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Drug Development and Disease Burden in India: Conflicting Priorities and Possible Solutions

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Introduction

Striking a right balance between healthcare priorities and pharmaceutical policies is a grave public health challenge for India given their mutually conflicting nature and interests. On the one side, the country has an expanding pharmaceutical and biopharmaceutical sector with a strong presence of domestic and multinational private companies. The sector, with an enormous state facilitation, could effectively position itself as the future engine of economic growth by rearranging itself to the new intellectual property and trade regimes. On the other side, we have a huge burden of diseases implicated by a gamut of public health problems, including the uneven distribution of demographic and epidemiological transition, resurgence and emergence of infectious diseases, burden of non-communicable diseases, increasing privatisation of healthcare, less regulated pharmaceutical market, low affordability of life saving medicines and most importantly the escalating out-of-pocket healthcare expenditure coupled with a poor financial risk protection. All these make the Indian healthscape not only diverse but extremely complex as well. Availability of medicines in the market has increased significantly in India with the expansion of domestic and multinational private companies. Nevertheless, we still do not know sufficiently whether medicine development in India is informed of the public health priorities of the country. Our aim is to understand whether the present organisation of medicine research in India, which includes generics, biosimilars, and New Chemical Entities (NCE), is responsive to the public health priorities of the country.

Methods

This policy brief is prepared based on the findings of a research project titled "Research and Development (R&D) in Preventive and Therapeutic Healthcare in India: Implications for Public Health". Sources of data for the study are as follows: Data on the drugs approved for marketing in India from 2001 to 2017 were obtained from the database of Central Drugs Standard Control Organization (CDSCO), Government of India. These drugs were then further organised according to their therapeutic areas. Data on NCEs in pipeline till 2016 were taken from Differding (2017). Data on disease-specific mortality was collected from the mortality database of health statistics and information systems of World Health Organisation (WHO) for the years 2000, 2005, 2010 and 2015. This data was further disaggregated across four age-groups. Data on prices of various brands of recently approved generic medicines were compiled from the web portal of National Pharmaceutical Pricing Authority, Ministry of Chemicals and Fertilizers, Government of India.

Disease Focus of Drug Development

We examined 1635 new drugs (biosimilars) approved for marketing in India for the period from 2001 to 2017 and grouped those based on the disease focus (see figure 1). Out of these drugs, as high as 87% was for treating non-communicable diseases (NCD) and the remaining for communicable diseases (CD). Within NCDs, the highest number of new drugs that came to market was for cancer (153), followed by hypertension (103), antibiotics (94), cardiovascular diseases/cholesterol (92), to list a major few. Among CDs, the lowest number of new drugs that came to the market was for leprosy (1), followed by Kala-Azar (2) and Tuberculosis (2). Diarrhoeal diseases (23) and malaria (19) received the highest attention in drug development within CDs. The therapeutic focus of NCEs in the pipeline has also been predominantly on NCDs (see figure 2). It should be mentioned that the data provided here detail only compounds developed at different stages of drug development. It should also be mentioned that out of these only three compounds have reached up to phase 3 level of development while only one has been launched so far by the Indian pharmaceuticals. Out of 227 NCEs in the pipeline, the therapeutic focus of nearly 84 % was on NCDs. Within NCDs, the highest was for endocrine and metabolic disorders (50) and oncology (50) followed by immunology (26), neurology (21) and pulmonary (21). It should be highlighted that 35 NCEs are in the pipeline for various kinds of infections. The anticancer drug was an important priority for both biosimilars and NCEs. Research focus on NCEs was more for those therapeutic indications of NCDs which have less number of medicines available in the market.

