

Tracking the Pharmaceutical Pipeline: Clinical Trials and Global Disease Burden

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Abstract

Aggregate data about pharmaceutical research and development (R&D) tend to examine Phase III trials. Hence, there are few published data about investigational drugs in earlier phases of clinical development that might fail. It is also unclear how well R&D corresponds to disease burden. We track the pharmaceutical pipeline using data from industry publications that provide otherwise unreported information about industry-sponsored clinical trials. The sample includes 2,477 unique drug entities in 4,182 clinical trials. The majority of drugs targeted neoplasms (26.20%), neurological diseases/diseases of the sense organs (13.48%), infectious and parasitic diseases (10.5%), and endocrine, metabolic, nutrition, and immunity disorders (9.45%). Less than 6% of drugs targeted diseases of the circulatory system, which represent the most prevalent causes of global mortality. Detailing the pharmaceutical pipeline, our findings suggest that pharmaceutical development does not adequately address global disease burden. Future research on the under-reported details of Phase I and II clinical trials is needed to understand how the industry operates and how its resource-allocation matches global health concerns. *Clin Trans Sci* 2014; Volume 7: 297–299

Keywords: clinical trials, phase I, phase II

Introduction

The pharmaceutical industry has been criticized for the high cost and low relevance of its products.^{1–3} Previous studies of the relationship between clinical research priorities and various measures of disease burden indicate that medical needs and drug development are disconnected from the needs of the global population.^{4–7} The World Health Organization claims that circulatory system diseases represented the top two causes of mortality in the world in 2004, accounting for 23.6% of all deaths.⁸ Additionally, diseases of the respiratory system were the third and fourth leading causes of death worldwide in 2004 (a combined 12.1%). Many chronic diseases also have limited drug development activity, although the most glaring drug development failures may be in the area of infectious diseases, responsible for more than 1,500 deaths per day.²

While the majority of the literature on drug development examines pivotal Phase III trials for drugs available on the market, published findings rarely report on earlier-phase trials or of drugs that have not been submitted to the FDA for market approval.^{4–7} Most reports indicate that Phase III trials have a high success rate; approximately 80% of products that enter this phase of testing will receive FDA approval. However, fewer than 40% of all investigational drugs ever commence Phase III testing, with little known about the disease focus of drugs that do not reach Phase III testing.⁹ This suggests that the majority of the pharmaceutical industry's R&D portfolio is absent from the published literature and phases I and II are largely unexamined aspects of the clinical development pipeline. As a result, research is needed that tracks early phases of pharmaceutical research and the correspondence between global health concerns/disease burden and the resource investment of the industry.

Methods

To better assess the industry's clinical development, we created a database to track the pharmaceutical pipeline using industry-sourced news and information (CenterWatch Weekly

[CWW]) about clinical trials reported over a 5-year period (2006–2011). CWW is a subscription-only weekly publication produced by CenterWatch, the clearinghouse for information on industry research and development. In each issue, CWW reports information on investigational drugs and clinical trials. While targeting industry members, data from this publication may be more conservative and inclusive of Phase I and II trials than the clinical trials registered at clinicaltrials.gov, which suffers from duplication and under-reporting of trials.¹⁰

We extracted data on the company name, drug name, trial phase, the therapeutic area designated for each drug, and the appropriate International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM) code for each drug. Each "Therapeutic Area" was assigned an appropriate code, using an online resource for classification (<http://www.icd9data.com>). Entries that were not easily labeled were discussed with a second reviewer to reach consensus. In order to count the number of unique drugs in the pipeline, the first appearance (chronologically) of a particular drug was assigned a "unique" variable status and subsequent appearances were classified as "nonunique."

Results and Discussion

The database consisted of 3,816 cases, representing 2,477 unique drug entities and 4,182 trials. See *Table 1* for the distribution of drugs across ICD-9 disease categories. Neoplasms (ICD-9-CM code #2) was the most common disease category targeted by drugs in the pipeline ($n = 649$, 26.2%), followed by neurological and sense organs (code #6, $n = 334$, 13.48%), infectious and parasitic diseases (code #1, $n = 260$, 10.5%), and endocrine, metabolic, nutrition, and immunity (code #3, $n = 234$, 9.45%). The least represented codes were complications of pregnancy (code #11, $n = 1$, 0.04%), perinatal conditions (code #15, $n = 1$, 0.04%), and congenital anomalies (code #14, $n = 6$, 0.24%). Results were consistent across the 5 years. Of the 4,182 trials, 36% were Phase I, 46% were Phase II, and 18% were Phase III.

