Original Article

A descriptive study of new drug approvals during 2017–2021 and disease morbidity and mortality patterns in India

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Abstract

Aim: Studies show the presence of a mismatch between drug research and disease burden. A study conducted in the European Union found that new drug development was restricted to certain diseases. A study of biosimilar approvals in India found that 87% of drugs were for treating noncommunicable diseases. This study aimed to determine the new drugs approved in India from 2017 to 2021 and the top ten causes of morbidity and mortality and detect the presence of any discordance between these.

Methods: A descriptive study was conducted using data on new drug approvals accessed from the Central Drugs Standard Control Organization website. The top ten causes of mortality and morbidity in India from 2015 to 2019 were identified from the Global Burden of Diseases database. Descriptive statistics were used to compare the drug approvals and the leading diseases.

Results: One hundred twenty-six drugs were approved during the study period. Antineoplastic drugs constituted 19.84% of the approvals, antimicrobials 18.25%, and cardiovascular drugs 9.52%. Ischemic heart disease and chronic obstructive pulmonary disease were the two leading causes of morbidity and mortality. Diarrheal diseases, lower respiratory tract infection, and drug-susceptible tuberculosis were among the top ten causes. Ten antibacterials, including four antitubercular drugs, were approved during this period. Two drugs were approved for rare diseases.

Conclusion: Our study showed that the drugs approved were largely in line with the prevalent disease burden, and there was no significant discordance observed. Some diseases, such as ischemic stroke/intracranial hemorrhage, require further efforts in bringing forth newer pharmacotherapy options.

Keywords: Drug approval, investigational new drugs, morbidity, mortality, noncommunicable diseases

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INTRODUCTION

Drug development is the process of bringing a new pharmaceutical compound to the market once a lead substance has been identified through the process of drug discovery. Health-care costs in the past years have increased tremendously, which means companies go by the value-for-money approach in the process of innovation.[1] Ideally, there needs to exist a balance between what research is conducted to produce new drugs and what the public health-care system needs in a country.[2]

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In the recent past, many clinical research organizations have been shifting their focus from developed countries toward developing countries, including India, as the country offers a good potential for the development and testing of new drugs in terms of large population and patient diversity. However, what remains to be seen is whether this research is directed toward the medical needs of the country or caters to the international market. The health system, including research, in any country needs to be aligned to the needs of the population they serve, and this needs to be assessed regularly as well.[3] Innovative medicines should be seen as investments and not merely expenses to the company.[1] Earlier studies conducted in this regard have shown that a mismatch does exist between drug research and the health burden, especially in developing countries.[4] Also to be considered are the ethical and scientific implications of the global clinical trials being conducted in India in the zeal to have "faster" and "cheaper" trials since these may have an indirect implication on the research–disease burden gap.[5]

In India, the Central Drugs Standard Control Organization (CDSCO) regularly releases a list of newly approved drugs, categorized as new drugs as per the regulatory definition, and this data can provide insight into the pattern of new drugs being approved for marketing in the country.[6] Comparing this with the prevalent disease pattern in India can provide a reasonable idea regarding the presence of any potential gap in areas of drug development in the context of the predominant health-care needs of the country that need to be addressed.[7] Hence, the objective of our study was to determine the new drugs approved in India from 2017 to 2021 and the top ten causes of morbidity and mortality and detect the presence of any discordance between these.

METHODS

A descriptive study was conducted using the data on new drug approvals and leading causes of morbidity and mortality in India available from online data sources. The study was approved by the Institutional Ethics Committee. The data regarding new drug approvals were accessed from CDSCO, the regulatory body which grants approval for marketing of drugs in India. The data for the period 2017–2021 were extracted from publicly accessible documents via the CDSCO website.[6]

The morbidity and mortality data for India were extracted from the Global Burden of Diseases (GBD), Injuries, and Risk Factors Study 2019 database.[7] GBD provides incidence, prevalence, mortality, and disability-adjusted life year (DALY) estimates for 369 diseases and injuries for 204 countries and territories.[8] Each year, the estimates are updated based on the availability of new data and changes in estimation methods. The data, available for different age and sex groups, span the past three decades, allowing comparisons over time, across age groups, and among populations. These data are being used by policymakers in many countries including Brazil, India, China, and the United Kingdom to assess the health of the population and to plan the available resources accordingly.[7] Since drug development is based on diseases of significance identified over the preceding years, data for the 2015–2019 time period, 2 years preceding the new drug approval time period, were collected.