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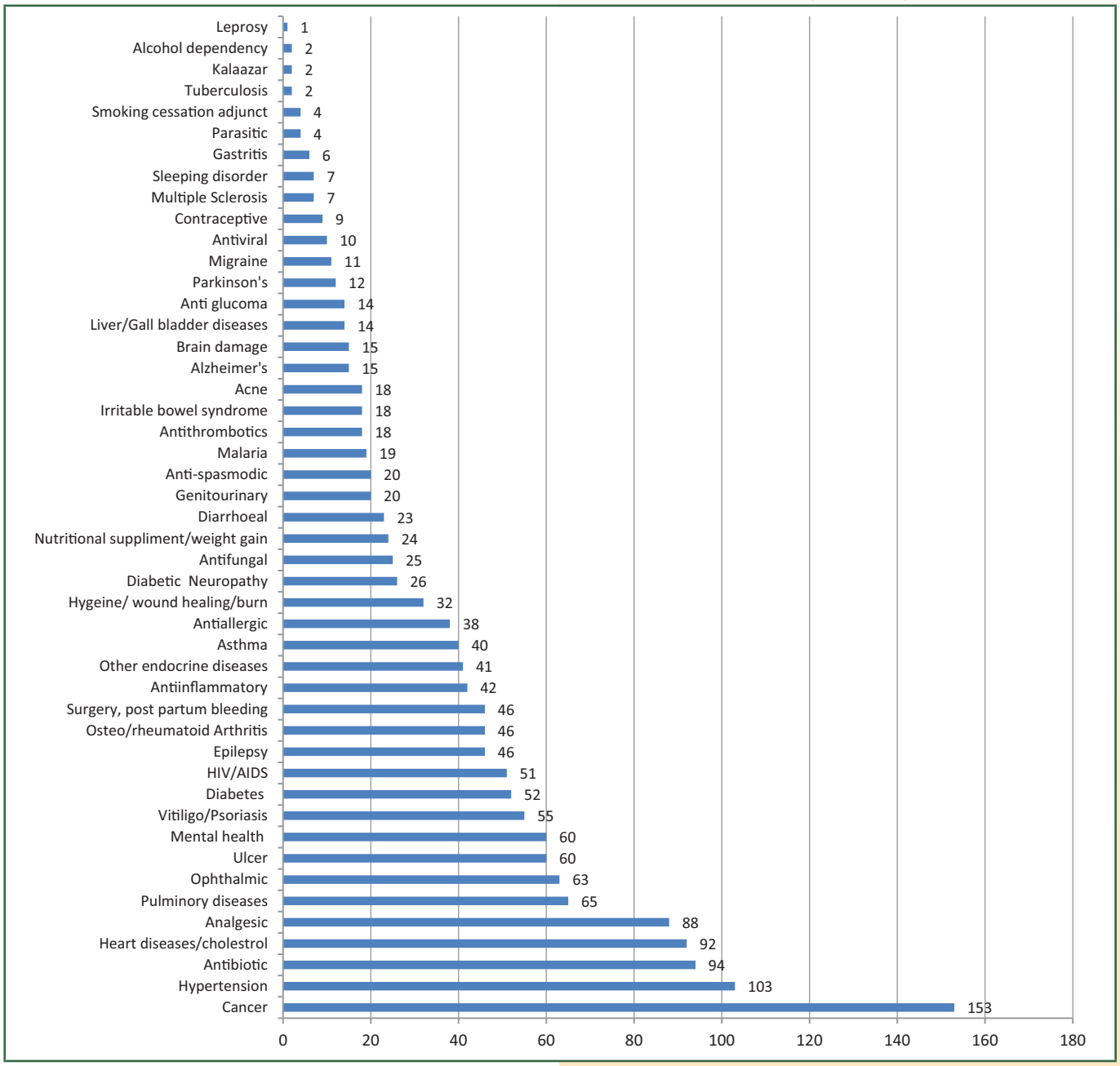
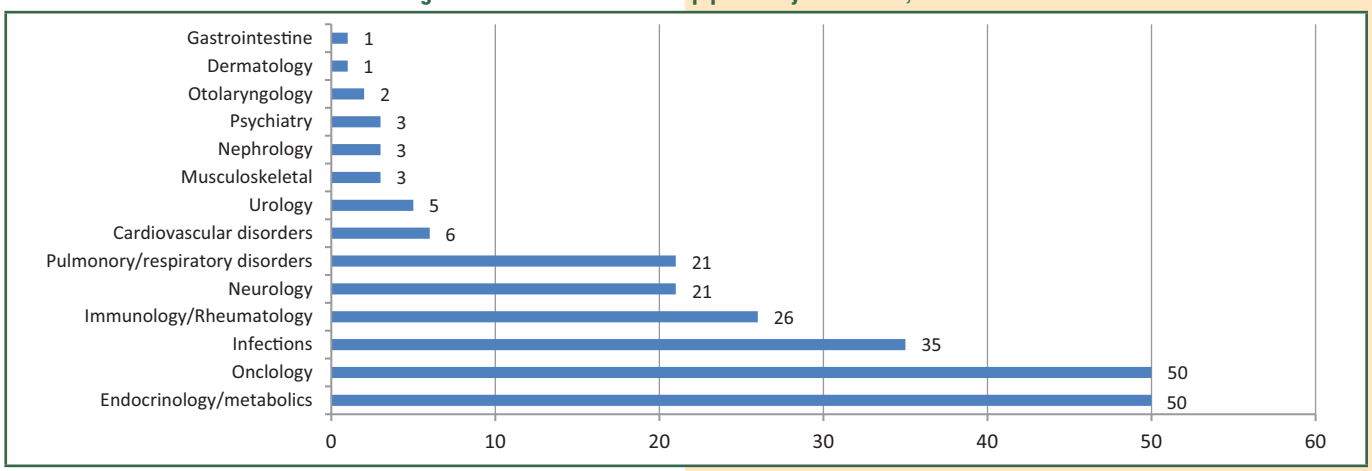
Figure 1 Number of new drugs approved for marketing across indication (2001-2017)