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DOI: 10.1111/cts.12163

ICD-9-CM	Therapeutic area	Total entries	
		n	%
1	Infectious and parasitic diseases	260	10.5
2	Neoplasm	649	26.2
3	Endocrine, nutritional and metabolic diseases, and immunity disorders	234	9.45
4	Diseases of the blood and blood-forming organs	57	2.3
5	Mental disorders	102	4.12
6	Diseases of the nervous system and sense organs	334	13.48
7	Diseases of the circulatory system	147	5.93
8	Diseases of the respiratory system	168	6.78
9	Diseases of the digestive system	100	4.04
10	Diseases of the genitourinary system	71	2.87
11	Complications of pregnancy, childbirth, and the puerperium	1	0.04
12	Diseases of the skin and subcutaneous tissue	98	3.96
13	Diseases of the musculoskeletal system and connective tissue	119	4.80
14	Congenital anomalies	6	0.24
15	Certain conditions originating in the perinatal period	1	0.04
16	Symptoms, signs, and ill-defined conditions	50	2.02
17	Injury and poisoning	63	2.54
Suppl V	Supplementary classification of factors influencing health status and contact with health services	11	0.44
Suppl E	Supplementary classification of external causes of injury and poisoning	6	0.24

Table 1. ICD-9-CM codes and totals for the 2,477 unique drug entities.

Results suggest a disconnect between pharmaceutical development and the global burdens of disease.^{2,4-6} Given worldwide mortality rates, one would expect that the most needed drugs would be those developed to treat diseases of the circulatory and respiratory systems (ICD-9-CM codes #7 & #8). According to the World Health Organization, circulatory system diseases represented the top two causes of mortality in the world in 2004, accounting for 23.6% of all deaths.⁸ Additionally, diseases of the respiratory system were the 3rd and 4th leading causes of death worldwide in 2004 (a combined 12.1%). Our study, however, found a surprisingly small number of drugs under development for circulatory system disorders ($n = 147$, 5.93%) and diseases of the respiratory system ($n = 168$, 6.78%). An even more surprising finding from our study was the over-representation of drugs in development to treat various types of cancer. While specific cancers ranked as the 8th, 17th, and 20th disease-based causes of mortality in 2004, these diseases nonetheless represented fewer than 5% of deaths worldwide.⁸

On average, 40% of drugs transition from Phase II to Phase III,⁹ yet some therapeutic areas in our database exhibit much lower percentages of Phase III studies than would be expected. Of the 403 trials targeting infectious and parasitic diseases (for 260 unique drugs), 178 trials were in Phase I (44.2%), 173 were in Phase II (42.9%), and 52 were in Phase III (12.9%). Notably, this suggests that the industry is investing in drugs that target these diseases at Phase I, but this investment does not carry over into Phase III testing.

Although our database does not represent the movement of particular drugs across phases, it is a concern that there were less than one-third as many Phase III trials for infectious and parasitic diseases as there are Phase II trials. This translates to fewer drugs and vaccines that will treat these diseases. Likewise, there are 557 Phase I (41.1%) and 603 Phase II trials (44.5%) for neoplasms, but only 195 Phase III trials (14.4%). One possible interpretation of these data is that the number of products in the pipeline is simply a function of the success of clinical development with some therapeutic areas proving more difficult to find safe and effective therapies.

This study tracked investigational drugs in the pharmaceutical pipeline and their targeted therapeutic areas. Industry drug development priorities are not in sync with the prevalence of diseases. Results suggest significant investment in oncology trials, neurological diseases, and infectious diseases with far fewer drugs in development for cardiovascular and respiratory conditions. Tracking the prevalence of these drugs across Phase I, II, and III trials rather than simply assessing the rate of drug approvals provides a more complete picture of the drug development pipeline.

Acknowledgments

The research was supported in part by the US National Institutes of Health, National Cancer Institute (grant 5R21CA131880) with additional institutional support for REDCap provided by the Vanderbilt CTSA and the NIH National Center for Research Resources (grant 1UL1RR024975).

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