the marketing divisions of the pharmaceutical companies also aid the proliferation of antidepressant prescriptions among the lowest
qualified doctors, including RMPs. While talking to people working at different levels of the same marketing division, we saw that people who are in the ‘field’, actually visiting the doctors, would go an extra step to meet their sales target for the quarter. The marketing division of the pharmaceutical companies follow the same pattern of reporting. It is a five tier system with medical representatives at the bottom tier with ‘area sales managers’ in the tier above them. The area sales manager reports to the zonal or regional marketing manager of the division, who in turn reports to the national marketing head. The vice president of the division works closely with the national marketing head and is responsible for the overall progress of that division. We spoke to the national marketing head, the regional marketing manager and an MR of a leading fluoxetine brand in South Asia on who they perceive as their target customers. According to the national marketing head, the company caters “only to psychiatrists, neurologists and neurosurgeons, people who deal with the brain.” The regional marketing manager, however, includes GPs and other select non specialists like cardiologist as his target customers though ‘by policy’ RMPs are not targeted. Yet, for the MR working under him, the RMPs play a crucial role in meeting his targets: “if we wish to increase our business, we have to go to them ... Market potential is there. How to exploit it depends upon us.” For all different customers there are different strategies as he explains:

...we have to arrange something for the doctors like camps and perhaps premium payments. But in the interior parts, sometimes, an emotional part comes into play. There, you go from Kolkata and tell the RMP that you’re coming from a long distance away and, ‘as you know, fluoxetine is a very good drug, so please help me out by giving me three or four prescriptions a day.’ There’s a form of sympathetic dealing.

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.

IV

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 WHO methodologies 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. The willingness to prescribe antidepressants might be more of a cause for alarm, than otherwise.

It might seem easy to dismiss the findings on 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. When specialists and non specialists alike are prescribing antidepressants in all the three sites of the study, then in all likelihood, antidepressants have established a much larger market for themselves than what some other numbers might indicate.
Any strategy for better mental health treatments in South Asia must take into account how much antidepressants are already used in the region. Interviews in local medicine shops on what brands of antidepressants are on sale and who the main prescribers are of these drugs can yield far more useful information far more quickly than any of the data sets used by the WHO to date.

References:


Meeting Local Needs in Global Times
Case of Universal Vaccines in India

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and Development Studies (CSIR), New Delhi

Abstract: This article analyses access to stable and affordable supply of vaccines that are needed for mass immunisation programmes, during the post liberalisation period and new IPR regimes. The article points out that the Indian experience of sudden shift from public sector to private sector and preference to public private partnership models at the cost of public sector has not ensured access to universal vaccines to Indian children. The lack of good governance, strict regulation and an evidence-based rational national vaccine policy are major stumbling blocks on the road to a sustainable, affordable stable universal vaccine supply in India.

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I
Introduction

In January 2008, the Drug Controller General of India abruptly suspended production in the three vaccine public sector units (PSUs), the Central Research Institute (CRI, Kasauli, in Himachal Pradesh), Pasteur Institute of India (PII, Coonoor, Tamilnadu) and the BCG Vaccine Lab, (BCGVL, Chennai, Tamil Nadu) alleging that they do not comply with the current World Health Organisation’s (WHO) Good Manufacturing Practices (cGMP). This put the national immunisation programme under crisis. Around this time, the Union Health Ministry announced the upcoming new vaccine park in Chengalpattu in Tamil Nadu based on public-private partnership model that was expected to meet the upcoming Universal Immunisation Programme (UIP) vaccine requirements by 2011 [Ramachandran 2008].

This raised several eyebrows and some pertinent questions such as 1) Why PSUs were not given a chance to upgrade to WHO-cGMP compliance, when they were under the very same union health ministry, especially at a time when their productions had peaked and the vaccine demand supply gaps were narrowing down, and there had been no complaints at all on the quality of the vaccines produced? 2) Why were PSUs asked to stop production even before the proposed centralised GMP compliant vaccine park
became operational at Chengalpattu, Tamil Nadu? 3) How would the Government meet the demand-supply gap of universal vaccines till the new vaccine park commences production, especially at a time when there is a short supply of primary vaccines the world over (http://www.unicef.org/supply/index_vaccine_security.html>) (Fig.1) with very few primary vaccine manufacturers? What was the economic logic of spending over Rs.150 crore on building a new vaccine park when modernising existing PSUs would have cost less than Rs. 50 crore? Will the new companies that come up in the vaccine park really manufacture the vaccines indigenously or repackage them from the imported bulk?

If they import, what is the point in achieving GMP compliance at the cost of indigenous manufacturing ability? If dependence on private sector supply or import is inevitable, how will the government tackle concerns of biosecurity and strategic national health security? [Madhavi 2008]

Fig 1: Global Shortage for EPI vaccines

![Graph showing global shortage for EPI vaccines]

Though several Indian PSUs involved in vaccine production have been closed down in the last 15 years (Table1), and despite the role of the remaining PSUs in narrowing demand-supply gaps for universal vaccines by 2006 (Table 2), demand-supply gaps for universal vaccines peaked during 2008 (Table 3) with the closure of three vaccine public sector units that have major contribution to the country’s UIP vaccine requirement (~70 per cent of DTP and 100 per cent BCG). Despite the private sector’s promise of meeting UIP vaccines at par with the prices of PSUs, the shortages for UIP vaccines continue.
till today [Ramachandran 2009]. In this context, this paper traces and analyses the trajectory of public and private sector’s roles and access to stable and affordable supply of vaccines needed by the national immunisation programme, especially in the current context of changing socio-economic-political scenario, and implications for national vaccine policy.

Procurement of UIP vaccines

The Bhore Committee Report 1946 indicated that the child mortality due to infectious diseases was very high in India and it needed to improve child health status to improve the health of the nation [GOI 1946a]. Though there was house-to-house BCG vaccination programme after BCG vaccine laboratory was set up in 1948 in Chennai (then Madras), regular vaccination of children against infectious diseases in India was adopted only in 1978 in alignment with WHO’s policy of “Health for all by 2000AD” that underlined primary health care approach. India adopted tetanus toxoid (TT), diphtheria toxoid (DT), diphtheria, pertussis, tetanus toxoid (DPT), oral polio vaccine (OPV), Bacillus Calmette Guerin (BCG) and Typhoid vaccines under its Expanded Programme on Immunization (EPI) to vaccinate children regularly under primary health care. These vaccines are provided by government in India free of cost in all primary health care centers. Since they were launched as EPI programme they are referred to as EPI vaccines. These vaccines are also called primary or universal vaccines as they are under the national immunization programme and vaccines against diseases such as Japanese Encephalitis, Cholera, Yellow fever, Hepatitis B etc., were classified as secondary vaccines as they are given as per the demand.

Subsequently, primary or EPI vaccines have come to be known as universal vaccines, with the launch of Universal Immunisation Programme (UIP) in 1985 aimed to achieve ~85 per cent immunization coverage in children and pregnant women by 1990. In 1985, measles vaccine was introduced under UIP and typhoid vaccine was excluded. The UIP was adopted as a Technology Mission launched by the Ministry of Health and Family Welfare with the Department of Biotechnology (DBT) as the nodal agency to support the UIP programme by promoting vaccine R&D towards self-reliance in vaccine technology and self-sufficiency in vaccine production (GOI 1987-88). This was the first time some policy aspects of vaccine development, production and immunization were articulated by the Union Government, though a clear, coherent and comprehensive national vaccine policy was never adopted. This is partly the reason why national vaccine production in general and PSUs in particular drifted away from the original objectives of self-reliance and self-sufficiency.

It was not difficult for India to meet the objectives of UIP with its fairly institutionalized
### Table 1: Fate of Vaccine Public Sectors Units (PSUs) in India By 2008

<table>
<thead>
<tr>
<th>Vaccine PSU</th>
<th>Year of Establishment</th>
<th>Vaccines/Sera Produced</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Haffkine Institute, Mumbai. (then Bombay Bacteriological Laboratory)</td>
<td>1898</td>
<td>DT, TT, Plague, Cholera, typhoid, rabies, gas gangerene anti-toxins, anti-dysentry, anti-snake venum</td>
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<tr>
<td>2. Pasteur Institute of India, Kasauli.</td>
<td>1900</td>
<td>Anti-rabies, (closed down)</td>
</tr>
<tr>
<td>3. King Institute of Preventive Medicine, Guindy, Chennai. (then Madras)</td>
<td>1898</td>
<td>Vaccine lymph, TT, Typhoid, cholera (production suspended in 2005)</td>
</tr>
<tr>
<td>4. *Central Research Institute, kasauli.</td>
<td>1905</td>
<td>Typhoid, cholera anti-snake venum, anti-rabies (production suspended in Jan 2008)</td>
</tr>
<tr>
<td>7. The Pasteur &amp; Medical Research Institute, Shillong, Assam.</td>
<td>1917</td>
<td>Typhoid, cholera, anti-rabies treatment (closed down in 2006)</td>
</tr>
<tr>
<td>8. Vaccine Lymph Department, Belgaum.</td>
<td>1904</td>
<td>Vaccine lymph (production stopped, closed down in 1980s)</td>
</tr>
<tr>
<td>9. Vaccine Lymph Department, Calcutta.</td>
<td>1890s</td>
<td>Vaccine lymph (closed down in 1980s)</td>
</tr>
<tr>
<td>10. The Cholera Vaccine Lab, Calcutta.</td>
<td>1890s</td>
<td>Cholera (closed down in 1980s)</td>
</tr>
<tr>
<td>11. Pasteur institute, Calcutta.</td>
<td>1910</td>
<td>Anti-rabies (not satisfactory functioning, now it is a teaching institute) (closed down in 1980s)</td>
</tr>
<tr>
<td>12. The Bengal public health Lab, Calcutta.</td>
<td>1900</td>
<td>Cholera, now conducts sterility tests of other govt. labs (since mid 1980s)</td>
</tr>
<tr>
<td>13. The Provincial Hygiene Institute, Lucknow.</td>
<td>1900</td>
<td>Cholera (closed down recently)</td>
</tr>
<tr>
<td>14. The vaccine Lymph Dept., Patwada Nagar (now called State vaccine Institute)</td>
<td>1903</td>
<td>Vaccine lymph, anti-rabies (closed down 2003)</td>
</tr>
<tr>
<td>15. The vaccine Institute, Ranchi.</td>
<td>1900</td>
<td>Vaccine lymph, cholera, anti-rabies (closed down recently)</td>
</tr>
<tr>
<td>16. The School of Tropical Medicine, Calcutta.</td>
<td>1921</td>
<td>Epidemiological and other routine diagnostic services. No vaccine production (since 1980s)</td>
</tr>
<tr>
<td>17. Institute of Preventive Medicine, Hyderabad. (Then Plague Department).</td>
<td>1870</td>
<td>Plague, Smallpox (since 1910), rabies (since 1976-77)TT (since 1978) (production of anti-rabies, TT stopped in 2002 and the company was closed down in 2005)</td>
</tr>
<tr>
<td>No.</td>
<td>Institution</td>
<td>Year (established)</td>
</tr>
<tr>
<td>-----</td>
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<tr>
<td>18.</td>
<td>Vaccine Institute, Vadodara. (became PSU in 1973)</td>
<td>1973</td>
</tr>
<tr>
<td>19.</td>
<td>Public Health Laboratory, Tiruvananth Puram.</td>
<td>1937</td>
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<tr>
<td>20.</td>
<td>Public Health Laboratory, Patna.</td>
<td>1900</td>
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<tr>
<td>21.</td>
<td>Public Health Laboratory, Bangalore.</td>
<td>1900</td>
</tr>
<tr>
<td>22.</td>
<td>Indian Immunologicals Ltd., Hyderabad.</td>
<td>1983</td>
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<tr>
<td>23.</td>
<td>Bharat Immunological and biologicals Ltd., (BIBCOL), Bulandshar Delhi.</td>
<td>1989</td>
</tr>
<tr>
<td>26.</td>
<td>Bengal Chemicals and Pharmaceuticals ltd., Kolkata. (established in 1901 as private company, became PSU in 1980)</td>
<td>1901</td>
</tr>
<tr>
<td>27.</td>
<td>Smithstrain Street Pharmaceuticals Ltd., (established in 1821 as private company, became PSU in 1977)</td>
<td>1821</td>
</tr>
<tr>
<td>28.</td>
<td>Vaccine Institute, Nagpur. (established in 1959 and became PSU in 1980)</td>
<td>1959</td>
</tr>
<tr>
<td>29.</td>
<td>West Bengal lab Calcutta (became PSU in 1980)</td>
<td>1980</td>
</tr>
</tbody>
</table>

* suspended production in Jan 2008.

Source: Compiled from Annual reports of health and Family Welfare, Health Information of India, MOHFW, GOI, New Delhi.

Vaccine R&D and production. Several institutions that were set up during British India were restructured to produce DTP group of vaccines since 1978. BCG vaccine was supplied by BCGVVL for the entire country. However, 100 per cent of OPV and measles vaccine was imported to meet the I requirements of UIP. Measles vaccine was not produced in the country, as technology was not available. Since 1992, the entire measles vaccine required for UIP has been met by a private company, Serum Institute of India,
Table 2: Demand and Supply of UIP vaccines

<table>
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<tr>
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<tbody>
<tr>
<td></td>
<td>Demand</td>
<td>Supply</td>
<td>Demand</td>
<td>Supply</td>
</tr>
<tr>
<td>DPT</td>
<td>1320.24</td>
<td>1270.30</td>
<td>1362.20</td>
<td>182.50</td>
</tr>
<tr>
<td>DT</td>
<td>350.00</td>
<td>650.82</td>
<td>360.00</td>
<td>820.00</td>
</tr>
<tr>
<td>TT</td>
<td>1190.00</td>
<td>2319.71</td>
<td>140.00</td>
<td>529.00</td>
</tr>
<tr>
<td>BCG</td>
<td>500.60</td>
<td>168.50</td>
<td>550.00</td>
<td>350.00</td>
</tr>
<tr>
<td>OPV*</td>
<td>1550.60</td>
<td>*950.50</td>
<td>534.00</td>
<td>600.00</td>
</tr>
<tr>
<td>Measles</td>
<td>500.00</td>
<td>680.00</td>
<td>550.00</td>
<td>700.00</td>
</tr>
</tbody>
</table>

Source: Compiled from Annual Reports of Health Information of India 1991-92 and National Health Profile 2008, DGHS, India. *All imported Source

Pune, that bought technology from elsewhere [Madhavi 1997]. Since 2002, Indian Immunologicals Ltd., Hyderabad (IIL), a PSU under National Dairy Development Board (NDDB) also started the manufacture of measles vaccine indigenously and supplies some amount to UIP. BCG supply from BCGVL became self-sufficient since 2002. OPV was also produced indigenously since late 1990s in HBPCL Mumbai that supplied OPV to UIP. Though, PII Coonoor produced polio vaccine indigenously between 1967-76, due to unexplained reasons, OPV production was stopped abruptly [Madhavi 2007]. Since then OPV has become a major import. Thus, DTP, TT, DT and BCG are produced indigenously in the country in the public funded organizations that largely took care of UPI requirements, though a few private companies (Bengal immunity ltd., Bengal Chemicals and Pharmaceuticals Ltd., etc.) also supplied small quantities to UIP. The country was able to meet the annual UIP requirements by importing some quantities of DTP group of vaccines whenever there was insufficient production and supply of UIP vaccines and the demand-supply gaps for UIP vaccines were met to a large extent by 2007.

In 2008, the dramatic suspension of the 3 major vaccine PSUs that catered to most of the UIP needs created the paradoxical situation that still exists in India: while there exists a critical shortage of childhood vaccines, there is also an abundance of new expensive vaccines and their combinations in the market, being promoted heavily through media advertisements, industry campaigns, medical dealers, private practitioners, professional bodies and others. The lack of a national vaccine policy has facilitated the growth of the new vaccine Market, while the current crisis for universal vaccines peaked. The success of a country’s immunisation programme is determined by several local factors such as pathogen variations, incidence levels that qualify for mass vaccination, efficient
disease surveillance system, development and/or procurement of vaccines, choice of technologies, choice of selective vs. universal vaccination (even among childhood vaccines), logistics, cost-benefit analyses, and resource mobilization [Madhavi 2005]. While these factors are important and complimentary to each other, this article focuses on only the fate of Indian indigenous vaccine production capacities and its implications for access to stable and affordable supply of universal vaccines.