Source: Central Drugs Standard Control Organization (CDSCO)

Figure 2 Number of NCEs in pipeline by indication, India



Source: Differding (2017)

Disease Burden

Table 1 details the causes of death in India for the year 2015 for ten diseases/conditions within CDs and twelve disease/conditions within NCDs for the age groups of 0-14, 15-49, 59-69 and 70+. The data show that although the epidemiological transition is a reality, CDs were the causes of death for nearly 78% in the age group of 0-14. Within this group, the neonatal conditions accounted for the death of 43%. While respiratory infections caused 14% of deaths, diarrhoea accounted for nearly 10% of deaths in this age group. Similar to the overall trend, NCDs are the major causes of death in the age group of 15-49, followed by injuries and CDs. The largest single cause of deaths in this group was cardiovascular diseases (17.4%), followed by cancer (11.2%), tuberculosis (9.1%) and digestive diseases (9%). The leading cause of deaths in the age group 50-69 is also the cardiovascular disease (36%), which is followed by cancer (13%), respiratory diseases (12%), tuberculosis (6%), digestive diseases (6%) and diabetes and endocrine diseases (4%). Cardiovascular diseases (32.16%), respiratory diseases (18.85%) and respiratory infections (9.87%) were the major causes of deaths, among others, in the 70+ population.

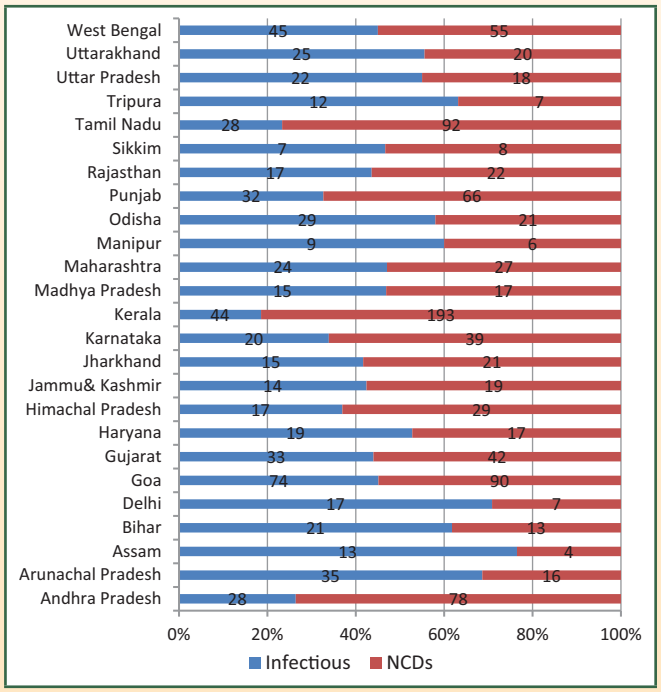
Table 1: Percentage contribution of causes of death by age group, India, 2015