The anatomical, chemical, and therapeutic (ATC) classification was used to categorize each new drug approved,[9] and the approved indications for their use were coded using the International Classification of Diseases (ICD) version 10.[10] When a complete ATC code was unavailable for a drug, we recorded the ATC code for the drug group if present. Similarly, when an ICD-10 code was unavailable for a specific indication, we recorded the ICD code for a broader indication to which the disease could be assigned. All types of finished drug formulations were considered; drugs approved as bulk powders were considered only when a finished formulation of the same was not available. A drug was defined as a new drug in accordance with the New Drugs and Clinical Trials Rules 2019;[11] accordingly, a drug which represents minor changes in the chemical/pharmacokinetic/pharmacodynamic profile, a me-too drug, was also considered a new drug. Different drug strengths or dosage formulations of the same drug approved for different indications or different severity classes of the same disease were considered different drugs. Regarding the indications for drug use, we considered only the approved indication(s) as listed on the regulatory document. The top ten causes of mortality and morbidity in India were identified from the GBD database for a 5-year period (2015–2019),[7] and the average contribution of each disease (in terms of percentage of the total) over this time period was calculated to obtain a final list of top ten causes of mortality and DALY, which was used to compare with the new drug approvals. DALY, which represents the years of life lost due to premature death and disability, was used as an indicator of disease morbidity; one DALY equals loss of 1 year of full health. Drugs approved for rare diseases, debilitating lifelong diseases or disorders with a prevalence of one or less per 1000 population, were identified; rare diseases as listed in the National Policy for Rare Diseases, 2021, were considered.[12] The mechanism of action of the approved

drugs, in terms of whether they act via receptors, enzymes, ion channels, transporters, or other mechanisms, was identified. In the case of fixed-dose combinations, the mechanism of action of the newer active ingredient in the combination was considered.

Statistical analysis

The new drug approval data were extracted onto a Microsoft Excel worksheet (Microsoft Corporation, Redmond, Washington, United States). The ATC codes for the approved drugs and the ICD-10 codes for the approved indications were added as described earlier. The data have been presented using descriptive statistics, based on the year of approval and pharmacological and therapeutic categories.

RESULTS

One hundred twenty-six drugs were approved from 2017 to 2021. The number of new drugs approved each year is shown in Figure 1. The highest number of new drug approvals (32/126, 25.39%) occurred in 2017. The various classes of new drugs approved are shown in Table 1. Antineoplastic drugs constituted 19.84% (60% were protein kinase inhibitors) of the approvals followed by antimicrobials at 18.25% (43.47% were antibacterials) and cardiovascular drugs at 9.52% (25% were angiotensin receptor blockers). Ten antibacterials, including four antitubercular drugs, were approved during this period.

The major causes of mortality and DALY in India during the time period 2015–2019 are shown in Table 2. Ischemic heart disease and chronic obstructive pulmonary disease were the leading causes of mortality; ischemic heart disease and diarrheal diseases were the leading contributors to DALY. Diarrheal diseases, lower respiratory tract infection, and drug-susceptible tuberculosis were among the top ten causes of morbidity and mortality.