II

Indian Vaccine PSUs

It would unjust if India forgets its past glory in vaccine research and production for over 100 years, and how these oldest vaccine institutions stood up to meet national needs in testing times (the first and second world wars and during epidemics), despite overloaded service functions, inadequate manpower and poor patronage from the state. India’s venture into modern medical research began with vaccine research that was fairly institutionalized during British colonial rule in India. For example, i) a plague vaccine was developed first in India at the Haffkine Institute Mumbai; ii) CRI Kasauli was the first laboratory in the world to produce anti-Rabies vaccine, it is the only one of its kind in the South East Asia region for yellow fever vaccine, and also a certifying authority for all the vaccines produced in the country; iii) PII was the first institute in India to clinically evaluate the anti-rabies serum-vaccine therapy in 1917 in the treatment of human beings---PII Coonoor developed tissue culture rabies vaccine indigenously, and also manufactured relatively cheaper DTP-HB indigenously just before its closure [Ramachandran 2008] ; iv) the King Institute of Preventive Medicine, Chennai developed smallpox vaccine indigenously, through minor innovations, improved yields of anti-cholera vaccine and TT vaccine; and v) BCGVL proudly claims that it is the first and the only Institute under the Ministry of Health & Family Welfare, that was awarded ISO 9002 by M/s Bureau Veritas Quality International (BVQI), London to get international accreditation including WHO cGMP requirements in 1994, and BCGVL became self-sufficient in BCG vaccine required for the entire country since 2002 (http://mohfw.nic.in/dghs.htm). Many of these PSUs also undertook minor process/protocol innovations in vaccine development and production that improved yields and reduced costs of production. There were three private companies set up between 1890-1910 to produce synthetics, dyes and other pharmaceutical products, that have also produced vaccines and sera against infectious diseases [Kumar 1998]. However, it is the public funded vaccine institutions that mainly developed, produced and met all national vaccination needs.

R&D and production were traditionally under the same roof to facilitate coordination,
Table 3: The Demand-Supply Gap Following Vaccine Procurement from Private Suppliers 2008-09 (in Lakh doses)

<table>
<thead>
<tr>
<th>Supplier</th>
<th>Vaccine</th>
<th>Total order placed</th>
<th>Total requirement</th>
<th>Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>B.E Ltd., Hyderabad</td>
<td>TT</td>
<td>1,360.00</td>
<td>1,708.00</td>
<td>348.00</td>
</tr>
<tr>
<td>B.E Ltd., Hyderabad</td>
<td>DPT</td>
<td>800.00</td>
<td>1,579.87</td>
<td></td>
</tr>
<tr>
<td>SII, Pune</td>
<td></td>
<td>300.00</td>
<td></td>
<td></td>
</tr>
<tr>
<td>IIL., Hyderabad</td>
<td></td>
<td>63.00</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>1,163.00</td>
<td></td>
<td>416.87</td>
</tr>
<tr>
<td>B.E Ltd., Hyderabad</td>
<td>DT</td>
<td>375.00</td>
<td>432.66</td>
<td>57.66</td>
</tr>
<tr>
<td>Bharat Biotech Ltd., Hyderabad</td>
<td>OPV</td>
<td>1,350.00</td>
<td>1,581.86</td>
<td></td>
</tr>
<tr>
<td>HBPCL, Mumbai (pipeline)</td>
<td></td>
<td>180.50</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>1,530.50</td>
<td></td>
<td>51.36</td>
</tr>
<tr>
<td>SII, Pune</td>
<td>Measles</td>
<td>360.00</td>
<td>391.20</td>
<td></td>
</tr>
<tr>
<td>IIL., Hyderabad</td>
<td></td>
<td>90.00</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>450.00</td>
<td></td>
<td>58.80</td>
</tr>
<tr>
<td>Excess procurement</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SII, Pune</td>
<td>BCG</td>
<td>600.00</td>
<td>759.21</td>
<td>159.21</td>
</tr>
</tbody>
</table>


Table 4: Declining Budgetary Allocations

<table>
<thead>
<tr>
<th></th>
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<tbody>
<tr>
<td>BIBCOL</td>
<td>10</td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>(For both)</td>
<td>550</td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>(For both)</td>
<td>453</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
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<tr>
<td>(For both)</td>
<td>4.09</td>
<td>0.2</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>3.0</td>
<td>5.31</td>
<td>0.05</td>
<td>0.05</td>
<td>0.00</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IVCOL</td>
<td>0.91</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>1.5</td>
<td>0.0</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Source: Compiled from DBT Annual reports. BIBCOL: Bharat Immunological and Biologicals Ltd., IVCOL: Indian Vaccine Corporation Ltd.

technology transfer and commercialisation. A few centrally sponsored institutions such as Central Research Institute Kasauli, BCGVL Chennai, and others set up under the respective states during British India to develop vaccines and sera against dog bites, snake bites, insect bites and infectious diseases that were a major public health threat at that time got restructured and reoriented to produce EPI vaccines since the launch of EPI in 1978. For instance, institutions such as PII Coonoor, CRI Kasauli, Institute of Preventive Medicine (IPM), Hyderabad etc., that were initially set up to develop vaccines and sera against rabies, also started production of DTP group of vaccines. With the declaration 88 Meeting Local Needs in Global Times: The Case of Universal Vaccines in India / Madhavi of India smallpox free in 1976, institutions such as KIPM, Chennai, Vaccine Institute Belgaum, Pasteur Institute Shillong etc., stopped smallpox
vaccine production and started the manufacture of TT, DT and DTP. At that time Hathi committee felt that the existing conventional technologies for the production of TT, DT and DTP were fine and recommended use of same techniques of production [GOI 1975]. These aged institutions continue to carry out multiple tasks including epidemiological investigations, water testing, production of reagents, diagnostic services, blood bank services, training of S&T staff, vaccine research, development, production and supply of vaccines even today, though the Hathi committee felt that the production and R&D functions should be separated and regional centres should be established to carry out supply functions [GOI 1975].

Another significant development during mid 1970s was the government take over of private companies such as Bengal Chemicals and Pharmaceutical (BCPL) (1980), Bengal Immunity Limited, (BIL) (1977), Smith Strainstreet Pharmaceuticals Ltd., (SSPL) (1977), West Bengal Lab (1980) based in Calcutta (now Kolkata), Vaccine Institute Baroda (1973), and Vaccine Institute Nagpur (1980). Thus, the public sector units that produced primary vaccines increased in number by 1980s [Madhavi 2007]. Ironically, it is these very units that were closed down in post 1990s owing to liberalization in India.

Though, DBT was formally established in 1986, it was functioning as board since 1982 to harness biotechnology for mankind and vaccines are one of main focus areas of the health under biotechnology. In the late 1980s the launch of UIP under Technology Mission gave a further boost to indigenous vaccine R&D and production and DBT was entrusted with the i) production of newer vaccines for UIP, and ii) to promote R&D for new and improved vaccines. DBT set up three expert/technical committees in 1988 evaluated the state-of-the-art technologies for the production of oral polio vaccine (OPV), inactivated polio vaccine (IPV) and vaccines against measles and rabies. For the production of IPV and rabies vaccine, the committees opted for the Vero cell (micro-carrier) fermentation technology and for the production of the measles vaccine the chick embryo fibroblast cell culture, and for OPV primary monkey kidney cell culture based technology [GoI various years]. Thus, DBT took the initiative to meet the demand-supply gaps for universal vaccines [GoI 1987-88].

In 1989 DBT setup two public sector units, Bharat Immunologicals and Biologicals Ltd. (BIBCOL), Bulandhshhar and Indian Vaccine Corporation Ltd. (IVCOL), Gurgaon) to meet demand-supply gaps for universal vaccines. IVCOL was to produce 20 million doses of measles vaccine, 50 million doses of IPV and 40 million doses of DPTP. IVCOL was closed down in 1992 as technology for the production of measles was
Table 5: Reported Shortages of EPI Vaccines from Different States between Jan-Oct 2008

<table>
<thead>
<tr>
<th>State</th>
<th>Vaccine shortage</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Haryana</td>
<td>TT for pregnant women (TT Pw), DPT</td>
</tr>
<tr>
<td>2. Andhra Pradesh</td>
<td></td>
</tr>
<tr>
<td>3. Arunachal Pradesh</td>
<td>BCG</td>
</tr>
<tr>
<td>4. Andaman and Nicobar Islands</td>
<td>BCG</td>
</tr>
<tr>
<td>5. Assam</td>
<td>DPT, Measles</td>
</tr>
<tr>
<td>7. Chandigarh</td>
<td>TT Pw, DPT, BCG</td>
</tr>
<tr>
<td>8. Chhattisgarh</td>
<td>DPT</td>
</tr>
<tr>
<td>9. Delhi</td>
<td>TT Pw, DPT, yellow fever (No DPT vial stock since mid July 08. No stock of yellow fever vaccine for last 4 months)</td>
</tr>
<tr>
<td>10. Gujarat</td>
<td>TT Pw, DPT</td>
</tr>
<tr>
<td>11. Himachal Pradesh</td>
<td>DPT</td>
</tr>
<tr>
<td>12. Jharkhand</td>
<td>TT Pw</td>
</tr>
<tr>
<td>13. Karnataka</td>
<td>TT Pw</td>
</tr>
<tr>
<td>14. Kerala</td>
<td>DPT, yellow fever (State requires eight lakh doses of vaccines a year against the 2.5 lakh doses provided by the Centre this year. The State cannot procure these vaccines locally as the Centre was not ready to fund their purchase)</td>
</tr>
<tr>
<td>15. Lakshwadeep</td>
<td>TT Pw, BCG</td>
</tr>
<tr>
<td>16. Madhya Pradesh</td>
<td>TT Pw</td>
</tr>
<tr>
<td>17. Maharashtra</td>
<td>TT Pw, DPT yellow fever</td>
</tr>
<tr>
<td>18. Orissa</td>
<td>TT Pw and shortages of DPT, BCG, OPV and measles was also reported from Koraput district</td>
</tr>
<tr>
<td>19. Punjab</td>
<td>DPT</td>
</tr>
<tr>
<td>20. Rajasthan</td>
<td>TT Pw</td>
</tr>
<tr>
<td>21. Tamil Nadu</td>
<td>TT Pw, yellow fever</td>
</tr>
<tr>
<td>22. Uttar Pradesh</td>
<td>TT Pw</td>
</tr>
<tr>
<td>23. West Bengal</td>
<td>TT Pw, DPT</td>
</tr>
</tbody>
</table>


not available from Pasteur Merieux Serum & Vaccines (PMSV), France, as it became private company and India was viewed as potential future market for measles vaccine (Madhavi 1997). BIBCOL that was WHO-GMP certified, aimed to produce OPV and plasma derived Hepatitis B indigenously by 1992. However, BIBCOL was declared sick and IDBI was appointed to prepare a revival package in 2000 [Madhavi 2007]. The declining budgetary allocations to both the PSUs (Table 4) imply that it is not mere coincidence that both the PSUs set up by DBT failed during post liberalization
The closure of PSUs in the last 15 years (See Table 1 and Fig. 2) has drastically affected the access to universal vaccines 30 years after the launching of EPI in 1978. As there was no demand for smallpox and cholera vaccines, five vaccine PSUs were closed down in 1980s. Around 14 Indian Vaccine PSUs were closed down during 2000-2008. Vaccine Institute Baroda, IPM Hyderabad, SVI Patwadanagar, Bengal Immunity, Kolkata, SVI Belgaum, BCPL Kolkata were closed down between 1995-2005, and PI Shillong was closed in 2006. In 2008, production was suspended in three PSUs (CRI, PII, BCGVL) and their conversion to testing labs was envisaged. However, the closure of PSUs in post 1990s seems to be slow withdrawal of state funding/support from these institutions due to the introduction economic liberalisation policies in India. By 2008 India was left with only three PSUs functioning one under Maharashtra state government (HBPCL, Mumbai), one under National Dairy Development Board (NDDB) and one under DBT (BIBCOL, Bulandshar). Though erratic production patterns (Fig. 3) and demand supply gaps for EPI vaccines were observed over the years (Table 2), demand-supply gaps for universal vaccines have peaked (Table 3) last year due to the suspension of production in three vaccine PSUs that made a major contribution of UIP vaccines, resulting into acute shortage in 23 states in India (Table 5 and 6).

Though, there have been national efforts since the launching of EPI in 1978, the changing roles of public sector and private sector in meeting vaccine requirements have precipitated last year’s crisis of acute short supply of primary vaccines in India. A glance at current vaccine scenario in India indicate that despite fair vaccine production system in the country, production patterns of universal vaccines has always been erratic (Fig. 3) and demand supply gaps (Table 2) increased for all UIP vaccines despite national efforts through DBT [Madhavi 1997, 2007]. Over the years, declining role of public sector (Fig 2) and increasing role of private sector (Fig. 2) during post 1990s leading to the

![Table 6: Demand and Supply](chart.png)
declined production of UIP vaccines (Fig. 4) and increased production of new vaccines (Fig. 5).

However, increased growth of private sector did not contribute to the increased production of UIP vaccines, due to private sector’s low interest in UIP vaccines (Fig. 4) and its high interest in new vaccines (Fig. 5) leading to the orphanization of UIP vaccines in post 1990s in India. Further, demand supply gaps for universal vaccines peaked (Table 3) during the last year (January 2008) due to the suspension of production in three vaccine PSUs that account for 70 per cent of DTP and 100 per cent BCG of county’s UIP requirement. This led to the severe shortages for UIP vaccines from 23 states within six months (Table 5). In some states even in urban areas some children did not receive 2nd and 3rd doses of vaccines due to their non-availability. It was reported that many states have run out of their supplies and the government has not allowed them to pick up even the existing stocks from the PSUs. Around 300 deaths were reported in a hospital in a remote village in Bihar out of 700 patients admitted suffering from diphtheria, tetanus and pertussis. According to the health ministry’s data, compared to 2007-08, DPT vaccination in 2008-2009 (from April to November) fell by 29.5 per cent in Orissa and 36.2 per cent in West Bengal. BCG vaccination fell 7.9 per cent in Uttar Pradesh and 11.5 per cent in Punjab [Varshney 2009]. In fact, how India will resolve the current crisis of short supply of UIP vaccines, especially in the context of a global shortage for primary vaccines resulting from the decline of primary vaccine production in many companies, is a moot question and has implications for access to vaccines in future.

**Changing production profiles of PSUs**

Experienced vaccine PSUs not only did multiple tasks, but also changed production profiles as and when required, even till recently. For instance, during the first and second world wars they were forced by import restrictions to become self-reliant and self-sufficient in vaccine production [GoI 1946b]. In 1957 during influenza epidemics, PII, Coonoor carried out research to isolate and culture influenza virus to make the vaccine [Pasteur Institute 1957]. In 1976 after the country was declared smallpox free, KIPM Chennai adapted itself to produce DTP group of vaccines [KIPM 1985]. Similarly PII Coonoor produced OPV between 1967-76 indigenously and DTP group vaccines since 1978 till recently as per government orders. In 2006, PII Coonoor that was set up initially as a philanthropic organization to develop a vaccine against rabies and treat patients with dog bites was asked to stop its production after more than 100 yrs of its service. PII has been doing service to the nation through innovative treatment methods against dog bites, and was also producing a tissue culture based human anti-rabies vaccine indigenously since late 1997. Union health ministry ordered PII to start the production of measles vaccine [Madhavi 2008].
PII did oblige the ministry’s request and bought measles vaccine from a newly set up private company Green Signal Bio Pharma based in Tamilnadu by the then PII director.

**Fig 2: Growth dynamics of PSUs and private vaccine firms**

![Graph showing growth dynamics of PSUs and private vaccine firms.](image)

*Source: Compiled from Annual Reports of Health information of India and National Health Profile 2008, DGHS, India.*

**Fig 3: Erratic production of UIP vaccines**

![Graph showing erratic production of UIP vaccines.](image)
for Rs.3.25 crore, which was otherwise available virtually for free from another PSU, Indian Immunologicals Institute, Hyderabad. Interestingly, the Health Ministry sanctioned PII Rs 17.80 crore for branching out into measles vaccine production only after it entered into the deal with Green Signal Bio Pharma. According to media reports, the entire deal was allegedly executed to help the private company, as it stipulates that the PSU would produce measles vaccines from the seed and give away 70 per cent of the profit to Green Signal Bio Pharma [Gopikrishnan, 21st May 2008]. Objections have been raised in an audit on the misuse of financial powers and bypassing of procedures that were overlooked by the top functionaries of the ministry. Interestingly, Green Signal Bio Pharma could purchase BCG seed from the PSU, BCGVL (also headed at that time by the then PII director), for a mere Rs. 1.05 lakh, indicating that private firms get PSU resources for a song, whereas PSUs buy even free resources from favourite private firms by paying them the moon [Madhavi 2008]. One wonders, why PII was asked to change its production profile from anti-rabies to measles vaccine, when there was enough supply of measles vaccine from SII, Pune for UIP. It appears on the face of it that the indigenous manufacture of measles vaccine is being encouraged/shifted to PSU by the union health ministry. However, on the contrary, media reports indicate that this is only to favour two new private vaccine companies based in Chennai. While the reasons for changing production profiles in PSUs may be political, PSUs always obliged the parent ministry’s orders and were willing to adopt to the changes as and when required despite difficulties.