Disease/condition	Age groups				
	0-14	15-49	50-69	70+	All Ages
Communicable, Maternal, Perinatal and Nutritional Conditions	**78.31**	**23.17**	**16.13**	**20.21**	**28.09**
Tuberculosis	0.98	9.13	6.16	3.32	4.92
HIV/AIDS	0.52	2.88	0.30	0.00	0.70
Diarrhoea	9.65	2.16	3.32	4.62	4.51
Other common infectious diseases	7.00	3.05	1.29	0.79	2.28
Malaria and tropical diseases	1.10	1.48	0.63	0.43	0.79
Other Infectious Diseases	1.72	0.26	0.31	0.44	0.56
Respiratory Infections	13.90	1.16	3.20	9.87	6.80
Maternal conditions	0.00	2.44	0.00	0.00	0.45
Neonatal conditions	42.59	0.00	0.00	0.00	6.30
Nutritional deficiencies	0.84	0.60	0.91	0.73	0.78
Non-communicable diseases	**13.65**	**47.30**	**76.21**	**74.07**	**60.85**
Neoplasms	0.71	11.25	13.08	5.63	8.24
Cardiovascular diseases	0.57	17.48	35.75	32.16	25.89
Respiratory diseases	0.68	2.18	11.66	18.85	10.87
Digestive diseases	1.62	9.07	5.94	4.22	5.26
Neurological conditions	0.84	1.62	1.01	3.49	1.99
Diabetes and endocrine diseases	0.66	1.17	4.00	5.15	3.39
Congenital anomalies	7.89	0.20	0.02	0.01	1.21
Genitourinary diseases	0.44	3.12	3.86	3.48	3.08
Mental and substance use disorders	0.00	0.97	0.23	0.10	0.29
Skin diseases	0.04	0.09	0.11	0.17	0.12
Musculoskeletal diseases	0.01	0.15	0.53	0.81	0.49
Other Non-communicable diseases	0.17	0.14	0.08	0.07	0.03
Injuries	**8.04**	**29.53**	**7.66**	**5.72**	**11.06**
Total	100	100	100	100	100

Source: Mortality database of WHO

Similarly, at all India level, morbidity burden due to NCDs was noticeably higher than CDs across all age groups, excepting 0-14 wherein infectious diseases accounted for a substantial morbidity burden. However, State wise data showed some variations in the morbidity pattern (see figure 3). For instance, while the prevalence of NCDs was more than infectious diseases as a whole for India, some states including Arunachal Pradesh, Assam, Bihar, Delhi, Haryana, Manipur, Odisha, Tripura, Uttar Pradesh and Uttarakhand reported infectious diseases more than NCDs.