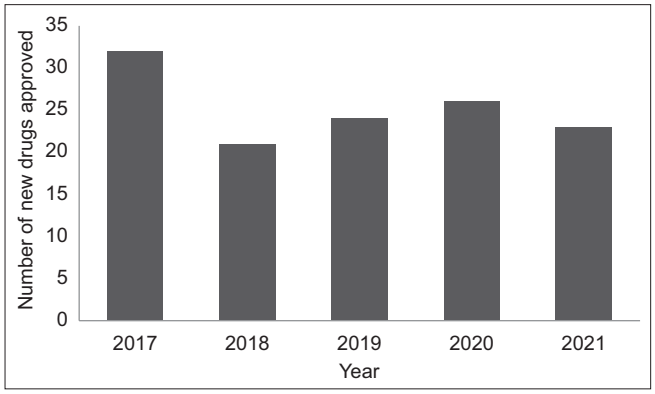

Figure 1: New drug approvals in India during 2017–2021

Table 1: Categories of new drugs approved in India during 2017–2021

Drug class	Number of drugs approved
Alimentary tract and metabolism products	6
Anti-obesity	2
Synthetic bile analog	1
Antiemetic	1
Laxative	1
Enzyme inhibitor	1
Drugs for peptic ulcer and GORD	1
Proton pump inhibitor	1
Hypothalamic and pituitary hormones and analogs	3
Somatostatin analog	1
Oxytocin analog	1
Adrenocorticotrophic hormone	1
Sex hormones and modulators of genital system	5
Progestogens	3
Progesterone receptor modulator	1
Gonadotropin	1
Cardiovascular drugs	15
Calcium channel blockers	3
Endothelial receptor agonist	1
Soluble guanylate cyclase inhibitor	1
ARB	3
ARB and calcium channel blocker combination	1
Adrenergic and dopaminergic agonists	2
Anti-arrhythmic	1
Antithrombotic	2
For hypovolemic shock	1
Dermatologicals	6
Cicatrizant	1
Proteolytic enzyme	1
Topical antibiotic	1
Antiseptics/anti-infectants	3
Antidiabetics	2
Sodium-glucose cotransporter-2 inhibitor	1
Dipeptidyl peptidase-4 inhibitor	1
Nervous system drugs	9
Antipsychotic	1
Antidepressants	2
Hypnotic/sedative	1
Antiparkinsonian	1
Anti-epileptics	2
Others	2
Ophthalmologicals	5
Antiallergic	2
Antiglaucoma	3
Antineoplastic drugs and immunomodulators	31
Proteasome inhibitor	1
Protein kinase inhibitors	15
Alkylating agent	1
Antimetabolites	2
Anti-estrogen	1
Anti-androgen	1
Cytotoxic drug	1
Others	3
Immunosuppressants	6
Antivirals	9
Polymerase inhibitor	1
Nucleoside/nucleotide/reverse transcriptase inhibitors	3
Direct-acting	5
Antibacterials	10
Antitubercular	4
Aminoglycoside	1
Beta-lactams	3
Fluoroquinolones	2

Contd...

Table 1: Contd...

Drug class	Number of drugs approved
Urologicals	4
Adrenergic agonists	2
Phosphodiesterase-5 inhibitor	2
Others	20
Antifungals	2
Antimalarial	1
Intestinal anti-infective	1
Antihistamines	2
For musculoskeletal disorders	1
For obstructive airway disease	2
Cough suppressant	1
Chelating agents	2
Contrast media	2
Diagnostic radiopharmaceutical	1
Others	1
No ATC codes	4

ARB=Angiotensin receptor blocker, ATC=Anatomical, chemical, and therapeutic GERD=Gastro-oesophageal reflux disease

Table 2: Top ten causes of mortality and disability-adjusted life years in India during 2015–2019

Cause	Mortality*	DALY*
Ischemic heart disease	1	1
COPD	2	4
Diarrheal diseases	3	2
Lower respiratory infections	4	3
Drug susceptible tuberculosis	5	6
Intracerebral hemorrhage	6	-
Ischemic stroke	7	-
Diabetes mellitus type 2	8	9
Falls	9	-
Asthma	10	-
Neonatal preterm birth	-	5
Other neonatal disorders	-	7
Dietary iron deficiency	-	8
Self-harm by other specified means	-	10

*The numbers indicate the overall cause ranking for the time period 2015–2019. DALY=Disability-adjusted life years, COPD=Chronic obstructive pulmonary disease

