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Profitability of Large Pharmaceutical Companies Compared With Other Large Public Companies

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IMPORTANCE Understanding the profitability of pharmaceutical companies is essential to formulating evidence-based policies to reduce drug costs while maintaining the industry's ability to innovate and provide essential medicines.

OBJECTIVE To compare the profitability of large pharmaceutical companies with other large companies.

DESIGN, SETTING, AND PARTICIPANTS This cross-sectional study compared the annual profits of 35 large pharmaceutical companies with 357 companies in the S&P 500 Index from 2000 to 2018 using information from annual financial reports. A statistically significant differential profit margin favoring pharmaceutical companies was evidence of greater profitability.

EXPOSURES Large pharmaceutical vs nonpharmaceutical companies.

MAIN OUTCOMES AND MEASURES The main outcomes were revenue and 3 measures of annual profit: gross profit (revenue minus the cost of goods sold); earnings before interest, taxes, depreciation, and amortization (EBITDA; pretax profit from core business activities); and net income, also referred to as *earnings* (difference between all revenues and expenses). Profit measures are described as cumulative for all companies from 2000 to 2018 or annual profit as a fraction of revenue (margin).

RESULTS From 2000 to 2018, 35 large pharmaceutical companies reported cumulative revenue of $11.5 trillion, gross profit of $8.6 trillion, EBITDA of $3.7 trillion, and net income of $1.9 trillion, while 357 S&P 500 companies reported cumulative revenue of $130.5 trillion, gross profit of $42.1 trillion, EBITDA of $22.8 trillion, and net income of $9.4 trillion. In bivariable regression models, the median annual profit margins of pharmaceutical companies were significantly greater than those of S&P 500 companies (gross profit margin: 76.5% vs 37.4%; difference, 39.1% [95% CI, 32.5%-45.7%]; $P < .001$; EBITDA margin: 29.4% vs 19%; difference, 10.4% [95% CI, 7.1%-13.7%]; $P < .001$; net income margin: 13.8% vs 7.7%; difference, 6.1% [95% CI, 2.5%-9.7%]; $P < .001$). The differences were smaller in regression models controlling for company size and year and when considering only companies reporting research and development expense (gross profit margin: difference, 30.5% [95% CI, 20.9%-40.1%]; $P < .001$; EBITDA margin: difference, 9.2% [95% CI, 5.2%-13.2%]; $P < .001$; net income margin: difference, 3.6% [95% CI, 0.011%-7.2%]; $P = .05$).

CONCLUSIONS AND RELEVANCE From 2000 to 2018, the profitability of large pharmaceutical companies was significantly greater than other large, public companies, but the difference was less pronounced when considering company size, year, or research and development expense. Data on the profitability of large pharmaceutical companies may be relevant to formulating evidence-based policies to make medicines more affordable.

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Editorial pages 826, 829, and 831

Supplemental content

CME Quiz at jamacmelookup.com and CME Questions page 889

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Policy makers face growing pressure to reduce the cost of drugs in the United States.[1-6] This pressure arises from concern that essential drugs are increasingly unaffordable and that excessive pharmaceutical company profits contribute to high drug prices.[1,5,7-11]

Large, for-profit companies play a central role in providing medicines to the public. Virtually all of the US Food and Drug Administration–approved medicines in the United States were developed by for-profit corporations.[12] The 25 largest pharmaceutical companies accounted for 73% of all pharmaceutical sales in 2015.[5] As such, it has been argued that pharmaceutical companies have an obligation to balance their responsibility to patients and the profit expectations of their shareholders.[1-7,10,13]

Thus, evidence-based policy aimed at reducing the cost of medicines requires a detailed understanding of both drug costs and company profits. While there is extensive literature on the adverse consequences of high drug prices, there has been little research on industry profits.[1] The objective of this study was to compare the profitability of large, publicly traded companies engaged in the research, development, manufacture, marketing, and sale of pharmaceutical products with that of other large, publicly traded companies.

Key Points

Question How do the profits of large pharmaceutical companies compare with those of other companies from the S&P 500 Index?

Findings In this cross-sectional study that compared the profits of 35 large pharmaceutical companies with those of 357 large, nonpharmaceutical companies from 2000 to 2018, the median net income (earnings) expressed as a fraction of revenue was significantly greater for pharmaceutical companies compared with nonpharmaceutical companies (13.8% vs 7.7%).

Meaning Large pharmaceutical companies were more profitable than other large companies, although the difference was smaller when controlling for differences in company size, research and development expense, and time trends.