Figure 3 Self reported disease prevalence across selected Indian states, 2014 (per '000 population)



Source: Paul and Singh (2017) based on NSSO 71st round (2014)

Conflicting Priorities

The critical question now is whether drug development in India is sensitive to this complex disease burden of the country. We juxtaposed the data on drug development with disease burden across age groups and drew the following inferences to answer this question. First, the disease burden of 0-14 age group was disproportionately prioritised in drug development. Excepting diarrhea for which 23 new drugs came to the market between 2000 and 2017, all other major disease causes of deaths in the 0-14 age group did not figure in the development of new drugs. Secondly, while several new medicines came to the market for treating cardiovascular diseases,

hypertension, cancer and digestive disorders, tuberculosis, which is resurging in several parts of the country (with increasing incidence of multi-drug resistant cases) in the age group of 15-49, did not receive sufficient attention in drug development. Only two new drugs came to the market for tuberculosis treatment between 2000 and 2017. Thirdly, when we come to the age group 70+, it is found that most of the major causes of deaths excepting cardiovascular diseases (35% of death in the age group) were not in the priority areas of drug development in India. Most importantly, infectious diseases were prioritised even lower than drugs for cosmetic treatments (acne, weight loss, hair removal, general dermatology). In short, R&D of the Indian pharmaceutical and medical-biotechnology industries have focussed less on the overall diseases burden of several Indian states as well as population including children and elderly and more on the economically active age group of 15 to 69, which constitutes its potential customer target group.

Conflicts in the priorities of drug development and disease burden have posed several public health challenges to India. First set of issues relates to the preparedness for resurging and emerging infectious diseases. Availability of vaccines and drugs plays an important role in controlling infectious diseases along with the provision of better social determinants of health like nutritos food, safe drinking water and sanitation facilities. We have recently seen the resurgence and emergence of several infectious diseases including cholera, tuberculosis , diphtheria, dengue, chikungunya, malaria, avian influenza, Japanese encephalitis, leptospirosis, nipah to list a few, across different regions of India in a major way (George et al 2018). The existing focus of the drug industry is not sufficiently addressing this issue. Second set of issues relate to the pricing of drugs and their affordability to poor people. Although India is one of the major manufacturers and exporters of generic medicines, these are predominantly sold under brand names in the domestic market – leading to significant price differences for the same product. Prescription practices of doctors, hence, have an important role in the purchasing of medicines by patients. The doctor who prescribes medicine is the sole authority in a highly power-ridden paternalistic profession of medical practice in India. Aggressive marketing of medicines by pharmaceutical companies through networks of practitioners and the incentive sops offered by pharmaceutical companies to doctors for prescribing a particular brand of medicine could be a major cause of cost escalation as there is no regulation on drug prescription in the country at present.

Policy Suggestions

The mismatch between the priorities of drug development and public health is a critical public policy concern in India. The study proposes the following recommendations in this regard:

- It is important for India to have an independent R&D agenda in respect of drug development, which is informed from the demographic, epidemiologic and other diverse public health concerns in the country. At present, R&D priorities of Indian firms are the extension of priorities of the global pharmaceutical giants due to the international division of innovations where India is still at the bottom of the hierarchy (Abrol et al, 2011).
- To begin with, there is an urgent need for assessing the current state of health R&D in view of the increasing burden of diseases, the need for new knowledge and the medicine/vaccines required to deal with the present and future threats of diseases.
- Setting of R&D agenda also comes along with funding. The state should promote fundamental research in universities and research laboratories with generous funding.
- As it is well known, development of new drugs, vaccines and diagnostic technology is a highly expensive and time consuming endeavour with a huge risk of failure. Public funded R&D, hence, in the present organisation of healthcare innovation may not be always feasible. Perhaps, what is feasible is the restriction of state facilitation to innovations that are in tandem with public health priorities.
- India has moved from cost-based pricing to market based pricing policies with regard to drugs and pharmaceuticals. Our analysis show that this does not bring down the prices of drugs rather it justifies the prices of largest selling drugs. Hence, it is important to go back to cost-based pricing or work towards new initiatives like value based pricing, which is now gaining popularity in the developed world.
- Medicines constitute the largest component of medical expenditure. It is important to have a pharmaceutical cost containment policy in India and also to include newly coming high impact drugs for NCDs under price control.
- Similarly, standardisation of medical prescriptions is another issue that needs attention, as we have found that prescription practices could influence the cost of medical care considerably, especially considering the price variations drugs across brands. The government should come up with a standard treatment protocol for treating each disease and strictly implement the same.

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