![Fig 4: Primary vaccine Suppliers to Indian EPI in The Last Four Decades](image)

Source: Compiled from Annual Reports of Health Information of India 1991-92 to 2004-05 and National Health Profile 2008, Directorate General of Health Services (DGHS), India.
These instances illustrate that unfortunately that PSU resources (raw material, skilled manpower, know-how, etc.) were often utilized to the full in such a manner that the PSUs benefited the least and the private sector the most. To cite few more examples, the famous private vaccine company Serum Institute of India, based in Pune was formed with erstwhile employees of Haffkine institute in 1960s. Even the newly set up Shantha Biotech in late 1990s derived inputs for Hepatitis B indigenous production from public funded organizations for developing technology, skilled manpower as well as infrastructure and institutional support [Hari 1997]. Moreover, Shantha Biotechnics which developed an indigenous hepatitis-B vaccine and was the most pampered by Indian government as a model for home-grown, government-supported private enterprise, has now been taken over by the French multinational company (MNC), Institut Merieux and is being eyed up by another MNC GlaxoSmithKline. This situation not only increased the uncertainty in availing affordable vaccines, but also affected public sector scientists who transferred technologies, as Shantha no longer honours its commitments to them. Hindustan Health Care Limited (earlier Hindustan Latex Ltd.) a PSU given charge of upcoming vaccine park (under public private partnerships) is also planning to access technologies from the existing PSUs for primary vaccine production in vaccine park, while new vaccine production is envisaged through public private partnerships.

It is not an exaggeration to state that today Indian private sector’s indigenous capacity would not have existed if there is no indigenous public sector. Thus, promoting private sector at the cost of PSUs amounts to killing indigenous vaccine capacities/strengths,
especially at a time when developed countries like US, UK are reconsidering to revive their PSUs in view of biosecurity/national security [Bunn 2008; Blume and Geesink 2000]. In some European countries like Netherlands, vaccine PSUs have traditionally been serving the national vaccine needs and continue to do so today. The Netherlands Vaccine Institute (RVI) is an agency of the Dutch Ministry of Health, whose core task is to guarantee the supply of vaccines for national immunisation programmes, by in-house production or by manufacturing vaccines under license from pharmaceutical companies. A US Institute of Medicine report on vaccine development recommended a government-owned vaccine research and production facility to produce vaccines against emerging disease threats and bioterrorism. In United States, shortages of several paediatric vaccines occurred between 2000-2002 due to the private manufacturers changing production profiles from UIP (eg.TT) vaccines to new vaccines (pneumococcal vaccine). This left only one other national producer, which did not have enough time to meet the shortfall. In 2004, the MHRA suspended Chiron’s manufacturing license for its influenza plant in Liverpool due to contamination. The company was scheduled to supply approximately 48 million doses to the US; it did not produce vaccine for a year whilst addressing the problems [Anon ]. Seasonal influenza vaccine manufacturing problems affecting the UK’s supply occurred in 2005 and 2006. However, this did not affect the number of doses reaching patients since more than one manufacturer contracted by the Department of Health was producing the vaccine. This illustrates how reliance on a single supplier can leave the national health systems exposed, a concern raised by the House of Commons Public Accounts Select Committee in 2003 [PAC 2004]. It is evident that even in developed countries UIP has been affected because of its reliance on single and private manufacturer.

Indian PSUs have done dependable services to the national immunization needs by developing, manufacturing and supplying UIP vaccines, besides carrying out a range of other public health services. Yet, they did not receive enough patronage from the ministries under which they were functioning, despite their inherent interest. The case of Haffkine Institute is a reflection of state of affairs in many older vaccine institutions [Madhavi 2000].

The government support received by these public sector units was for only enhancing production capacities, and they did not receive much deserved support for upgrading infrastructure, R&D, technological growth and compliance to good manufacturing practices (GMP). Moreover, there were no changes in their governing bodies since their inception and lack of vision on their part to promote R&D through incentives that can be inbuilt with in the institutional structures, neglect, and bureaucratic controls added.
to the systematic decline of the state patronage of PSUs. Even the policies of economic liberalization in 1990s did not enhance the functional autonomy of the vaccine PSUs. It is ironic that no money was sanctioned for their cGMP upgradation worth (Rs 50 crore), while generous sanction was given to the tune of Rs 150 crore on the upcoming vaccine park. On the contrary, supporting and reviving PSUs became politically unfashionable and blaming the PSUs and manufacturing political consent for their closure became the favourite pastime of the powers that be. Operationally, starving and stifling PSUs till they failed to meet some regulatory requirements was a safe strategy, as the action taken on the PSUs would seem like an act of good governance [Madhavi 2008]. Thus, the attenuation of PSUs has severely affected the indigenous manufacturing capability, and has also led to the orphanization of primary vaccines. While some of the remaining vaccine PSUs have already become importers and repackaging units over the years, skeptics fear that the Hindustan Healthcare Ltd., though a PSU (does not have the technology, experience or credibility to manufacture world-class vaccines as compared to any of the Indian vaccine PSUs) likely to go down the same path of bottling and repackaging of imported stocks or enter into the public-private partnerships [Ramachandran 2008].

The fate of PSUs in this country and their credibility in meeting national vaccine needs and with private sector’s uncertain behaviour indicate that the private sector at best can be complementary to public sector with good governance in place, but it cannot be a replacement in view of national public health and bio security concerns. How the government is going to meet the current crisis of short supply of UIP vaccines, with private sector going back on its promise and vaccine park coming up only in 2011 is bigger challenge to face.

### III

**Private Sector in Vaccines**

Indian vaccine private sector began to grow in late 1980s. Today there are around 30 companies (Table 7, Fig. 2) manufacturing and marketing vaccines in contrast to three functional PSUs in the country. One would have expected that the growth of private sector would meet the void (for universal vaccines) created by public sector’s closure. That has not been the case. The private companies policy of prioritizing their new

<table>
<thead>
<tr>
<th>Vaccine Institute</th>
<th>Year of establishment</th>
<th>Vaccines/sera produced</th>
</tr>
</thead>
<tbody>
<tr>
<td>Company</td>
<td>Year</td>
<td>Products Offered</td>
</tr>
<tr>
<td>----------------------------------------------</td>
<td>--------</td>
<td>----------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>2. Shantha Biotech, Hyderabad</td>
<td>1993</td>
<td>r-Hb, DTP-HB (2005) and JE vaccine</td>
</tr>
<tr>
<td>5. Cadila Laboratories</td>
<td>1952</td>
<td>Typhoid</td>
</tr>
<tr>
<td>7. Zydus Cadila (a division of zydus biogene manufactures vaccines)</td>
<td>1995</td>
<td>R-HB, typhoid, anti-rabies, chicken pox vac</td>
</tr>
<tr>
<td>9. LG Lifesciences India Pvt. Ltd.,</td>
<td>2002</td>
<td>r-HB</td>
</tr>
<tr>
<td>10. Unichem Laboratories Ltd., Mumbai</td>
<td>1944</td>
<td>but ventured into biotech business in 2001 including vaccines</td>
</tr>
<tr>
<td>11. VHB Life sciences Inc</td>
<td>1946</td>
<td>R-HB, typhoid, anti-rabies, varicella vaccine</td>
</tr>
<tr>
<td>12. Solvay Pharma India Ltd., Mumbai</td>
<td>Since 2004</td>
<td>Markets Netherland’s Influenza vaccine</td>
</tr>
<tr>
<td>13. Intas Biopharmaceuticals Ltd., Ahmadabad</td>
<td>2000</td>
<td>r-HB</td>
</tr>
<tr>
<td>14. Pfizer India Ltd.</td>
<td>Mid 1990s</td>
<td>Markets r-HB made in USA and also shantha biotechs Hb vac</td>
</tr>
<tr>
<td>15. Wyeth India Ltd., Mumbai</td>
<td>Started as ledrle lab ltd in 1947 and later changed its name to cynamid Uindia ltd and in 1962 and became Public sector. In 1998 3 copanies merged as Wyeth Ledrle ITd and in 2003 as Wyeth Ltd., a MNC company now.</td>
<td>Markets Hib, DTP, prevenar since late 1990s</td>
</tr>
<tr>
<td>16. Chowgule &amp; Co. (India)</td>
<td>Late 1940s</td>
<td>Triple antigen</td>
</tr>
<tr>
<td>17. GlaxoSmithKline India</td>
<td>Established in 1924 used to produce vaccines and in 1970s it business is more on other medicines and in post 1990s ventured into new vaccines</td>
<td>Varicella, DTP-HB, Hib, Hib conjugate, DPT, Hepatitis A, Hib-TT</td>
</tr>
<tr>
<td>18. Sanofi Pasteur India Ltd.,</td>
<td>1997</td>
<td>Typhoid, Hib, anti-rabies, varicella, OPV, combination vacs, Pneumococcal, Hib, Hepatitis A, meningococcal</td>
</tr>
<tr>
<td>19. Zydus Cadila Healthcare Ltd., Ahmadabad</td>
<td>2002</td>
<td>Varicella, typhoid,</td>
</tr>
<tr>
<td></td>
<td>Company Name and Address</td>
<td>Year of Establishment</td>
</tr>
<tr>
<td>---</td>
<td>--------------------------</td>
<td>-----------------------</td>
</tr>
<tr>
<td>20.</td>
<td>Chiron Behring vaccines Ltd., Ankelswar India</td>
<td>In 1978, and Hoechst sold its rabies manufacturing unit to Chiron Behring vaccines India Ltd., and taken over by Aventis and now by Sanofi pasteur</td>
</tr>
<tr>
<td>22.</td>
<td>Biomedical Private Ltd., Ghaziabad</td>
<td>2000</td>
</tr>
<tr>
<td>23.</td>
<td>Dano vaccine &amp; Bio hyderabad,</td>
<td>2000</td>
</tr>
<tr>
<td>25.</td>
<td>Transgene biotech Ltd., Hyderabad</td>
<td>2000</td>
</tr>
<tr>
<td>27.</td>
<td>Childcare Biotech Ltd., Jalgaon, Maharashtra</td>
<td>2000</td>
</tr>
<tr>
<td>28.</td>
<td>Ruchi Networks, New Delhi</td>
<td>Post 2000</td>
</tr>
<tr>
<td>30.</td>
<td>Rajgarhia Drug Agencies, Ranchi</td>
<td>1982</td>
</tr>
</tbody>
</table>

Source: Compiled from websites and annual reports of companies [http://pharmaceuticals.indiabizclub.com/directory/vaccines; http://mohfw.nic.in/dofw%20website/family%20welfare%20programme/vaccines.ht and (http://www.nature.com/nbt/journal/v25/n4/fig_tab/nbt0407-403_T4.html](http://www.nature.com/nbt/journal/v25/n4/fig_tab/nbt0407-403_T4.html)


Vaccine business (Fig 5) over UIP vaccines (Fig 4) has only aggravated the situation. Though private sector set up DTP production plants, they are more interested in making new non-UIP vaccines or their dubious value-added combinations, rather than supplying the DTP for the government’s UIP. While it may be true that the overall production in
the last couple of years (till the public sector units were closed) has increased to meet the demand, this growth in production may have come from two sources. 1) The PSU’s themselves pushed up their production in the last few years, perhaps in a last ditch attempt to prevent their imminent closure- which itself may have diverted their attention from GMP. 2) The private sector seems to have recently enhanced its production of UIP vaccines (strangely enough, considering their earlier disinterest despite mounting shortages), in anticipation of the closure of the PSUs.

It is evident from last year’s (2008) experience that the shortages of UIP vaccines in 2008-09 are much more when compared to previous years (Table 6), even with few sinking PSUs by 2006 and despite private sector’s promise to the union health ministry that it would supply to Indian UIP at par with PSU prices. On the other hand the private sector units that promised to supply UIP for one year at subsidized prices started complaining by July 2008 that their revenue has gone down by 22 per cent due to this supply and they may not be able to supply UIP vaccines at the same price in the following year (Biospectrum 2008). The situation has not improved even after one year. In fact, the health ministry was forced to get vaccines illegally from the very public sector manufacturers it suspended previous year (2008). In 2008-2009, the government has bought DPT worth Rs 1.1 crore; DT worth Rs 30 lakh and Rs 1.2 crore worth of TT from the Central Research Institute, Kasauli [Varshney 2009]. This indicates that it is the public sector that is responding to UIP needs in the midst of its own crisis for survival. According to some officials in the procurement wing of health ministry, private manufacturers had hiked prices and not supported the nation during a crisis. The vaccine cost for diphtheria, pertussis, tetanus and BCG for 2008-09 turned out to be Rs 64.29 crore, compared to Rs 32.20 crore the previous year. It was also not clear from table 3, why ministry has placed order for more quantity of measles vaccine than required [Varshney 2009].

Clearly, it makes economic sense to depend on the public sector for the supply of affordable vaccines for the universal immunization programme, rather than leaving the health security of the country to the mercy of the private industries and politicians. These instances prove that the private sector in no way matches public sector’s willingness and promptness in meeting national needs unless they are made to do so. Only good governance with good regulatory system in place can ensure access to vaccines through private sector.

**Regulations ensuring access to universal vaccines**

Vaccine production was stopped abruptly in three existing PSUs (CRI, Kasauli, PII, Coonoor, and BCGVL, Chennai, TN), in Jan 2008, by Drug Controller General of
India (DCGI) alleging that they were not compliant with current “Good Manufacturing Practices” (cGMP). It was pointed out by the health ministry that they had no option but to close these units as WHO would derecognise the Indian National Regulatory Authority (NRA), if Indian companies do not meet WHO-cGMP standards. WHO-GMP is a certification of a process adopted by the World Health Organisation to ensure that products are consistently produced and controlled according to quality standards. It’s objective was to set up uniform global standards to minimize the risks (contamination, causing damage incorrect labels on containers, insufficient or too much active ingredient, ineffective treatment or adverse effects, etc.) involved in any pharmaceutical production that cannot be eliminated through testing the final product. Many countries have formulated their own requirements for GMP based on WHO-GMP. India’s Schedule M is comparable to WHO-GMP, that is awarded and certified on behalf of WHO by the DCGI under ministry of health and family welfare (MOHFW).

Though, these PSUs could meet GMP standards earlier in 2001 and 2004, they could not meet them in 2007 as they were made more stringent, referred to as current GMP standards (cGMP), and companies have to become cGMP complaint every time with the latest modifications in WHO-GMP guidelines. The stringent rules in the current GMP standards are related to structural, process and documentation deficiencies, and the institutes could rectify process deficiencies but could not rectify structural and documentation deficiencies [Ramachandran 2008]. The institutes stated in their reply to the DCGI that limited funds and lack of functional autonomy in recruitments, promotions, maintaining staff, finances, structure etc., and the lack of flexibility in running these biological industrial units due to bureaucratic limitations as the reasons for their inability to comply with the GMP norms [Madhavi 2008]. While it is desirable that PSUs should become cGMP complaint, government’s action of closure in haste without making reliable alternative arrangements (till vaccine park comes up) to meet resultant short supplies of UIP vaccines met severe criticism. The government had the following options to exercise, yet, it did not, that led to skepticism.

1. Since the expenditure of making PSUs WHO-cGMP compliant is meager compared to costs on upcoming vaccine Park, the health ministry should have sanctioned the money by giving a chance to PSUs. Critics wondered why the ministry, that owns and governs the vaccine PSUs, could not wait till they were made compliant with the increasingly stringent GMP norms, before taking such a drastic action on them, despite PSUs request to sanction money in order to become GMP-compliant.

Moreover, the health ministry did not accept the WHO offer to help them to become cGMP compliant[Rajya Sabha Secretariat 2009]. It is not a big deal to make these PSUs GMP complaint as many of Indian pharmaceutical companies including Indian private
vaccine companies such as serum institute of India, Shantha biotech, Panacea biotech, have WHO-GMP certification and have complied with much tougher requirements of US FDA and EU and WHO’s pre qualification requirements for export. About 800 Indian drug companies including big, medium, and small are WHO-GMP complaint for making a wide range of liquids, tablets, capsules, injections, bulk drugs and vaccines and sera. And about 40 Indian drug companies (very few of them MNCs) have been approved by international regulatory agencies of UK, USA, Australia, EU, Brazil, etc. (www.pharmabiz.com). Spending a few crores of Rupees on vaccine PSUs is meager when compared to the money spent on vaccine park that would come up only after 3 years, and also when compared to the costs of purchasing imported vaccines from private companies. Most importantly, costs on child health due to non-availability of universal vaccines and the possibility of rise of childhood diseases and treatment costs would be of grave national public health concern.