Methods

This cross-sectional study compared the profitability of large pharmaceutical companies with companies in the S&P 500 Index from 2000 to 2018 using information from annual financial reports.

Data

Audited financial data for fiscal years 2000 to 2018 were retrieved from Compustat (Wharton Research Data Services), including end of fiscal year stock price; common shares outstanding; revenue; gross profit; net income; research and development expense; in-process research and development expense; selling, general, and administrative expense; and earnings before interest, taxes, depreciation, and amortization (EBITDA). Calculated data included market capitalization (end of fiscal year stock price × common shares outstanding); cost of goods sold (revenue − gross profit); research and development expense (research and development expense [Compustat variable] + in-process research and development expense); selling, general, and administrative expense (selling, general, and administrative expense [Compustat variable] − research and development expense [Compustat variable]); gross profit margin (gross profit/revenue); EBITDA margin (EBITDA/revenue); and net income margin (net income/revenue). Financial terms are described in the **Box** and the eAppendix in the Supplement. Financial metrics are presented in US dollars adjusted for inflation to 2016 using the Consumer Price Index for All Urban Consumers data.

Pharmaceutical, S&P 500, and Health Care Data Sets

The pharmaceutical data set comprised companies involved in research, development, manufacture, marketing, and sale of pharmaceutical products from the S&P 500 Index or PharmaExpert "top 50" in 2018. Companies without data in Compustat were excluded.

The S&P 500 data set comprised companies listed in the S&P 500 Index in 2018, excluding (1) companies categorized as pharmaceutical, biotechnology, or health care products; (2) companies with data in the financial services format (mostly banks, savings and loans, insurance, or real estate investment trust); and (3) fiscal years without necessary data in Compustat. S&P 500 companies were classified by the Bloomberg Industry Classification System as communications, consumer discretionary, consumer staples, energy, health care (excluding companies in the pharmaceutical data set), industrials, materials, technology, utilities, or other. "Other" included primarily banks, savings and loans, insurance, or real estate investment trust with data in the industrial format.

The health care data set combined the pharmaceutical data set and the health care sector of the S&P 500 data set. These companies were subclassified as pharmaceutical; distribution, retail, information; insurance, health services; or other products. The list of companies and sector classifications is provided in eTable 1 in the Supplement.

Subset analyses included (1) data from fiscal years with reported research and development expense (research and development >0), (2) data from fiscal years that companies were listed in the S&P 500 Index, and (3) data only from the years 2014 to 2018. Sector analysis compared pharmaceutical companies with companies in each sector and to a set of the largest technology companies: Alphabet (Google), Amazon, Apple, and Microsoft.

Outcomes

The primary outcome was the difference between the profits of companies in the pharmaceutical data set and the S&P 500 data set from 2000 to 2018 expressed as percent of revenue (margin) and calculated by median regression. Three distinct measures of corporate profit were examined: gross profit, representing the difference between revenue and cost of goods sold; EBITDA, representing the pretax profit from the core business activities of the company; and net income (earnings), representing the difference between all revenue and expenses.

Box. Accounting and Finance Terms[a]

Revenue
Total amount of sales after discounts, credits, or rebates.

Market capitalization
A measure of company size calculated as the stock price multiplied by the number of shares outstanding.

Expense metrics

Cost of goods sold
Costs of producing or purchasing products that are sold.

Research and development expense
Costs of both basic research and development.

Selling, general, and administrative expense
Costs of marketing and sales as well as administration and management.

Profit metrics

Gross profit
The difference between revenue and cost of goods sold. Gross profit margin is gross profit as a percentage of revenue.

Earnings before interest, tax, depreciation, and amortization (EBITDA)
The difference between revenue and expenses related to the core business, but not expenses related to interest, taxes, or the reduction in the value of assets over time. EBITDA margin is EBITDA as a percentage of revenue.

Net income
The difference between all revenues and expenses, often referred to as the *bottom line* or *earnings*. Net income margin is net income as a percentage of revenue.

[a] A detailed description of accounting and finance terms is provided in the eAppendix in the Supplement.

Financial terms are described in the Box and defined in the eAppendix in the Supplement.

Statistical Analyses

Cumulative financial metrics were calculated as the sum of annual values from 2000 to 2018. Normality of data was assessed using the Kolmogorov-Smirnov test. Descriptive analysis included calculation of median and interquartile range, Mann-Whitney tests of significance, and Hodges-Lehman estimator of median difference. The Hodges-Lehman estimator accounts for variation within data sets and is not equivalent to the difference of the medians. Because this analysis involved 20 comparisons, significance was interpreted with a Bonferroni correction of 20, meaning that $P < .0025$ was considered significant.