Neonatal preterm birth was the 10th leading cause of death in 2015–2016 but was later replaced by asthma. Neonatal encephalopathy due to birth asphyxia and trauma in 2015 and intracerebral hemorrhage in 2016 and 2017 were the 10th leading causes of DALY, respectively. The drugs approved for the leading causes of mortality in India are listed in Table 3; 21.43% (27/126) of drugs were approved for such diseases. In terms of individual causes, 9 drugs were approved for ischemic heart diseases (including hypertension), 6 for diabetes mellitus (including drugs approved for associated conditions such as diabetic foot ulcer and obesity), and 4 each for tuberculosis and lower respiratory tract infections. No new drugs were approved during the study period for diarrheal diseases, intracerebral hemorrhage, and ischemic stroke.

Regarding the mechanism of action of the approved drugs, 44.44% (56/126) of drugs act via enzymes, 26.19% (33/126) through receptors, 6.35% (8/126) by binding to ion channels, 3.17% (4/126) through transport proteins, and 19.84% (25/126) by other mechanisms. Two drugs were approved for rare diseases. A capsule formulation of eliglustat for the long-term treatment of adult patients with Gaucher disease type 1 who are CYP2D6 extensive, intermediate, or poor metabolizers as detected by an appropriate test, and powder formulation of risdiplam for the treatment of spinal muscular atrophy in patients 2 months of age and older, approved in the years 2017 and 2020, respectively. Besides the drugs approved for rare diseases, new chemical entities or drugs acting by a novel mechanism of action included delamanid and pretomanid for tuberculosis; midostaurin for acute myeloid leukemia and advanced systemic mastocytosis; olaparib for ovarian and breast cancer; lorcaserin for chronic weight management; fixed-dose combination of sacubitril and valsartan for chronic heart failure; fingolimod for relapsing forms of multiple sclerosis; ripasudil and netarsudil for glaucoma; diperoxochloric acid for wound healing in diabetic neuropathic ulcers; endoxifen for acute treatment of manic episodes; pixantrone for relapsed or refractory aggressive non-Hodgkin's B-cell lymphoma; ozenoxacin for the topical treatment of impetigo; 2-deoxy-D-glucose for moderate-to-severe COVID-19 infection; cetilistat for the treatment of obesity; and tafamidis for the treatment of wild-type or hereditary transthyretin amyloidosis in adult patients with cardiomyopathy. There were four drugs approved which did not have a specific ATC code. Some diseases which were leading contributors to mortality and DALY, such as falls and self-harm, are mainly managed by nonpharmacological measures.

DISCUSSION

We studied the drug approval patterns in India during 2017–2021 and the leading causes of mortality and DALY during 2015–2019. The drugs approved during the study period, in general, addressed the diseases of interest to varying extents. As per the New Drugs and Clinical Trials Rules 2019, new drug development should take into consideration the risk–benefit ratio, the existing drugs and the relative advantages over these, and the unmet medical needs of the country.[11] Noncommunicable diseases have witnessed a steep rise over the past decades in India, accounting for more than 60% of the total deaths; this rising disease burden prompted the launch of the National Programme for Prevention and Control of Cancer, Diabetes, Cardiovascular Diseases and Stroke to strengthen the health system in tackling the problem.[13] The approval of a significant number of drugs for cardiovascular disease,

Table 3: Drugs approved during 2017–2021 for the top ten causes of mortality in India