2. PSUs should have been allowed to produce UIP vaccines till they become cGMP compliant, as there is no complaint about the quality of vaccines produced by these PSUs. It is not clear whether stringent application of GMP norms were applicable only to vaccine PSUs or to the Pharmaceutical industry as a whole, since there seem to be many private Pharmaceutical companies that operate without GMP certification. The 34th Parliamentary Committee pointed out that the GMP status of private company Biological Evans that supplies vaccines to UIP is not very clear. The ministry did not hesitate to import Japanese Encephalitis vaccine in 2006 from GMP noncompliant Chinese manufacturers. The ministry is also aware that Chinese exports were neither hit due to their non-compliance, nor was the Chinese NRA de-recognized by the WHO [Ramachandran 2006]. Clearly, the Chinese Government seem to handle the WHO and its NRA better than the Indian Government [Ramachandran 2008].

3. Since cGMP is required for exports through WHO-UNICEF, the DCGI had the option of banning PSUs from exports until they were made cGMP complaint and till the vaccine park come up. Critiques pointed out that if Indian NRA is derecognised by WHO it would hit private vaccine units rather than PSUs. According to former health minister Ramadoss, “Derecognising Indian NRA as a country means even private units that are CGMP certified will not be able to export. Today India exports vaccines worth nearly Rs.1,000 crore to international agencies, such as UNICEF, all of which will be cancelled.” It appears that the ministry was more interested in private sectors exports, than the consequences of sudden closure with the resultant severe short supply of UIP vaccines. Compliance with WHO-GMP is mandatory only for exporting vaccines or buying them through the UNICEF vaccine procurement system and not for indigenous
That means that the DCGI and the health ministry had the option of suspending only exports till the PSUs became GMP compliant to meet indigenous demand, considering the fact that there was no complaint on the quality of the vaccines produced in those PSUs. Vaccine Institute (RIV) under the Dutch ministry in Netherlands improved Salk’s injectable polio vaccine (IPV) vaccine, and the incentive came both from the country’s commitment to a particular immunisation schedule (the combined polio and DPT vaccine) and from technical achievements that reduced dependence on wild monkeys, and this vaccine has been insulated from market forces as the Dutch ministry was not interested in exports [Blume and Geesink 2000]. Indeed China, Netherlands and other countries have effectively exercised this option to protect their PSUs and indigenous public health needs from the vagaries of international regulation. India is making quality medicines and vaccines for years without a WHO-GMP and by following their own idea of aseptic clean manufacture, and without any reported fatalities, it is argued that that the setting up uniform global standards such as good manufacturing practices (GMP), good lab practices (GLP), global intellectual property regimes (IPR) tend to become trade barriers in the form of International Conference on Harmonization (ICH), to inhibit countries like India from entering the international trade (personal communication, Srinivasan, LoCost). Before the last General Elections, there were rumours in the media that these three PSUs were going to be reopened due to public furore.

However, other reports [Nagarajan 2008] pointed out that the ministry may simply be buying time till the upcoming elections of May 2009. Even though the PSUs would be revived, they would not be asked to produce anti-rabies, DTP and BCG, but other vaccines. That means by not allowing Vaccine PSUs to produce vaccines in which their expertise lies, that comprises 80 per cent of the Indian UIP market, the PSUs would be rendered redundant. On the other hand, since the closure of CRI affected private companies’ vaccine exports, (worth 1,500 crore) as CRI Kasauli certifies all vaccines before release for consumption, It is predicted that the government might reopen these units, though the threat to convert these institutes to testing labs still remains. In September 2008, WHO did not approve any new vaccine from India temporarily as Indian NRA failed its quality bench marks [Mathew 2008]. Companies like Shantha Biotech, Panacea Biotech and Serum Institute of India are eagerly waiting to supply new vaccines to WHO-UNICEF procurement system, while they refused to meet national UIP vaccine shortages. The same private companies, beneficiaries of PSUs closure, that were very critical about PSUs GMP standards, also justified their closure. However, the same private vaccine companies were very eager by September 2008 that these PSUs should be revived, since derecognition of Indian NRA by WHO would be a deathblow.
to private sector vaccine business. According to the consultancy firm KPMG, vaccines dominate the Indian biopharma market and contribute about 51 per cent of its $1.4 billion revenues. [Varshney 2009].

4. The health ministry could have exercised the choice of making the private sector supply to UIP vaccines at affordable prices with appropriate regulations till the PSUs become GMP compliant and till the Vaccine Park is ready. Indian experience reveals that private sector is not a reliable option for stable and affordable supply of vaccines. Doubts have been expressed regarding the upcoming Vaccine Park, and whether the public sector unit, Hindustan Healthcare Limited (HHL) (then HLL) that does not have any expertise in vaccines whatsoever (except that it mediated occasional import of some vaccines to the government), would be able to manufacture quality vaccines and remain WHO-cGMP compliant forever in the upcoming park. Moreover, there is no guarantee that HHL would not meet the same fate as these three public sector units in the near future. Also, whether the public private partnerships (PPP) in the Vaccine Park are going to be cGMP complaint and produce quality vaccines or are they going to supply imported vaccines is anybody’s guess. Most, importantly, how is the Indian government prepared to deal with any similar crisis that may arise in future? Given that the plan for vaccine park and future vaccine market in India was projected by Earnst & Young, a US based consultancy organization, many wonder whether this vaccine park through PPPs is not surreptitiously meant for multinational corporations to produce or supply new vaccines.

It is not that regulatory issues have come up only today, as many instances in the past reveal that the Indian vaccine PSUs have been made victims despite producing quality products. It is interesting to note that the OPV was indigenously prepared in PII Coonoor between 1967-1976 with the coordinated efforts of Government of India, World Health Organization (WHO) and Dr. Sabin, the discoverer of OPV vaccine. However, in 1976 the Government of India ordered PII to stop production alleging that some of the batches were found reactogenic. They samples were sent to the Haffkine Institute and facilities abroad for testing if they were virulent, just before the launching of EPI in WHO member countries. Since then OPV is one of the major imports among EPI vaccines until late 1990s [Madhavi 2007]. But later, it was found that the OPV batches from PII were perfectly safe and according to S. Archetti of WHO, that particular batch of Indian OPV were of excellent quality and the toxicology report of National Institute of communical diseases (NICD) was faulty [Ramachandran 2008]. It is intriguing to note that even then, the indigenous OPV production was not revived. There have been studies indicating
that the indigenous production is more economical compared to its imports [John 1981]. Yet, India opted for imported OPV on the advise of WHO. Similarly, one of the public sector vaccine institutes wanted to grow monkey kidney cell culture for the indigenous production of OPV, but they were discouraged on the advice of WHO and it was only in late 1990s that Haffkine Biopharmaceuticals (HBPCL) was allowed to obtain seed virus from abroad for its indigenous production. Once again in 2000, the Maharashtra State Government refused to buy OPV from HBPCL alleging that it was not potent, and procured OPV from Radicura Pharma, a private company. HBPCL had to file a PIL against the Maharashtra Government that it was a false allegation designed to favour a private company [Madhavi 2000]. Even the ultramodern GMP-compliant vaccine PSUs that emerged during post 1990s under the Department of Biotechnology faced regulatory hurdles, when UNICEF refused to accept OPV supplies from Bharat Immunologicals and Biologicals made from bulk imported from a Russian PSU, alleging that the vaccine from Russia was not WHO GMP compliant. India had no option but to import OPV bulk from Smith Kline Beecham (SKB) on the advice of WHO and only then was BIBCOL continues to function as a repackaging unit [Madhavi 2007]. Given this background, there is no guarantee that the emerging Hindusthan Health Care-led vaccine park at Chengalpattu would not meet the same fate as the other vaccine PSUs.

Media reports indicate that the real reasons behind the closure of PSUs were rather political than scientific and legal to promote vaccine private sector, and the reasons of WHO-GMP compliant comes in handy to kill the existing PSUs [Ramachandran 2008; Madhavi 2008]. It is also not very clear whether the newly set up private companies --- Green Signal Biopharma and Vatsan Biotech, Tamil Nadu --- that have benefited from these three PSUs for raw material, skilled manpower and finances (according to media reports) are WHO-GMP compliant! According to media reports, the Controller of Audit had raised serious objections regarding dubious financial dealings between the director of PII, BCGVL and the Green Signal Biopharma and Vatsan Biotech ltd., Tamilnadu, on the alleged corruption, favouritism, mismanagement and for not following procedural norms [Gopikrishnan, May 23d 2008]. It was pointed out by the 34th parliamentary standing committee on health, that the ministry did not take the offer of WHO to help in making these PSUs GMP complaint, rather it closed them and was not discussed in the cabinet before the units were closed (Rajya Sabha Secretariat 2009). Meanwhile, public health activists filed a public interest litigation (PIL) in view of the emerging child health crisis due to acute shortages of primary vaccines [Mudur 2009].
IV

Conclusion and Discussion

The President of India in her first address to the nation after the elections in May 2009, announced [Ray 2009], (backed up by health ministry’s endorsement under its 100 days agenda) that the three vaccine units that were suspended in January 2008 would be reopened is welcome a step, though the fate of these PSUs is still uncertain as government is planning to introduce pentavalent vaccine (DTP-HB-Hib) in its national immunization programme [http://www.indianexpress.com/news/pentavalent-vaccine-likely-to-be-introduced/480971/]. Since PSUs do not produce pentavalent vaccine, government would procure pentavalent vaccine from private companies, making public sector’s 70% of DTP production in the country redundant.

Secondly, the scientific rationality of introducing such combination vaccines under UIP becomes questionable and controversial as there is no unanimity among scientific community regarding its safety, protection efficacy and cost-efficacy in Indian population. Scientific evidence from India indicates that children develop immunity against Hib during infancy [Puliyel et al 2001]. Very few studies in India indicate that the incidence is very low in Indian population. [Minz et al 2009, IBIS 2002], Moreover, evidences from other countries show that in Hib vaccinated populations, some highly virulent Hib mutant strains are reported to have replaced the native strains [Bruce et al 2008, Lipsitch 1998, Muhalman 1996]. Hib vaccine induced Type 1 diabetes in children in some countries have been reported [Classen and Classen 2001 & 2002]. Srilanka launched pentavalent vaccine in its national immunization programme in Jan 2008 and in Oct 2009, SriLankan government suspended vaccination of pentavalent vaccine following four deaths after vaccination. [http://www.kuenselonline.com/modules.php?name=News&file=article&sid=13837]. Similarly, in Oct 2009 Bhutan suspended Pentavaent vaccination after 8 children died after vaccination[http://www.kuenselonline.com/modules.php?name=News&file=article&sid=14972], though WHO climed in NOV 2009 that these deaths were not due to vaccine[http://www.southasianmedia.net/index_story.cfm?id=618737&category=Frontend&Country=BHUTAN&pro=0]. These examples only underscore the need to establish the necessity, efficacy and safety of Hib vaccine in Indian population based on scientific evidence. from India Therefore, Hib vaccination becomes highly contentious and unethical, whether alone or in combination, without its proven efficacy and safety..

In general, the safety and efficacy aspects of combination vaccines are not proven beyond doubt [Girard 2005; Comenge & Girad 2006; Beri et al 2002, MIMS India
Nov 2009, Beeching et al 2004], and it is reported that they are less protective when compared to their individual components [FDA 1997; American Academy of Pediatrics 1999; Buttery et al 2005; Greenberg et al 2000; Kalies et al 2004; White et al 1997


Combination vaccines do not have price advantage either. Most combinations, including the pentavalent vaccine, are not multivalent by design but are simple cocktails, which means that industry adds vaccines and multiplies prices. Pentavalent vaccine is costly, and may increase immunisation costs, as combination vaccines in general are more expensive than the existing primary vaccines. For instance, DTP vaccine that comes for Rs. 3 per dose from PSU and by combining DTP with Hepatitis B increases the price of DTP several fold (17-100 times fold) costlier [Madhavi 2006], indicating that the combination vaccines are nothing but meant for IPR and pricing advantages..

Worse, virtually every combination vaccine combines one of the universal vaccines with one or more of the new vaccines whose need for mass immunization has not been established beyond doubt. These are ingenious ways of ‘value addition’ invented by private sector in India and abroad marketing vaccines to increase its margins to sell to governments and individuals, just because they are available off the shelf.

If the pentavalent vaccine is introduced into UIP, the private sector will have no incentive to supply DTP at its original price (less than one-fiftieth the price of pentavalent), and will either stop selling it or increase the price of DTP substantially. Private sector refused to supply UIP vaccines at par with the prices of PSUs 6 months after the closure of the three PSUs, as it complained of loss in its revenue from vaccine sale. This experience with private sector during the suspension of 3 public sector units certainly indicates that the country cannot rely entirely on private sector for stable and affordable supply of UIP vaccines. Thus, pentavalent would adversely affect the DTP availability & pricing.

Introduction of Pentavalent vaccine in Indian UIP will kill PSUs even before revival, as pentavalent is produced only by private sector so far. Government purchase of pentavalent vaccine from private sector for UIP will deprive the PSUs of their earnings from DTP (their main source of income), while the government will waste public money
on buying dubious DTP+ combinations. The government should ban UIP and Non-UIP combinations to prevent market distortions and to meet shortages of the 6 UIP vaccines on priority basis.

Thus, introducing a pentavalent combination vaccine (DTP-HB-Hib) in UIP would be additional crisis, while country is not even prepared to set its house first, by resolving the current crisis of increased demand-supply gaps for UIP vaccines. One wonders why national governments have to pay money while private companies benefit at the cost of child health.

Thirdly, by over emphasising the logic of convenience in giving multiple vaccines together (often at the expense of lack of scientific evidence for their need, efficacy and safety), private companies have specialized in the art of adding vaccines and multiplying prices. This creates an artificial scarcity for affordable UIP vaccines, while the market is flooded with costly UIP-nonUIP combinations. It is estimated that the introduction of DTP-HepB in Indian UIP, would cost twice that of the national TB control programme [Madhavi 2006]. Combination vaccines are basically industry’s ploy to capture UIP market that ensures future markets for their new vaccines through backdoor entry.

The current crisis of short supply for UIP vaccines must be resolved to ensure stable affordable supply of UIP vaccines as a priority by reviving and restrengthening Indian PSUs, and Indian indigenous capacity should not be compromised before introducing any new vaccine in Indian UIP. Several Indian studies indicate that many of the new imported vaccines may not be cost-effective and beneficial in Indian population keeping in view of epidemiology of prevailing diseases and protection efficacies of those vaccines [Phadke 2000; Arora and Pulivel 2005; Madhavi 2003, 2006]. Therefore, scientific, economic rationality and suitability must be established in Indian population, before introducing any new vaccines (and their combinations) in Indian UIP and these studies should be made transparent to win public confidence.

It is important to strengthen indigenous vaccine capacities not only to access universal vaccines, but also to tackle recent health emergencies such as swineflu. The recent emergence of swineflu in April 2009 and its spread in India, almost entirely from United States (US) originating passengers has prompted India to request the US to screen and retain outgoing passengers. While this could have retarded the spread, there have been embarrassing moments when patients ran away from the abysmal conditions in government hospitals in the national capital of Delhi and had to be brought back with police help. The state of the public health system in the country is far too well known,
The ongoing battle against H1N1 (swine) flu has many lessons for developing countries already battling their ailing economies. One wonders whether Tamiflu (which was stock piled in case of emergent epidemic) would be protective against any future epidemic if H1N1 virus gets mutated. This also indicates that after all disease control is not about fire fighting against outbreaks, but of proper planning.