Disease condition	Approved drug	ATC code	Year of approval	Approved indication(s)*	ICD-10 code
Ischemic heart disease	Argatroban hydrate injection 250 mg/2.5 mL	B01AE03	2017	Prophylaxis or treatment of thrombosis in adult patients with heparin-induced thrombocytopenia	3B64.12
	Efonidipine hydrochloride ethanolate tablets 10/20/40 mg	C08CA	2017	Hypertension; renal parenchyma hypertension; angina	BA00.Z, BA02, BA40.7
	Azilsartan + chlorthalidone (40+12.5/25 mg)	C09DA09	2018	Mild-to-moderate hypertension	BA00.Z
	Fimasartan potassium trihydrate film-coated tablets 30/60/120	C09CA10	2018	Mild hypertension	BA00.Z
	Sacubitril + valsartan 50 (24+26)/100 (49+51)/200 (97+103) mg film coated tablets	C09DX04	2018	Chronic heart failure (NYHA Class II–IV) and reduced ejection fraction	BD1Z and XT8W
	Azelnidipine tablets 16 mg	C08CA	2019	Stage II hypertension	BA00.Z
	Azelnidipine tablets 8 mg	C08CA	2020	Stage I hypertension	BA00.Z
	Azelnidipine + telmisartan tablets (8 mg+40 mg)	C09DB	2020	Stage II hypertension	BA00.Z
	Cangrelor tetrasodium injection 50 mg/vial	B01AC25	2021	Adjunct to percutaneous coronary intervention in patients who have not been treated with a P2Y12 platelet inhibitor and are not being given a glycoprotein IIb/IIIa inhibitor	NA
COPD	Fluticasone furoate + vilanterol trifenatate (100+25 μg)	R03AK10	2017	Maintenance treatment and to reduce exacerbation of COPD	CA22.0, CA22.Z, CA21.Y
Diarrheal diseases	Nil			Nil	
Lower respiratory infections	Arbekacin injection 200 mg/4 mL	J01GB12	2017	Methicillin-resistant *Staphylococcus aureus* infection	MG51.00
	Ceftazidime + avibactam (2+0.5 g) powder for concentrate for solution for infusion	J01DD52	2018	Complicated intra-abdominal and urinary tract infections, hospital-acquired pneumonia with susceptible Gram-negative microorganisms	NA
	Isavuconazole sulfate capsules 100 mg	J02AC05	2020	Invasive aspergillosis and mucormycosis	1F20.0, 1F2C
	Isavuconazole sulfate powder 200 mg	J02AC05	2020	Invasive aspergillosis and mucormycosis	1F20.0, 1F2C
Drug susceptible tuberculosis	Delamanid tablets 50 mg	J04AK06	2017	Multidrug-resistant tuberculosis	MG52.00
	Rifapentine tablets 150 mg	J04AB05	2019	Latent tuberculosis in adults and children 2 years and older who are at high risk of progression to tuberculosis disease	1B14
	Pretomanid tablets 200 mg	J04AK08	2020	Extensively drug-resistant or treatment intolerant or nonresponsive multidrug-resistant tuberculosis	1B10.0
	Isoniazid + rifapentine (300/300 mg) tablets	J04AM02	2021	Latent tuberculosis	1B14
Intracerebral hemorrhage	Nil			Nil	
Ischemic stroke	Nil			Nil	
Diabetes mellitus type 2	Cadexomer iodine ointment 500 mg (contains 0.9% w/v iodine)	D03AX01	2018	Chronic exuding wounds	EH90, BD54
	Evogliptin tartrate tablets 5 mg	A10BH07	2018	Type 2 diabetes mellitus	5A11
	Lorcaserin hydrochloride tablets 10 mg	A08AA11	2018	Chronic weight management in obese or overweight	5C1Z
	Remogliflozin etabonate tablets 100 mg	A10BK	2019	Type 2 diabetes mellitus	5A11
	Diperoxochloric acid topical solution	D08AX	2019	Diabetic neuropathic ulcers	BD54
	Cetilistat tablets 120 mg	A08AB	2021	Obesity	5B81
Falls	Droxidopa capsules 200/300 mg	C01CA27	2019	Symptomatic neurogenic orthostatic hypotension	8D87.0Y
Asthma	Fenspiride hydrochloride extended-release tablets 80 mg	R03DX03	2019	Acute rhinosinusitis, moderate persistent asthma add-on therapy	CA01, CA23
	Benzonatate capsules 100 mg	R05DB01	2021	Refractory cough	MD12

*The indications have been abbreviated. COPD=Chronic obstructive pulmonary disease, ATC=Anatomical, chemical, and therapeutic, NYHA=New York Heart Association, ICD=International Classification of Disease, NA=Not available

diabetes, and cancer indicates that the drug discovery and development is largely in line to address the priority health-care needs of the country.