Table 8: Prices of Vaccines Produced by Public and Private Sector

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Quantity</th>
<th>Public Sector (Indian Rupees)</th>
<th>Private Sector (Indian Rupees)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary (UIP) Vaccines</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>OPV</td>
<td>10ml</td>
<td>9.22</td>
<td>52.11</td>
</tr>
<tr>
<td>DPT</td>
<td>5ml</td>
<td>13.75</td>
<td>~15.00 - 215.00</td>
</tr>
<tr>
<td>TT (adsorbed)</td>
<td>5 ml</td>
<td>~2.40 to 5.12</td>
<td>37.50</td>
</tr>
<tr>
<td>TT</td>
<td>5 ml</td>
<td>2.68</td>
<td>5.83</td>
</tr>
<tr>
<td>DT</td>
<td>5ml</td>
<td>5.75</td>
<td>-</td>
</tr>
<tr>
<td>Measles</td>
<td>1 ml</td>
<td>None</td>
<td>~56.84 to 1125.</td>
</tr>
<tr>
<td>BCG</td>
<td>1dose</td>
<td></td>
<td>~10.00</td>
</tr>
<tr>
<td><strong>New/Improved Vaccines</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hepatitis B</td>
<td>Pediatric dose</td>
<td>None</td>
<td>~45.00 to 181.00</td>
</tr>
<tr>
<td></td>
<td>Adult dose</td>
<td></td>
<td>~190.00 to 345.00</td>
</tr>
<tr>
<td>DTP-Hepatitis B conjugate</td>
<td>Adult dose</td>
<td>None</td>
<td>~97.00 to 225.00</td>
</tr>
<tr>
<td>R-Vac (against rubella)</td>
<td>1 dose</td>
<td>None</td>
<td>36.80</td>
</tr>
<tr>
<td>MMR</td>
<td>0.5ml</td>
<td>None</td>
<td>66.05</td>
</tr>
<tr>
<td>Anti-Rabies</td>
<td>0.5ml</td>
<td>~147.00 to 184.50</td>
<td></td>
</tr>
<tr>
<td>HAVRIX (for hepatitis A)</td>
<td>1ml</td>
<td>None</td>
<td>~294.00 to 1125.66</td>
</tr>
<tr>
<td>Meningococcal A&amp;C</td>
<td>Adult dose</td>
<td>None</td>
<td>1360.00</td>
</tr>
<tr>
<td>Influenza type B</td>
<td>1 dose</td>
<td>None</td>
<td>48.85 to 370.00</td>
</tr>
<tr>
<td>Typhoid</td>
<td>0.5ml</td>
<td>None</td>
<td>~185.00 to 400.00</td>
</tr>
<tr>
<td>HPV vaccine</td>
<td>1 dose</td>
<td>None</td>
<td>~3000.00</td>
</tr>
<tr>
<td>Anti-rabies vaccine</td>
<td>1 dose</td>
<td>~290.00 to 1112.50</td>
<td></td>
</tr>
<tr>
<td>Chickenpox</td>
<td>1 dose</td>
<td>None</td>
<td>~1430.00 to 1500.00</td>
</tr>
<tr>
<td>Hib-TT</td>
<td>1 dose</td>
<td>None</td>
<td>~400.00</td>
</tr>
</tbody>
</table>

Source: Compiled from MIMS India 2008

India must revive its indigenous capacities in view of price advantage (Table 8), and private sector should be made to meet national immunisation/health needs through...
good governance and regulations. The presence of PSUs acts as a market deterrent to prevent monopolies in key areas of public health, make affordable products available for mass use (therefore saving the government health budget that goes into vaccine purchase), as well as to ensure health sovereignty (by avoiding imports or aid politics) and health security (biosecurity, biowarfare and defence concerns). Indigenous private sector can supplement and complement the government’s efforts, but cannot be seen as a substitute.

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Irrational Pharmaceutical Promotion Practices

Amitava Guha*

Abstract: Brand promotion is double edged: it is necessary to effectively market a product; but can also harm the interests of consumers. This is especially so with medicines. Unethical promotion practices of the pharmaceutical industry have caused grave harm, as this article illustrates.

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Pharmaceutical companies spend large sums of money on the promotion of their products. In an absolute sense this is not surprising, since the pharmaceutical sector is very large: in 1996, 1.2 per cent of GDP in industrialised countries was spent on pharmaceuticals. But pharmaceutical promotion outlays are large in a relative sense as well. In the entire economy, firms spend an average of 2 per cent of their revenues on promotion. For pharmaceutical firms this percentage is much higher; estimates imply that around 15 per cent-25 per cent of their revenues are spent on promotion.

--Windmeijer, de Laat, Douven and Mot, 2004

The term promotion explicitly involves profit as the role of information and dissemination of knowledge. Promotion itself is aimed to generate demand which may or may not pre-exist. It may be debatable issue whether a medicine is required to be promoted even if it is essential; yet promotion has become a very integrated term with medicines. One can argue that medicines are part of business not charity, and therefore profit is also a key motive for the pharmaceutical industry. Brand promotion with inflated claims for other commodities can be acceptable with some limitations. Brand promotion for medicines is acceptable provided that the drug industry adheres to a framework of ethics. In the absence of ethics, regulation or application of sparsely available law, this industry can do enormous harm as is evident from a closer look at India.

Three Cs of Promotion

The three Cs of promotion generally adopted by the pharmaceutical industry all over are convince, confuse and corrupt. Medicine are a commodity where the consumers have no choice. It is the sole responsibility of a prescribers to select the medicine or rather the brand of medicine for their patients thus making industry’s job easier to simply convince the prescriber. A number of strategies adopted in promotion to convince a prescriber may not act, and then comes the need to confuse the prescriber in some other way. In case both these process do not yield results, the easy way to achieve success is to corrupt the prescriber.

Let me illustrate this with a story in a write up of Senator Henry A. Waxman published
in the *New England Journal of Medicines* *(Volume 352:2576-2578; June 23rd, 2005).* While marketing rofecoxib, an inhibitor of cyclooxygenase-2 that had been marketed as Vioxx since May 1999, an anti-inflammatory medicine, Merck company was very careful to suppress the fact that it increases cardiovascular risk. The medicine became a blockbuster after its introduction in 1999. Then a large sized randomised, controlled trial sponsored by the same Merck company known as VIGOR study showed that though the medicine has fewer gastrointestinal complications than naproxen, yet those who used this medicine had four times as many myocardial infarctions as those who were given naproxen. While promoting Vioxx, Merck carefully avoided the later findings of VIGOR trial. The medicine was prescribed to 100 million patients alone in US before its withdrawal from the market.

Then on February 7, 2001 US FDA directed Merck to inform medical profession about the observations of the trial on the potential danger of the medicine. From the next day Merck directed its sales representatives to avoid any discussion on VIGOR trial. Instead they circulated a ‘Cardiovascular Card’ indicating that rofecoxib was associated with 1/8 the mortality from cardiovascular causes of that found with other anti-inflammatory drugs. All the references used in this card are from pre-approval studies where the medicine was used in low dose that too for short term. None of these studies were designed to find out cardiovascular effect of the medicine. Countering the statement of pharmaceutical association that many physicians learn about new drugs — indeed, about ongoing research in their areas of specialization — largely through information provided by the companies that market new products, Senator Waxman commented, “But if the primary goal is sales, not education, and the information provided to physicians is slanted or misleading, the health consequences for patients can be serious.”

**Corruption**

This process is very widely used by the pharmaceutical industry in nicely decorated coats so that society does not at a glance consider them as simple bribes.

In 2002 the state of Vermont in the US introduced a ground breaking law to remedy the situation of uncontrolled promotional expenditure of pharmaceutical industry by requiring the medicine companies to publicity report promotional gifts and payment to physicians.

The second round report of the committee which looks after the implementation of the law published disclosure made by the pharmaceutical company (See report by Attorney General William H. Sorell and Assistant Attorney General, Julie Brill dt. May 10, 2005). The report informed that for the period from July 1, 2003 to June 30, 2004 (FY 04) 48 companies spent $ 3.11 million towards fees, travel expenses and other direct payments to physicians, hospitals, universities and others. This amount if projected for estimation
of national level expenditure would arrive at a figure telling that US Pharmaceutical industry spends $1.45 billion outright to pay to physicians and universities to earn prescription of their medicines in FY 04.

The Vermont report does not include requirements, free samples, compensation for clinical trials, payments under the head of continuing medical education, educational scholarship and any single payment under $ 25. Therefore it does not provide total sales promotion expenditure of the medicine companies. It also stated that in six months 25 recipients accepted $900,804 or 62 per cent of the money sprinkled while 426 recipients or 5 per cent accepted $ 1,450,750 in that FY04 [Cha 2005].

Primary Mechanism of Sale of Non-Essentials Medicine

For any essential materials including essential medicines the primary requirement of access is reach ability and the price. Yet for medicines one can add appropriate information as a third dimension. In third world countries for any essential materials no marketing or sales promotion is visible. Materials for our daily consumption do not even bear brand names excepting those, which are promoted in big shopping malls. Incidentally for medicines aggressive marketing is the only process for survival of a company at sizes big, medium and small. Is it then absolutely necessary for sale of a medicine aggressive marketing is inseparable component of business or it is a tool to push medicines, which are in- essential, but fetches more profit.

In the global level ‘me too’ medicines having no significant advantage over the existing advantage over the existing ones are quite large in number. During the period 1981 to 1988, of the new medicines marketed by the top 25 US pharmaceutical companies, a mere 12 or only 3 per cent ‘made an important contribution to existing therapies’; 13 per cent made a ‘modest potential contribution’ and the rest 84 per cent made ‘little or no potential contribution’. According to the US Food and Drug Administration (FDA), effective new chemical entities represent 361 out of 1035, or 35 per cent of those marketed in the US between 1998 to 2000 [NIHM 2002]. It is notable that all these 84 per cent non-potential medicines are sold in the market and are highly priced.

It is not easy to produce a blockbuster medicine always so that a medicine company can monopolise global market and earn exclusive profit for years together form it. In fact the ‘golden decades’ of 1940 to 1980 no longer persists when scores of new medicines of different therapeutic groups were introduced. Today this flow has nearly dried up. The medicine companies have therefore become busy in producing medicines which are not required.

In 2004 nearly 1300 new brands were allowed to be introduced in India [Annual Report of AIMS 2005]. The major instrument of sale of these medicines in the developed countries and more for the sale of irrational medicines in our country is aggressive sales
promotion, often do not await ethical practices or codes.

**Product First, Indication Later**

It is also important to analyse the mechanism of introduction of new medicine in the market particularly in the perspective of proliferation of irrational combinations. An interesting article published in BMJ (2003) explains how a new medicine can be introduced in the market overcoming any social and legal hassles those might involve. The authors offered formation of a hypothetical company, HARLOT Plc and said at the very onset of the write up that “the authors have amalgamated the world’s two oldest professions in a new niche company, HARLOT plc, specialising in How to Achieve positive Results without Lying to Overcome the Truth.”

The authors described that for the methodologies of introduction of a new medicine, the company would insist on the following:

a) Choosing a ‘new’ medicine which would generate a good profit margin.

b) E-Zee-Me-Too Protocol team provides ‘stepped care’ service to drugs or devices and useless screening tests. The Plc would provide guarantee for a positive trial.

c) The Plc would fabricate umpteen numbers of fake trial data to establish very firmly efficacy and safety of the medicine by their Research Administration Team (RATs).

d) The Plc would turn the phoney data over to BS (Biological Sociology) brain trust, which would supply a minimum of highly plausible theories to support their otherwise patently unbelievable subgroup result.

e) After the data are wonderfully established a SAFE (Say Anything For a Euro) team of experts will prepare ghost writing and at the drop of banknote would appear on television, chummy up reporters or write favourable commentaries in leading clinical journals.

That’s how many medicines usually have seen the light of the world pharmaceutical market. Then comes the marketing team who after a hair-splitting debate would find out what could be the indications for the medicine. Further the team would prepare elaborate promotional plan to fool the market forces, primarily the prescribers.

The Drugs and Cosmetics Act, 1940 confines the power of approval of any new medicine to the Drug Controller General of India (DCGI) and not to the state drug authorities (See Rule No 122E of Drugs and Cosmetics Act, 1940). Any combination of two or more separately approved medicines are also considered by the same Act as a new medicine (Schedule Y; Annexure, Drugs and Cosmetics Act, 1940). The DGCI has recently announced that it has not approved about 294 fixed dose combinations of medicines but that they have been approved by the state drug controllers. Why is this
open violation being tolerated by the DCGI for so long. Secondly, what has been done to these unapproved medicines by DCGI? All such unapproved medicines together with many others are even now freely available in the market. India has perhaps the dubious distinction of having the highest number of irrational medicines, courtesy, central and state drug control authorities.

**Irrational Medicines**

For a brief analysis to understand the enormity of the above statement, data was collected from ORG-IMS survey. The yearly sales 603 top selling medicines during 2006 were taken up. While selecting the irrational medicines, the following criteria was used.

- Whether such combinations are included in British National Formulary (available up to September 2007);
- whether they are included in the WHO Drug Formulary, and
- whether any evidences were presented to the medical profession during promotion.

The results are briefly presented in Table 1

In terms of percentages the irrational medicines sale in the retail market is 10.73 per cent but in terms of number of irrational brands to total top selling brands is 22.22 per cent. This is quite enormous for a country where medicines are dear. In the context that in India access to essential medicines are as poor as 35 per cent (2004), the sales of such a huge amount is a waste and in many cases are hazardous to health. In other words, a combination of ingredients that too in sub-therapeutic doses are sold to the extent of nearly Rs.10 million a year. The ingredients of Winofit marketed by Wockhardt are as given in Table 2.

There are instances where some of the irrational combinations approved are hazardous and nowhere else is approved. For example, the combination of two or more cardiovascular, two anti-diabetics with glitazones, paracetamol with nimesulide, etc. are found in the list.

It is obvious that the industry earn very high profit from selling such irrational medicines. Other benefit is that they industry get an added advantage to tell new stories to the profession about the newer and exotic combination of medicines. In doing so, they

<table>
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<th>Table 1: Sales of Irrational Medicines</th>
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<tr>
<td>Total medicines selected</td>
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<tr>
<td>Total Sales</td>
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<td>Total Number of irrational medicines found</td>
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<td>Total sales of the irrational medicines</td>
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invent various procedures for high pressure marketing machinery.

**Classification of Promotional Technique**
Promotional techniques in India have adopted innovative activities which would be second to none. First we may take instances of the standard techniques followed by the industry in the developed countries which most find highly objectionable.

A. Wazana (‘Physicians and the Pharmaceutical Industry – Is a Gift Ever Just a Gift?’) found the following techniques increased prescribing of a drug and/or generated a positive impression of the representative (and by association, the company):

- Visits by a pharmaceutical company representative;
- Gifts;
- Samples of medications;
- Industry paid meals;
- Conference travel;
- Speakers provided by the pharmaceutical company;
- Funding for continuing medical education; and
- Honoraria and research funding provided to doctors.

In each of the above, the Indian pharmaceutical industry had adopted novel methods. Only in the area of visit by a medical representative is very different in this country. In the cities, a doctor is visited by an average of 35 to 55 medical representatives in a day. The medicine companies insist their medical representatives to visit important doctors at least twice in a week!

Peter Mansfield described eight sub-section in the category of visit by medical representative: False statements, omission, fine print, evidence of poor quality, ‘red herring’ surrogate endpoints, statements of relative risk, ambiguity, widening the

| Table 2: Ingredients of Winofit marketed by Wockhardt |
|-----------------|---------|
| Vit C           | 100mg   |
| Zink Sulphate   | 7.5mg   |
| Folic Acid      | 2.5mg   |
| Manganese Sulphate | 2 mg |
| Vit A           | 30 per cent Beta Carotene |
| Chromium Sulphate | 100mcg |
| Selenium Dioxide | 40mcg |
| Eicosapentaenoic Acid | 90 mg |
| Docosahexaenoic Acid | 60mg |
| Vit E           | 200 mg  |
indications. These are the part of oral or visual presentations of the medical representatives which are given by the companies to do before a doctor. In all such process the only thing which is brutally killed is the evidence.

We shall examine such instances. It may look very trivial or insignificant yet they are very effective in influencing opinion of a large section. G. J. Kyle and others\(^2\) made an interesting complex graphical presentation of multifaceted coordinated promotional method in Figure 1

Figure 1 summarises the web of direct and indirect commercial influences that can be exerted on the prescribing process into a single visual representation. Prescribers make decisions about whether to prescribe or not, and if so, which drug to prescribe, within the paradigm of these commercial influences. The power of a coordinated marketing campaign utilizing multiple influencing factors, or channels of influence, can be seen.

**Misleading presentations**

One of the regularly promoted irrational medicines is combination of Methylcobalamin and other vitamins. Only one brand of such combination is **Neurobion**. E. Mark sells the largest amount of methylcobalamin or Vit-B12 which in sales turn over in 2006 was Rs. 54.14 crore. The company introduced ‘Met-Neurobion as the “first step in neuropathy management”. Only reference given in favour is in ‘ZhonghNeiKeZaZhi’ (!) possibly some Chinese magazine which very few Indians can read and verify. The company introduced ‘Met-Neurobion OD’ a combination of methylcobalamin and Alpha Lipoic Acid claiming that it was the “right equation in peripheral neuropathy”, and

**Figure 1: Multifaceted Co-ordinated Promotional Method**
therefore can be used in the therapy of “sciatica, lumbago and lumber disc herniation”.

Looking at the reference given by the company one can find the following:
1. www.Alzheimersupport.com (adapted); 2. J. Am. Boed Sam., This requires no no comment.
The other campaign for the medicine is for ‘Diabetic neuropathy’. Referring to certain Sydney-2 trial it is stated that the medicine induces improvement of symptomatic diabetic neuropathy. Here reference is from: Kamenova P. Hormones (Athens)’ It also claims that ‘methylecobalalmine promotes nerve re-generation’ and the reference is again-”www. Alzheimersupport.com(adapted)”
Another brand of similar combination is Meganuron OD which is a combination of Methylecobalamine, Alpha Lipoic Acid, Folic Acid, Biotin and Vitamine B6. Indication for which it is promoted are: diabetic peripheral neuropathy; post hepatic neuralgia; nerve compression disorder; degenerative nerve disorders, and post stroke.
In support, the literature referred the following: Alcohol and Alcoholism; Expert Opin Investing drugs, and Cochrane Database Syst Rev. A search in Cochrane found no reference on such an exotic combination.
E. Merck is also the largest seller of Evion, Vitamin-E fetched a yearly sale in 2006 reached to Rs. 30.68 Crores. Many other competitors have landed in the field by replicating same promotional process like Marck. To out bit them the company has
started to expand their product basket of Vit-E preparations in many combination form. One of them is ‘Evion LC’ which is a combination of Vit-E and Carnitine. This medicine is promoted as’ Dual Muscle Energiser’ in post operative cases and fractures, in muscle fatigue and muscle cramps. In support of their claims the only document offered was a web-site www.rxlist.com. On opening the site the following was found:

It has not been possible to determine which symptoms are due to carnitine deficiency and which are due to the underlying organic acidemia as symptoms of both abnormalities may be expected to improve with carnitine. The literature reports that carnitine can promote excretion of excess organic or fatty acid in patients with defects in fatty acid metabolism and/or specific organic acidopathies.

Therefore the only indication mentioned in the reference is’ For acute and chronic treatment with an in born error of metabolism that results in secondary carnitine deficiency.’

Merk India Limited, a German multinational company is the largest seller of Evion, Vitamin-E that fetched in 2006 Rs. 30.68 crore. Many other competitors have landed in the field by replicating the promotional process adopted by Merck. To out wit them the company has started to expand their product basket of Vit-E preparations in many combination forms. One of them is ‘Evion LC’ which is a combination of Vit-E and Carnitine. This medicine is promoted as’ Dual Muscle Energiser’ in post operative cases and fractures, in muscle fatigue and muscle cramps. In support of their claims the only
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**Gifts**

So far as the list of gifts offered to medical profession goes, it is endless and whatever is offered is gladly accepted with commitment of reciprocation. Sometimes the offers openly announce reciprocation.

Through the medical representatives, Torrent circulated a direct prescription related gift offer to doctors where they have not hesitated what that the kind of gift would relate to the quanta of prescription he would generate in a specific time. This type of
prescription dependant gift in cash or in kind is regularly offered by Torrent. In the recent time, Torrent floated a “gift-mela” by offering massive gifts of many kinds including gold coins to cash. Thousands of doctors happily joined and later a list of 350 ‘fortunates’ were also published with an assurance that he loosers woul get chance to join another mela.

Another such spree was recently worked out by Stancare division of Ranbaxy for promotion of ‘Roles SF’, a combination of rabiprazol with sodium bicarbonate. The provided prescription pad with carbonated foils to keep record each prescriptions which the medical representatives would collect at the end of every month.

Gifts of different values would then be given to the doctors after counting the prescriptions they have generated. Thus this kind of crude inducement is openly and generously practiced by the pharmaceutical industry in India. Here we can perceive that how the best students sent for medical education in our country are entrapped by the industry. Docors often do not keep track of what they are prescribing; for whom they are prescribing and what their commitment to society is. The bond between the industry and the profession has become so profound that ethics is sacrificed.
Ethics
Increasing concern has been shown by the medical profession on the unethical promotion adopted by the medicine companies. Almost all esteemed medical journals have published a lot of papers in this area. Following are some quotes from NEJM and JAMA.

When a great Profession and the forces of Capitalism interacts, drama is likely to result. This has certainly been the case where the profession of medicine and the pharmaceutical industry are concerned. On display and the grandeur and weakness of the medical profession—its noble aspiration and its inability to fulfill them (Journal of American Medical Association, Vol. No.18, November, 2003.)

And, when pharmaceutical companies court high-volume prescribers, writing prescriptions becomes an act not only with financial and health consequences for patients, but also with financial consequences for the physician (Notification: Ministry of Health, New Delhi, January 24, 1961).

In contrast one can be inquisitive about the ethical standards of the Indian Medical Journal, the largest circulated periodical in India published by the Indiam Medical Association. According to Drugs & Magic Remedies (Objectionable Advertisement) Rules, 1955 advertisement would be allowed if (Conditions) The advertisement contains
only such information as is required for guidance of registered medical practitioner in respect of matters relating to (a) the therapeutic indications of the drug; (b) its administration (c) its dosage and (e) the precautions to be observed in treatment with drug [Notification: Ministry of Health, New Delhi, the 24th January 1961].

JIMA does not appear to have any advertisement policy. It may not consider the provision of the Act in this area. No advertisement published in the journal follows the minimum conditions. Though in some cases strength of the medicines advertised is mentioned but never the precautions or contra indication. Here is an example from November, 2008 issue of the journal which advertise for a brand of medicine containing in 5ml: Ferrous Gluconate 129.5mg, Folic Acid 0.25mg Calcium Lactate 75mg and Vitamin B12. In the whole advertisement published nowhere dose, administration and precautions are mentioned. A study on all advertisements published in JIMA would be much more revealing.

**Marketing Code**

Today we found many marketing codes available in the world. Some of them had was created to aim improved image of the industry by the industry associations/federations and one is by WHO. We found following coded in the list.

2. Code of ethical marketing practices by PhRMA (organisation of pharmaceutical
3. Ethical Marketing of Medicines by World Health Organisation
4. Ethical Code of Marketing by Organisation of Pharmaceutical Producers of India (OPPI)
5. Code of Marketing Ethics by Indian Drug Manufacturers Association
6. Code of Ethics for marketing of Drugs by Health Action International

The codes prepared by industry associations are mostly written in vague terms. Though all of them assures that any violation of the code by their member companies would be dealt with punishment but since several decades no such actions have been noted.

In the recent times Torrent Pharmaceuticals spent Rs. 100 million in lifting hundreds of doctors through chartered flight to Bali, Fuket and other places for fun and frolic. When a formal complaint with evidences was made to IDMA on this activity of Torrent, nothing happened (Times of India, December 15, 2008).

Even the code prepared by WHO is as old as two decades which needs much modification yet no attempts is heard from them.

When the industry has openly corrupted the noble profession, our Govt. had only recently has held two meetings with the industry associations to express their concern and requested that unethical practices should be avoided.

The real pushing factor of irrational and harmful medicines is unethical promotion. This very factor if neglected, would allow proliferation of more irrational medicines would continue.

In the recent occasions concern on growing unethical marketing practices has become a global anxiety. In USA, several states are taking measures to halt such menace of the pharmaceutical industry. Massachusetts is going to give effect to a law on physician-industry relation of the pharmaceutical and medical devises manufacturers. Similarly the state of Vermont has introduced wider and stricter law signed on June 8, 2009, by Governor Jim Douglas. Vermont’s law bans gifts to physicians from manufacturers of prescription drugs, medical devices, and biologic products, with few exceptions. For the gifts and other expenditures that are allowed, the law requires disclosure of the product or products being marketed, if any, the name of the recipient, the recipient’s address and institutional affiliation, and the dollar amount (with no minimum). The law covers payments not only to doctors but also to other individuals and institutions, including pharmacists, health benefit plan administrators, nursing homes, hospitals, the state’s medical school, and professionals’ and patients’ organizations.

Most gifts to physicians are banned, including “any payment, food, entertainment, travel” or “anything else of value provided to a health care provider” that does not qualify as an “allowable expenditure.” The exceptions include the provision of drug
samples for free distribution to patients, the short-term loan of medical devices to permit their evaluation, and the distribution of journal articles and other items “that serve a genuine educational function.”

In our country, instead of the government making codes or any law the issue is till left to the industry for their voluntary adoption of codes. As reported by Chronicle Pharmabiz,4 “Faced with a rising public outcry against this unethical practice, the government asked the industry to evolve a common code of ethics for all the pharmaceutical industry in the country as existing codes do not cover members of all the pharma industry associations and the government felt that there is need for a uniform marketing code to cover the entire industry. The DoP conducted two industry-government meetings on the issue and asked the OPPI to take the lead to compile the marketing code in association with all major industry associations in the country.” The multinational dominated industry association OPPI taking this chance, had decided to approach Medical Council of India for preparing a Uniform Code of Marketing Practices. It is now a serious concern that when the credibility of MCI in the past several times were shaken regarding conflict of interest, the outcome may not be appropriate. The next most important question comes as to what obligation such code would establish unless it is given a legal authority and strong enforcement machinery?

References:


Note:
The author is solely responsible for the illustrations
I

Introduction

In 2007, the Citizen, Consumer and Civic Action Group (CAG) was invited to be part of a five-member working group of the Consumers International (CI). For the first time, consumer groups the world over were coming together on a common issue of relevance to consumers. This study followed from this partnership.

The study on pharmaceutical promotions seemed relevant in the context of various anomalies in the pharmaceutical sector: (a) Expenditure on drugs (outpatient) was the second largest reason for indebtedness. (b) There are a large number of irrational combinations in the top selling 300 drugs. (c) There is a great variation in the cost of drugs. The Citizen, Consumer and Civic Action Group (CAG), Chennai undertook a study looking primarily at the promotional chain of drugs and diagnostics at various levels.

*Email: peepultree@hotmail.com
3. To understand how diagnostic laboratories offered incentives to doctors and the lay public.
4. To understand how pharmacies responded to promotionals and how they stocked drugs.
5. To understand how hospitals procured their drugs and devices.
6. To obtain an understanding from medical sales representatives of pharmaceutical companies who visited doctors.

The selection of doctors for the survey was completely random to avoid any kind of bias. The choice of lay public again was random. However all participants in the study were literate--- could read, write and understand advertisements. Labs were chosen to ensure a mix of large, middle and small in terms of volume of clients serviced and facilities offered. Small to medium sized pharmacies (in terms of sales) were chosen randomly. Hospitals were the most difficult segment to sample as data was not forthcoming. There was a lot of suspicion and even a sample size of 9 was obtained after surveying more than 20. All the hospitals were in the <50 beds segment. Medical representatives were chosen company wise and for the segment (surgical, orthopaedic etc) that they serviced.

What follows is a brief synopsis of the results of the study.

<table>
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<th>Table 1: Sample Size</th>
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<tr>
<td>Doctors</td>
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<td>Lay Public</td>
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<td>Laboratories</td>
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<tr>
<td>Pharmacies</td>
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<tr>
<td>Hospitals</td>
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<tr>
<td>Medical Representatives</td>
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**Doctors**

The major source of information about drugs for doctors was journals and visits by medical representatives (almost equally distributed). 72 /92 used multiple sources. Kind of journal read was not verified.

When doctors were asked what kind of source they valued, the overwhelming response was the journal. Of the sample 62 doctors wanted another source preferably printed information.

While doctors valued journals unequivocally, 50 per cent used medical representatives as a source.

*Did gifts influence prescribing?* Here again the sample was almost equally divided. 60/92 said that it was acceptable to use gifts as reminders. Only 14/92 felt that it was an unacceptable practice.

*Did gifts lead to irrational prescribing?* 41/92 said yes and 35/92 said no while 16 were silent.

*Did gifts raise costs to customers?* 43/92 said yes and 31/92 said no while the remaining
maintained a diplomatic silence. Many doctors seem to feel that gifts are in a grey zone. Are doctors sitting on an ethical question here? Or maybe refusing to accept its consequences? There is overwhelming evidence to show that promotionals raise health costs to customers.

*How do doctors see sponsorships?* A majority of doctors, 78/92, felt that it was acceptable for pharma companies to sponsor CMEs organised by doctors’ associations. The response was not so unequivocal for pharma companies hosting their own CMEs. Most doctors see it as a pragmatic decision as it is difficult to get sponsorships otherwise. A small number, 20 doctors were. However, clear that sponsorships from non industry sources would be more ethical.

*Choice between the products of two companies:* Quality and cost seem to be the winning combination followed closely by regular visits by representatives. This sits strangely with the market analysis that the market leaders in terms of sales are the most highly priced brands!

*Drug combinations:* 65/92 proclaim that they use it selectively. Again contrast it with market figures of more than 120 irrational combinations in the top selling 300 brands.

*Banned drugs:* Doctors repose a lot faith in government and the industry to weed them out—(61/92); 32/92, however, feel that banned drugs exist in the market. Doctors inform themselves about banned drugs by reading bulletins.

*Diagnostic centres offering financial support to doctors:* The majority of the doctors felt that this practice leads to an increase in the number of unnecessary tests.

**Medical Representatives**
The survey of medical representatives, company-wise, was very revealing. We see a clear pattern emerging. Companies grade doctors primarily on the “business generated” for the company. So they knew about how many patients doctors saw in a day and the kind of fees charged.

A great variety of marketing strategies are used that included samples, small gifts, large gifts, frequent visits, sponsorships to conferences and discounts. Visual aids were the predominant mode used.

They felt that they briefed doctors both about the positive and the negative effects of drugs.

*Are doctors influenced by promotional incentives?* All of the representatives interviewed felt that doctors are influenced by promotional practices.

*Why are doctors influenced by promotionals?* There was an equal rating for “being influenced by the promotionals” and about “being convinced about drugs”.

*Pharmaceutical Drug Promotion and Consumers / Ramkumar*
How do doctors choose between products of two companies? On the basis of Services offered, 23; Effectiveness, 20; Cost, 15; Brand Name, 11.

Does giving benefits/sponsorships increase sales? The answer is an unequivocal yes.

Do doctors ask for gifts or are they offered without asking? 22 of 33 said that doctors expected gifts ‘we offer them as appreciation’ said 12/33; while 11 of the sample said that doctors asked for gifts.

Category of doctors: Supercore (trend setters and high volume sales for the company). So expenditures by the company on them are really high.

On an average, 6-12 gifts are given every year. The average field of one representative is 200 doctors. The number of representatives varies with the size of the company. The numbers are not clear from our study but the larger companies employ up to 400 people in one division. Average expenditures/year/doctor are too spread out to get an average: Ranges from Rs.500 to Rs.5 lakh for the chronic diseases segment.

The survey also covered labs, pharmacies, hospitals and public. Some highlights are reported here.

Diagnostic Labs
Laboratories focus on master health checks to entice customers. They too have representatives who promote their services to doctors. 11/20 labs offer incentives to doctors mainly in the form of cash incentives and discounts were the major incentives offered.

Public as Consumers
People are clearly swayed by advertisements for medicines. They remember brand names. The media that has been most successfully used for this is television.