In an earlier study conducted to observe the pattern of biosimilars approved over a 16-year period in India, grouped based on the diseases for which they were

indicated, it was found that almost 87% of the approved drugs were for treating noncommunicable diseases; most of the drugs were approved for the treatment of cancer, followed by hypertension and cardiovascular diseases.[2] While infectious diseases are still responsible for a large disease burden in India, epidemiological studies have shown that noncommunicable diseases are going to be the leading causes of morbidity and mortality; there is a need for upgrading the existing health-care system to address the increasing demand for appropriate treatment measures for these diseases. The finding of our study of approval of a large number of anticancer drugs, alongside antimicrobials, is in line with this view.

An earlier study by Charan *et al*. conducted to assess the correlation between drug approval compared to the disease burden in India found a significant mismatch between the two and also recommended an action plan to formulate research toward addressing the disease burden in the country.[3] Another study by Trouiller *et al*. which assessed the trend of drug development versus disease burden also pointed out this difference and a significant mismatch, especially with regard to tropical neglected diseases and new drugs being approved.[4] A study conducted in the European Union to assess if development of innovative medicines was focused toward global public health, by reviewing available information from 1995 to 2009, found that the development of new/innovative medicines was higher for certain diseases, and an imbalance was noted.[14] Furthermore, another study conducted in Brazil highlighted the issue of a decrease in the number of new drugs discovered and an increase in the number of me-too drugs.[15] It is to be noted that a number of drugs approved, as shown in the current study, belong to existing therapeutic groups and share the same/similar mechanism of action and do not constitute a truly new drug; this point becomes more obvious when the individual drugs approved for a disease condition are looked into. Hence, the observations of the earlier studies are not refuted by the current study data. Nonetheless, incremental advantages in terms of better efficacy and decreased adverse effects are a part of the drug development process. It is also to be noted that the development and clinical phase testing of a truly new drug takes several years, except in emergency situations, and hence, a short time frame of 5–10 years may not be appropriate.

Almost 70% of approved drugs act by interacting with receptors or enzymes. Some new drugs approved were new chemical entities that act by a novel mechanism or are unrelated to existing medications. Whether the availability and use of these novel drugs will translate into a significant clinical benefit in terms of better efficacy or decreased adverse effects will need to be determined by appropriately designed clinical studies and study of real-world data.

According to the available data for India, the conditions that accounted for a large proportion of DALY were those causing premature mortality, such as ischemic heart disease, perinatal conditions, chronic respiratory diseases, diarrhea, and respiratory infections.[16] Developing countries must have a therapeutic and research plan that makes the best use of available resources while addressing the major diseases that affect the people. The transition from communicable to noncommunicable diseases being the major health concern is also an important aspect to be considered in deciding on the allocation of scarce/limited resources for public health welfare. The difficulties associated with new drug discovery and development for diseases, such as tuberculosis, hypertension, and diabetes mellitus, where several drugs with different mechanisms of action are already available, strongly emphasize the need for greater commitment toward primordial and primary disease prevention efforts.[13] It is also to be noted that efforts toward improving the capacity for drug development and streamlining approval processes will not provide the desired results if not complemented by an equal effort toward monitoring the safety of approved drugs in the clinical setting by establishing robust pharmacovigilance systems and encouraging reporting of adverse drug events among health-care professionals and patients.

CONCLUSION

Our study showed that drug approvals in India were largely in line with the prevalent disease burden, although the additional therapeutic benefit provided by new drugs over the existing therapies for individual disease conditions may not always be significant. Some diseases, such as ischemic stroke/intracranial hemorrhage, require further efforts in bringing forth newer pharmacotherapy options. Furthermore, more effort is required to support the research and development of novel drugs while also focusing on disease prevention measures.

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Conflicts of interest
There are no conflicts of interest.

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