- 61/100 consumers actually bought the product advertised. Largely the medicines are OTC’s but there are a lot irrational medicines in that list including cough syrups. What is a cause of concern however is that drugs like aspirin, amoxicillin and a few NSAIDs also figure in the list of advertised products used.
- 62/100 feel that the drugs purchased this way have been effective.
- 68/100 have bought medicines without prescriptions. 46 of them mentioned the brand and 23 people had chemists recommending the brand to them. The reasons for not using the doctors prescription is that they have used the brand before (51/100) and 19 felt that they understood the medicine.
- 56/100 recommend drugs used to others.
- Just over a half used a lab recommended by the doctor (51/100). This is in contrast to the doctors’ survey where doctors said that they largely left it to patients to decide.
Table 2: Data from one sample company

<table>
<thead>
<tr>
<th>Gifts offered</th>
<th>Sponsoring CMEs</th>
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<tr>
<td>Samples</td>
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<tr>
<td>Small gifts eg., Pen, Pad</td>
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<tr>
<td>Large Gifts eg., Equipments for practice</td>
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<tr>
<td>Discounts for dispensing doctors</td>
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<table>
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<tr>
<th>No of doctors covered by the representative</th>
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<tr>
<th>Segments covered</th>
<th>Frequency of gifts</th>
<th>Amount (annual) Rs.</th>
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<tbody>
<tr>
<td>Diabetology</td>
<td>Once in 2 months</td>
<td>1-5 lakhs</td>
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<tr>
<td>Cardiology</td>
<td>Once in 2 months</td>
<td>1-5 lakhs</td>
</tr>
<tr>
<td>Physician (General Physician)</td>
<td>Once in 2 months</td>
<td>1-5 lakhs</td>
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<th>No of sponsorships/year</th>
<th>1-2 (conferences abroad)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No of representatives in the division</td>
<td>180</td>
</tr>
</tbody>
</table>

**Pharmacies**

- Most pharmacies stock 11-15 brands of each drug. They stock by doctors prescription and what they term as “fast moving”.
- Very few of the pharmacies surveyed actually have a systematic way of taking stock of drugs past the expiry date. 13 pharmacies said that the companies took back products that are not sold and six said that the companies did not. What happens to products not sold?
- 13/20 pharmacies said that they recommended brands to customers seeking advice. Their basis for doing so was ‘effectiveness’. 16/20 said it was based on the profit margin.
- 50 per cent said that the company provided information on side effects and 50 per cent said that they did not.
- What do pharmacies do when drugs on the prescription are not available? Most suggest alternatives.
- Are all pharmacies manned by pharmacists? Clearly not.
- All pharmacies said that pharma companies offer incentives that ranged from 10+1 to 10+10 on some drugs for the branded generic segments.

**Hospitals**

Hospitals proved to be the most difficult segment to survey. Very little information was forthcoming. Of the nine hospitals in our study none had a procurement policy with
clear guidelines. Many had clear procedures for procurement and some criteria like cost, quality, company name, doctors preferences. All hospitals had discounts offered to them and five of nine had sponsorships for conferences or Continuing Medical Education (CME) Programmes.

II

Important Questions for Consumers and Consumer Groups

There are more than 40,000 (conservative market estimate) brands of drugs in the market. For example, there are more than 1200 brands of paracetamol, which is a drug for fever (Source: CIMS India). Why is this an issue?

1. It is difficult for a customer or a doctor to choose rationally when there are so many brands of just one drug.

2. There is a great variation in prices among brands. The same company often makes more than one brand and prices them differently. Neither the doctor nor the patient is sometimes aware that there they may be cheaper alternatives for the same quality.

3. A myth of quality is generated. Doctors often observe that some brands have a greater efficacy on their patients than other brands and so they prescribe them. They feel, and rightly so, that quality considerations should override cost considerations. The question is: Is there a body of objective evidence to prove that brand A is better than brand B? Have a large number of other doctors validated this observation with verifiable data which is the hallmark of the scientific process? To quote S. Srinivasan of LOCOST, “The practice of evidence based medicine means integrating individual clinical expertise with the best available external clinical evidence from systematic research.”

Secondly, if the same company is making more than one brand and selling it at different prices, where does the question of quality come in? All manufacturers have an approved license to manufacture from the Drug Controller. So is the question of quality difference a real one? Yes, there are manufacturers who violate norms; there are spurious drugs in the market. However, quality control is not an issue for small companies alone. Many multinationals have also been taken to court for violation of quality norms. Where and how does the actual difference in cost structure between different brands of the same drug happen?

4. Manufacture: There are not too many variations in the manufacturing costs of a drug. There are only 500 active pharmaceutical ingredients (the actual medicinal component) on the whole and about 1300 bulk drug manufacturers make them.

5. Formulating: This is a process where the API is made into its usable form by making it into a tablet or syrup or capsule. Here there may be some little difference in the cost based on the quality control systems or the quality of materials used.

6. Marketing and distribution cost: This is where there is a substantial difference in the
cost. To cope with the competition that exists, Pharma companies use a variety of promotional tactics that increase the cost of the drug to the patient.

For the same reason, there is the huge trade margin given to pharma distributors and retailers thanks to competition between companies. This margin is not passed on to the consumer. For example, take the drug Olfloxacin. The distributors’ price was Rs.330 for 100 tablets and it had an MRP of 1600/100 tablets. (Source: *Impoverishing the Poor: Pharmaceuticals and Drug Pricing in India*, Local/ JSS 2004)

7. Promotional tactics: The bottom line is very clear. All promotional tactics have finally one aim---to increase sales. Who pays for the cost of the promotion? The consumer. They increase sales by creating a need. For example, vitamins. Prescription drugs cannot be advertised but ‘over the counter’ drugs can. There are more than 17 brands of vitamin supplements in the top selling 300 brands. Some of the claims in the marketing of these drugs are often misleading. (Source: *A Lay Person’s Guide to Medicines*). They aggressively market many irrational drug combinations.

Rational drug therapy means the use of drugs which are efficient, safe, low cost and easy to administer. Irrational use of drugs could be using irrational drugs available in the market or irrational prescription of rational drugs by doctors or irrational usage of drugs by patients.

In a study done by Gopal Dabade (Drug Action Forum Karnataka), 338 preparations for anemia were scanned. Only one drug ferrous fumarate, 200 mg tablet conformed to the WHO List of Essential Drugs, 2005 and other standard textbooks of pharmacology.

8. Increased cost due to the combinations: *The Report of the National Commission of Macroeconomics and Health* mentions that out of the top selling 25 brands in India, 10 were irrational. Even if we consider a conservative figure of 10 per cent of the overall preparations as being irrational, the turnover related to the sales would be more than Rs. 2,000 crore. This figure is more than the combined budgets of the Central and State governments on the procurement of drugs.

9. Wooing the doctors: The study clearly points to the expenditure on doctors through promotion. “The top 50 drug companies in India spend about 18. 56% of the total income on selling expenses, which is the highest among all manufacturing activities.” (ET Intelligence Group December 15, 2004). This raises ethical questions.
**How should the consumer movement respond to these challenges? What are some of the issues that it should build awareness about? What are some demands that it should raise?**

1. Drugs should be of good quality, that good testing facilities for quality exist. (Samples of less than 1 per cent of the batches of drugs manufactured in the country are exposed to scrutiny by the Government drug testing laboratories.)

2. That the state should put on public domain an independent source of information on the prices of the various brands so that consumers can compare costs and and make informed choices.

3. Promotions by drug companies should be regulated. Many other countries in the world have regulated promotions. Why not India?

4. Doctors should be mandatorily following Standard Treatment Guidelines and not succumb to irrational prescribing.

5. Equitable and fair prices for drugs should be ensured and the Government of India should take adequate steps to regulate pricing. Only 74 drugs are under price control. The open market has not ensured that the prices of drugs have become more affordable.

6. Should drug prices be regulated at all? The answer is a clear Yes. The industry argument is that price control results in the suppression of the free market dynamic of competition that keeps prices down. This is shown by surveys to be incorrect. The drugs that have been taken out of price control have shown a higher price rise than drugs which are not under price control. Drugs are essential and lifesaving. If prices go up or down we cannot shrink or expand requirement. Drugs that are market leaders in terms of market share are also the highest priced brands. This is a rather strange phenomenon happening as a result of marketing practices. It is very heart breaking in a country where health care is largely market dependent, where drug costs lead to indebtedness and more than 80 per cent of the population is either poor or middle class.

7. The consumer movement in many states is well networked. It should work closely with health and public rights groups to ensure that its demands are met. In the promotional sector there is a paucity of regulatory tools and the consumer movement can work towards rectifying this. CAG has completed a study of regulations regarding promotions and looks forward to coordinate a national network in this regard.

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**Note:**

The first part of the article is based on the report of a study, ‘A Taste of the Promotional Chain: Pharmaceutical Drug Promotion - A preliminary survey of doctors, pharmacies, hospitals, public, company salespersons’ conducted by the Citizen, Consumer & Civic Action Group. (CAG) Chennai. The team included Suchitra Ramakumar, Nandikes and Saroja from CAG. We received very valuable support from Vishwanathan and Sukumar from, Federation of Medical Representatives Association if India (FMRAI),Chennai.
I
Introduction

The study of health transition in India has occupied centre stage in the ongoing debate on the relationship between mortality and morbidity [Murray 1998]. While there has been a general decrease in mortality in India leading to significant gains in life expectancy, both at the country and state level over the last three decades, what has happened to morbidity is yet to be assessed. Evidence derived from studies conducted in developed countries indicates that due to morbidity, part of the expected life is liable to be lost through incapacitation. Although concerns have been expressed by the researchers and health policy planners about whether the disease burden due to morbidity follows the secular trend of mortality, there have been very few studies to examine the trends and patterns of morbidity prevalence across population groups for states in India.

Therefore, for making an objective assessment of disease burden of India and its many regions, population level estimates of morbidity are essential. It is also imperative to study the components of differential morbidity within its population. India is often described as a sub-continent with substantial regional rural-urban and social group
differentials in terms of standard of living and quality of life including human health. The purpose of this study is to examine the existing inequalities in non-fatal health outcomes between different subsections of population in India.

However, many researchers argued that the quantification of ‘inequality’ in morbidity prevalence among different population groups may not give a true picture because of the influence of subjectivity in measurement of morbidity. The reporting of ailments depends on the levels of awareness about health problems arising from various individual, household and community level factors in the population [Schultz and Tansel, 1996]. Despite these well-recognised problems and difficulties of measurement, the reported information of morbidity obtained in large scale surveys would be extremely useful, especially in the absence of clinically validated surveys [Sen, 1998; Dilip 2007].

**Review of Previous Studies**

Health is a multidimensional concept that is difficult to capture in a single measure. Conventional indicators such as infant mortality rate or life expectancy at birth, anthropometric measures or nutritional status are generally used to measure the health status of the population since they are comparatively simple to analyse and data is easily available. However, in recent times, many studies have used self-reported illness to measure health status because of its consistent relationships with future mortality in many countries and its direct link to policy changes, e.g., those who did not perceive the need would not be seeking health care even though the health care service is fully available [Nicholson, Bobak, Murphy, Rose and Murmot, 2005; Idler and Benyamini, 1997; Dilip, 2002; Duriasamy 1995; Murray, 1998].

Though a number of agencies in India such as NSSO and NCAER have been conducting national level surveys on ‘morbidity and health care’ on a periodical basis, fewer and limited attempts have been made in assessing the health status of the population across states using data from these sources. Studies that dealt with the evidence of differentials in morbidity are reviewed below.

The evidence of disaggregated morbidity prevalence in India showed a ‘J’ shaped relationship between age and morbidity, an indication that elders and children are susceptible to higher prevalence of illness [Kannan, et al, 1991; Shariff, 1995; Gumber, 1997; NSSO, 1998]. Gender differences are observed with women reporting significantly lower levels of morbidity than men. This suggests under-reporting of ailments among women [Iyer, 2000; Kannan, et al. 1991; Krishnaswami, 2004].

Studies found contrasting pattern of evidences about disease burden between rural and urban population with some reporting greater burden among rural population than in urban population [Gumber and Kulkarni, 2000; Duggal and Amin, 1989; Dilip 2002;
NCAER, 1992; Satya Sekar, 1997 NSSO, 1998] and others suggesting the opposite [Sundar 1995; Mahiwala, et al, 2000]. Existing evidence indicate that reported morbidity prevalence is negatively associated with educational attainment [Duraisamy, 1998; Ghosh, 2007; Navaneetham, 2006]. It is argued that better educated take more precautions against diseases which in turn reduces their morbidity. However, the nature of relationship between economic status of household and the risk of reporting morbidity is far from clear. While evidence from national level surveys suggests a positive association between self-reported morbidity prevalence and economic status of an individual [Dilip, 2002; Duraisamy 1998], the reverse is observed in regional studies ([Navaneetham, 2006; KSSP 2006; Kunhikannan and Aravindan 2000; Kannan et al. 1991]. Such differences can be attributed to the differences in definition, survey design and the level of health consciousness of the population of these studies.

However, very little information is available about the disease profile of different population groups in India. The level and prevalent pattern of morbidity in the country show that India has entered into the fourth stage of health transition [NSSO, 1998; 2006]. Therefore, understanding changing morbidity patterns and determinants with new data is important for devising and reviewing health intervention policies.

II
Data and Methods
In this study, data was drawn from National Sample Survey Organisation (NSSO) 52nd (1995-96) and 60th round (2004) survey on ‘morbidity and health care’. While for the 52nd round, the data collection period, July 1995-June 1996 was spread in four sub-rounds each comprising three months, in the 60th round, the survey was conducted in two sub-rounds of three months each during the period, January-June 2004. In the 52nd round, the survey covered 120942 households with 71284 in rural areas and 49658 in urban areas. Information was gathered about whether an individual suffered any illness during the last 15 days prior to survey date from 629888 usual residents of these households. However, in the 60th round, the survey conducted interviews in 73868 households with 47302 in rural areas and 26566 in urban areas in West Bengal. Information on whether an individual was ailing during the last 15 days is available for 383338 persons, the usual residents of the households.

The prevalence of ailments was calculated with information from the survey on any person who had fallen ill during the 15 days leading up to the survey. Since both the 52nd (1995) and 60th rounds (2004) of NSS surveys are based on similar survey design, concepts, definitions and reference period, the estimates from these surveys are comparable.
The prevalence of any ailment or its morbidity, is defined as

\[
\text{Morbidity} = \frac{\text{Number of ailing persons}}{\text{Total number of persons-alive in the sample households}} \times 1000
\]

The morbidity prevalence rate presented in this study gives the estimated proportion of persons reporting ailment suffered at any time during the reference period, which is not strictly the prevalence rate as recommended by the Expert committee on Health Statistics of the World Health Organisation (W.H.O). The WHO defines prevalence rate as the ratio between the number of spells of ailment suffered at anytime during the reference period and the population exposed to the risk. It measures the frequency of illnesses prevailing during the reference period; whereas here we present the number of persons reporting any ailment during a 15 day period per 1000 persons.

The variations in the morbidity prevalence rate across the states could be due to the differences in the age structure of different states. This is removed by standardising the rates for the year 2001 using the population of India as standard. The morbidity prevalence was also studied in terms of disease composition-broadly, acute and chronic. Ailments of less than 30 days duration are treated as ‘acute’ and those of more than 30 days duration as ‘chronic’ [NSSO, 1998]. Since the differences in reported morbidity prevalence levels by selected background factors will indicate the unequal burden of morbidity in the population, an attempt is made to examine the differences in morbidity levels by individual characteristics as well as household socio-economic characteristics. Probit regression model is applied to study independent effect of various predictor variables on the morbidity prevalence. However, interpreting the relative impact of different variables in a probit model is complicated by the fact that the model is non-linear in the explanatory variables, and as a consequence, the impact of independent variables on the probability of reporting illness depend on the value of that and other independent variables. Nevertheless, in this study, we assess the importance of different explanatory variables by looking at marginal changes in predicted probabilities for a representative individual controlling the effect of all other independent variables except the one of interest.
III
Levels, Trends and Regional Variations in Morbidity Prevalence

Figure 1 presents the trends in sex specific morbidity prevalence rates during the period 1995-96 and 2004. The morbidity prevalence rate has increased significantly from 54 to 91 per thousand population during the period 1995-96 to 2004. The increase in the prevalence of morbidity could be due to increased health consciousness among the people and better reporting by the respondents. Morbidity prevalence by sex indicate that although the morbidity prevalence has increased both for males and females, a greater increase in morbidity prevalence is seen among females compared to their male counterparts during the period 1995-96 to 2004.

Inter-state differentials in morbidity prevalence

State level sex-specific age-adjusted morbidity prevalence rates are presented in figure 2. It can be seen that even after the standardization of age, the morbidity prevalence is reported relatively higher for both sexes in the states of Kerala, West Bengal, Punjab, Uttar Pradesh, Maharashtra and Andhra Pradesh but sex differentials are greater and considerably higher among females in Punjab, Himachal Pradesh, Tamil Nadu and Haryana. The states where the reported rates of morbidity prevalence are relatively low are Bihar, Rajasthan, Madhya Pradesh and Karnataka.
However, it is not possible to establish any association between levels of socio-economic development and the prevalence of morbidity by looking at the levels and differentials of morbidity prevalence rate between states. Contrary to the anticipation, it is observed that states like Kerala, Punjab and West Bengal known for their achievements in improving social and economic conditions have recorded the highest morbidity prevalence in the country. On the other hand, the socio-economically poorer states like Bihar, Madhya Pradesh and Rajasthan have reported lowest morbidity rates.

Previous studies suggest that this type of variations occur because of variations in morbidity reporting as a result of health ideals, accessibility of health services and the socioeconomic background of the population or it could be due to variation in

Note: *The population of India in 2001 is taken as standard population.*
disease profile between the populations arising from varying levels of demographic and epidemiologic transition.

**Morbidity by Background Characteristics**

Table 1 shows the morbidity rates of respondents according to various background characteristics of individuals and households. The reported morbidity prevalence rate was higher among females (97 per thousand population) than among males (86 per thousand). Prevalence of morbidity was higher for children 0-9 years, followed by a declining trend till age group 10-19 with a rising trend again at higher ages.

Level of education and morbidity prevalence are found to be inversely related. The reported morbidity prevalence is highest among the illiterates with the prevalence rate of 110 per thousand population. However, the prevalence of ailments is about a third lower (79 per thousand population) among the people with post-middle education.

The monthly per capita consumption expenditure (MPCE) quintile which represents the economic condition of the household showed a positive relationship with prevalence of morbidity. Stark difference is noticed in the prevalence of ailments by the expenditure quintiles. The prevalence of ailments in the richest quintile (124 per thousand population) is almost twice than the poorest quintile (70 per thousand).

Surprisingly, the reported morbidity prevalence rate among the ST is considerably lower than other social groups. The morbidity prevalence rate of 58 per thousand among the scheduled tribes is almost half compared to “Others” group (106 per thousand). It is worth mentioning that their socio-economic conditions are very poor than other social groups in India. The lower prevalence of morbidity among them is plausible due to the fact that the awareness about health problems among the scheduled castes may be very low leading to poor reporting of ailments. The morbidity prevalence rate was reported higher in the urban areas than in the rural areas.

The burden of ailments was higher during January-March (97 per thousand population) compared to the period April-June (85 per thousand population) suggesting marginal seasonal variations. The spatial distribution of ailments provides some interesting results. The Southern region constituting the states of Kerala, Tamil Nadu, Andhra Pradesh and Karnataka reported highest morbidity prevalence (112 per thousand population). Compared to this, the morbidity rate in the states of eastern region is 82 per thousand population.

*Acute, chronic and ‘others’ ailments*

Both acute and ‘others’ ailments indicate significant age differences, with almost same pattern of age differentials in the prevalence of ‘acute’ and ‘others’ ailments as in the case of any morbidity prevalence. However, the results show a positive relationship
between age and prevalence of ‘chronic’ morbidity. Clearly, the aged are suffering from a disproportionate burden of chronic diseases. While sex differentials are marginal for acute and other diseases, the reported prevalence of chronic diseases is found to be considerably greater among females than males. Though the differences in the prevalence of acute ailments by education are not noted, the prevalence of chronic ailments is very high among the illiterates than the educated. Caste differences are also observed with the highest prevalence of ‘acute’, ‘chronic’ and ‘other’ diseases in ‘others’ and lowest in scheduled tribes. However, the caste differences are more striking for the prevalence of ‘chronic’ diseases with the prevalence rate being reported more than three times in ‘others’ than in the scheduled tribes. The analyses indicate that the prevalence of both acute and chronic disease differ marginally across income groups. Contrary to this, the prevalence of chronic ailments is reported three times greater in the highest income

<table>
<thead>
<tr>
<th>Table 1: Prevalence of ailments by selected background characteristics in India, 2004 (Per thousand population)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any ailment</td>
</tr>
<tr>
<td>-----------------</td>
</tr>
<tr>
<td><strong>Sex</strong></td>
</tr>
<tr>
<td>Male</td>
</tr>
<tr>
<td>Female</td>
</tr>
<tr>
<td><strong>Age</strong></td>
</tr>
<tr>
<td>0-9</td>
</tr>
<tr>
<td>10-19</td>
</tr>
<tr>
<td>20-49</td>
</tr>
<tr>
<td>50-59</td>
</tr>
<tr>
<td>60+</td>
</tr>
<tr>
<td><strong>Education</strong></td>
</tr>
<tr>
<td>Illiterate</td>
</tr>
<tr>
<td>Literate upto middle complete</td>
</tr>
<tr>
<td>Middle complete or higher</td>
</tr>
<tr>
<td><strong>Caste</strong></td>
</tr>
<tr>
<td>Scheduled tribe</td>
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<tr>
<td>Scheduled caste</td>
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<tr>
<td>Other backward caste</td>
</tr>
<tr>
<td>Others</td>
</tr>
<tr>
<td><strong>MPCE</strong></td>
</tr>
<tr>
<td>Q1</td>
</tr>
<tr>
<td>Q2</td>
</tr>
</tbody>
</table>
Regression Analysis of Factors Affecting Morbidity

Table 2 presents the results of the probit regression analysis which provide the independent effects of different background variables on the reported health status of the population. The results indicate the probability of persons suffering from any ailment compared to the reference category during the reference period, when the effects of other variables are controlled. The dependent variables are dichotomous in nature taking the value of one if it was reported that an individual had suffered from any kind of ailments during the 15 days prior to the survey. The explanatory variables included in this model are: age, sex, place of residence, caste, education, per capita consumption expenditure, season and region.

Age is found to be an important indicator. The predicted probabilities by age confirm positive relationship between age and morbidity. The dummy variable sex shows that females are more likely to report ailments than the males. The analysis also confirmed the caste differences observed in the bivariate analysis with the lowest probability for scheduled caste and highest probability for the ‘others’. Contrary to the finding of the bivariate analysis, it is observed that persons living in rural areas have greater probability to report morbidity than the urban people. The inverse relationship observed by the
bivariate analysis between education and morbidity prevalence, is also confirmed by probit regression. A positive association has emerged between MPCE and morbidity prevalence. While persons belonging to the highest expenditure quintile have the highest probability (Pr=0.11) to report illness, persons belonging to lowest quintile (Pr=0.07) have lowest probability of reporting sickness.

The seasonal variations in morbidity prevalence are found to be significant. As compared to months of January-March, the probability of becoming ill is lower for the months of April-June. Persons living in southern states have the highest probability to report an ailment, followed by their counterparts in north, north-central, west and eastern region.

<table>
<thead>
<tr>
<th>Table 2: Probit regression analysis</th>
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<tbody>
<tr>
<td><strong>Age (years)</strong></td>
</tr>
<tr>
<td>Background Characteristics</td>
</tr>
<tr>
<td>10-19</td>
</tr>
<tr>
<td>20-49</td>
</tr>
<tr>
<td>50-59</td>
</tr>
<tr>
<td>60+</td>
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<tr>
<td>Sex</td>
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<td>Male</td>
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<td>Other backward caste</td>
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<td>Education</td>
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### Summary

We presented evidence on levels, differentials and determinants of morbidity prevalence in India. The country has achieved significant gains in life expectancy in the last few decades but the overall health conditions of the population appear to have worsened as it is having a very high level of morbidity prevalence with considerable inter-state differences in morbidity prevalence. Though the demographically and socially advanced states like Kerala, Punjab and West Bengal have lower infant mortality and greater life expectancy, the reported morbidity prevalence rates in these states are the highest in the country. Contrary to this, socio-economically poorer states like Bihar, Madhya Pradesh and Rajasthan have reported lowest morbidity rates. Some researchers, commenting on this, have suggested that there may be serious flaw in the health care surveys, which is primarily dependent on the self-reported illness of the respondents [Sen 2002; Dilip 2002; Visaria 1994; Murray 1992]. The other common argument for the rise in reported morbidity prevalence is that the people with higher level of education and media exposure are more conscious in these states, which may lead to better reporting of ailments. These findings and the arguments warrant an immediate attention of the survey designers to adopt more appropriate methodologies to address the above issues.

The analyses clearly indicate that various demographic, social and economic characteristics are important determinants of ill health in India. Significant gender inequality is observed in morbidity prevalence with females at greater risk of ill health than males. This is inconsistent with the findings of other studies that had used the earlier rounds of NSS. This means that the present round of NSS gives better estimates of morbidity for females than the earlier rounds. However, it could be possible that even the present level of morbidity among the females is under-reported.

It is observed that prevalence of illness increase with age. While acute ailments is responsible for high morbidity prevalence among the children, chronic ailments has caused the rise in morbidity prevalence among the elderly. The high prevalence rate of chronic illness among the aged population points to the need for special targeting of health care services for the elderly.

<table>
<thead>
<tr>
<th></th>
<th>Probability</th>
<th>Confidence Interval</th>
<th>Season</th>
<th>Probability</th>
<th>Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Illiterate</td>
<td>0.099</td>
<td>(0.098, 0.102)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Literate upto middle #</td>
<td>0.086</td>
<td>(0.085, 0.087)</td>
<td>January-March</td>
<td>0.091</td>
<td>(0.089, 0.092)</td>
</tr>
<tr>
<td>Higher</td>
<td>0.073</td>
<td>(0.071, 0.074)</td>
<td>April-June</td>
<td>0.079</td>
<td>(0.078, 0.081)</td>
</tr>
</tbody>
</table>

Note: #Literate upto middle refers to those who have studied up to eighth standard. Predicted probabilities at population means for all variables except the one indicated.
Prevalence of ailments varied significantly among different social groups. People from the scheduled tribes and scheduled castes communities reported lower prevalence of ailments than people belonging to all other social groups. The scheduled tribe communities are mostly concentrated in areas where the availability of health care services is minimal, even non-existent. Therefore, low literacy, limited exposure to media and lack of health care services may lead to underreporting of ailments among the SC/ST people.

Surprisingly, it is found that the burden of the ailments is reported to be higher among better-off sections than the poor. This could be again largely due to underreporting of morbidity by the poor people. Furthermore, the higher reported prevalence of chronic diseases resulting from higher prevalence of life-style related diseases among the rich people could also have contributed to the greater burden of illness among them. Seasonal variations are observed, with morbidity being highest between January and March. Regional differences are striking, as the reported prevalence of ailments is higher in southern region followed by northern states compared to other regions in India. The greater social and economic development, coupled with greater accessibility of health care services could be responsible for the regional variations observed during the study. The rural-urban differences in reporting illness indicate that health conditions of the rural people are poorer than their urban counterparts. It is imperative that health budgets are necessary to target these populations with very different pattern of disease profile and health care access.

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**New from SAGE India!**

Improving Access and Efficiency in Public Health Services: Mid-term Evaluation of India’s National Rural Health Mission

Nirupam Bajpai, The Earth Institute, Columbia University, New York
Jeffrey D Sachs, Director, The Earth Institute, Columbia University, New York
Ravindra H. Dholakia, Indian Institute of Management, Ahmedabad

March 2010; Pp. 144 (Double Demy); Rs. 695.

This book presents a systematic mid-term evaluation of the processes of the National Rural Health Mission (NRHM), India’s biggest rural health programme. It discusses the challenges and successes of the Mission with the help of extensive field observations, data analysis using District Level Health Surveys (DLHS), National Family Health Surveys (NFHS) and Sample Registration System (SRS) datasets and inputs from experts on health and nutrition sectors focusing on maternal, newborn and child health issues and chronic diseases.

The book will be useful for all those concerned with the issue of health and public administration in general and rural health in particular, such as, NGOs, IGOs, journalists, columnists, public policy planners, civil servants, and other practitioners.

By Maarten Bode;
Orient Longman, Hyderabad/London;
2008; Pp 272, Rs 625.

Reviewer
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Email: bhushan.patwardhan@manipalu.com

Unprecedented advances in science and technology have created a global village of a sort, breaking geographical barriers and diffusing cultural boundaries. However, ironically on their very watch, in health care, world population seems to have become more granular and polarized. The quality of health care seems to be declining in every quadrant. The percentage of population that is denied sufficient quality health care is rising, though reasons may be different for different groups of population.

Over this background, Indian medical traditions such as Ayurveda and Unani are attracting increasing attention within the context of health care provision and health sector reform. The gamut of traditional knowledge covers a variety of topics including its definitions, scope, and relevance to public health, intellectual property rights, patents, commoditization and such. In this book the author has touched on important issues related to the Ayurveda and Unani industries covering a 20-year span. Being a well trained professional anthropologist the author provides clear anatomy of the study defining objectives, methods and processes. Topics like endorsement, validation of efficacy, regulation of safety, standardization of materials and the gap between humoral and modern pharmacology along with a commentary on the construction of an Indian modernity are covered very lucidly.

With a very unique study on traditional medical substances and its manufacturers, the author rightly distinguishes between Indian indigenous medical ‘products’ from ‘medicines’ that are made in kitchens of traditional physicians and families. The author has visited most of the prominent industries and has interviewed several Ayurvedic vaidyas,
hakims, and industrialists. He also has gathered data on market trends from authentic sources. The author has kept regional and cultural sensitivities in mind. For instance, he clarifies that term ‘kitchen’ is not being used to undermine the value of traditional medicine but primarily to differentiate it from the commercially manufactured products.

In the Chapter ‘The Kitchen, the Government and the Market’, he gives a good ‘flavor’ of home remedies and Indian ideas about health and disease that are linked to Ayurveda. Typically, this is an example of ongoing exchange and interaction between the great and little traditions. The author has given very good account of how the manufacturers make use of popular ideas on ingredients like sacred tulsi, neem, lotus, rose, mango, haldi, chandan, garlic, etc. for product promotion. He describes thinking in these systems on constitution or prakriti, primordial elements or panchamahabhoot, guna such as warm, cold, dry, wet, etc. and connects it to medicine, cooking and tissue building. This is true as Ayurvedic remedies are not considered medicines but a healthy way of life by most Indians. As an anthropologist he touches upon the religion and mythological references to gods, demons and lord Dhanvantari’s elixir of life. He further states rightly so that in India’s health traditions, medicine and religion are closely connected.

The author takes a quick review of the origin, philosophies and product range of a few Indian industries including Zandu, Dabur, Himalaya, Arya vaidya, Hamdard. The section on education in Ayurveda and Unani as well as a short description of available materia medica is informative. A review on various efforts on regulations, quality assurance, national policies, pharmacopoeia committees, research councils, and manufacturers’ associations, government and non government agencies involved in the Ayurveda and Unani industries is also very informative. He also touches upon registration and the licensing of products and further discusses issues related to the appropriateness of terms, brands and the logic of markets by taking a few examples like Chyavanprash and VepoRub.

The chapter ‘Manufacturers, Products and Markets, differentiates manufacturing by vaidyas or hakims for their patients and that by the small or large organized industry. The former does not come under any regulations and the latter is governed by the Food and Drugs Administration. The discussion is illustrated by case studies of some industries: Himalaya, Arya Vaidya Shala, Arya Vaidya Pharmacy and Hamdard and other suitable industries. He also discusses several other issues including, Good Manufacturing Practices, traditional or classical manufactur throwing light on strategies used by companies like, Dabur that moved from Ayurvedic medicines to consumer goods.

With help of informative tables, the author provides valuable data on over 7,000 small, medium and large manufacturers based on turnover. Case studies of five manufacturers gives details of the journey of selected companies such as Dabur from small producers to modern business organizations. How Ayurvedic companies are using popu-
lar media like television for marketing is also discussed with examples. The author compares Dabur and Zandu from strategy and marketing angles.

In the Hamdard case he particularly discusses the entrepreneurial spirit and various charity initiatives of the company. He calls S.K. Burman, Abdul Hameed, Zandu Bhatt and P.S. Varrier as great souls and modernizers of their traditions. The study elaborates the company’s efforts to make strong prescription brands and its aim at strengthening biomedical research support through science and clinical study. The case of Arya Vaidya Shala on the other hand illustrates a legacy where classical medicines and practices continue to be a strong foundation.

In the chapter ‘Reworking Ayurvedic and Yunani Medicines thru Modern Science and Technology’, the author mainly focuses on the gap between humoral and modern pharmacology. He reviews modern production technology and quality control. The traditional and modern hi tech methods for preparation of kashayas and kvathas; ghrita, tailam and such classic formulations has been discussed with examples. The importance of laboratory and clinical studies in reinventing humoral medicine especially for making remunerator like rasayanas using modern scientific approaches has also added value to the product. The research activities of government and semi government institutions such as AYUSH, CSIR, ICMR are also given their due. Due mention is made of the efforts of integrated system research champions like K.N. Udupa.

Various interviews of the founders, expert consultants and experienced technical or managerial staff working in industry have enriched the discussions. With numerous footnotes with descriptions, definitions and apt citations the book becomes a scholarly resource that is useful in understanding Ayurveda and Unani philosophies, status, approaches, industries and markets. The author also attempts a kind of gap analysis among the various systems that adds practical value to the book.

And yet, despite the vast scope of the book a few issues, such as the research and development strategies, true successes stories, or the global standing of this sector in detail. Some more critical analysis comparing these industries with modern pharmaceutical industry clearly indicating inadequacies, limitations or areas of improvement especially from quality assurance and R&D would have been useful for the future development of Ayurvedic and Unani industry. Nevertheless, this book is certainly a valuable reference resource for the industry and academia, especially to international readers who may not have much exposure to these systems.