The profit margins of pharmaceutical companies were compared with subsectors of the health care data set by Mann-Whitney tests and the Hodges-Lehman estimator. Because this analysis involved 3 comparisons, significance was interpreted with a Bonferroni correction of 3, meaning that $P < .016$ was considered significant.

As the normality of residuals of classic linear regression estimated by the Shapiro-Wilk W test was rejected ($P < .001$), primary outcomes were examined by median regression.[14] The linearity and additivity of explanatory variables in the median regression model were assessed via residual vs fitted values plots, and no evidence of a violation of the median regression assumption was found. Pseudo R^2 value was calculated to assess the explanatory power of the model.

The median and 95% CI of the difference in profit margins of pharmaceutical and S&P 500 companies were estimated by bivariable regressions for each profit measure. Two similar bivariable models with a single indicator variable (PHARMA) were used. In the first model, with PHARMA = 0 for pharmaceutical companies, the intercept estimated the median pharmaceutical profit margin and the coefficient estimated the median difference between pharmaceutical and S&P 500 companies. In the second model, with PHARMA = 1 for pharmaceutical companies, the intercept estimated the median S&P 500 profit margin and the coefficient estimated the median difference between S&P 500 and pharmaceutical companies.

The multivariable model included the PHARMA indicator variable set to 0 for S&P 500 companies and 1 for pharmaceutical companies, market capitalization as a proxy for company size, and year fixed effects to account for time trends. The model specification was as follows: $PROFIT\ METRIC_{i,t} = \beta_{0i,t} + \beta_1 PHARMA_i + \beta_2 Market\ Capitalization_{i,t} + \beta\ (Year\ Fixed\ Effects) + \varepsilon_{i,t}$.

Standard errors were estimated using the bootstrapping method (10 000 bootstrap replications; initial seed set equal to 495) with samples drawn from company clusters with replacement to address time-series correlation in the residual.[15] Bonferroni correction was unnecessary for these analyses.

Secondary analyses were the difference between pharmaceutical and S&P 500 profit margins in subsets of the data including (1) years with reported research and development expense (research and development >0), (2) years when these companies were listed in the S&P 500 Index, and (3) the years 2014 to 2018.

For sector analysis, the multivariable model eliminated the PHARMA indicator and included an indicator for each of the 10 industrial sectors (industry fixed effects): $PROFIT\ METRIC_{i,t} = \beta_{0i,t} + \beta_1 Market\ Capitalization_{i,t} + \beta(Year\ Fixed\ Effects) + \beta(Industry\ Fixed\ Effects) + \varepsilon_{i,t}$.

In this model, the coefficients for each sector indicator represented the difference in profit between pharmaceutical companies and that sector. Because 10 sectors were examined, significance was interpreted with a Bonferroni correction of 10, meaning that $P < .005$ was considered significant.

All tests were 2-tailed. Except where previously noted, a 2-sided P value less than .05 was considered significant. Kolmogorov-Smirnov and Mann-Whitney tests, as well as the Hodges-Lehman estimator, were performed using SPSS version 26. Median regression was performed using Stata/SE version 15.

Results

Data Description

The pharmaceutical data set comprised 35 companies and 631 fiscal years of data, the S&P 500 data set comprised 357 companies and 6258 fiscal years of data, and the health care data set comprised 87 companies and 1552 fiscal years of data.

From 2000 to 2018, the cumulative revenue of companies in the pharmaceutical data set was $11.5 trillion, with gross profit of $8.6 trillion (74.5% of cumulative revenue), EBITDA of $3.7 trillion (32.2% of cumulative revenue), and net income of $1.9 trillion (16.2% of cumulative revenue) (eTable 2 in the Supplement). The cumulative revenue of companies in the S&P 500 data set was $130.5 trillion, with gross profit of $42.1 trillion (32.3% of cumulative revenue), EBITDA of $22.8 trillion (17.5% of cumulative revenue), and net income of $9.4 trillion (7.2% of cumulative revenue) (eTable 2 in the Supplement).

The Kolmogorov-Smirnov test rejected the null hypothesis that corporate profit data was normally distributed ($P < .001$), indicating that statistical tests comparing mean values were not appropriate, so analyses were performed using tests of median values.

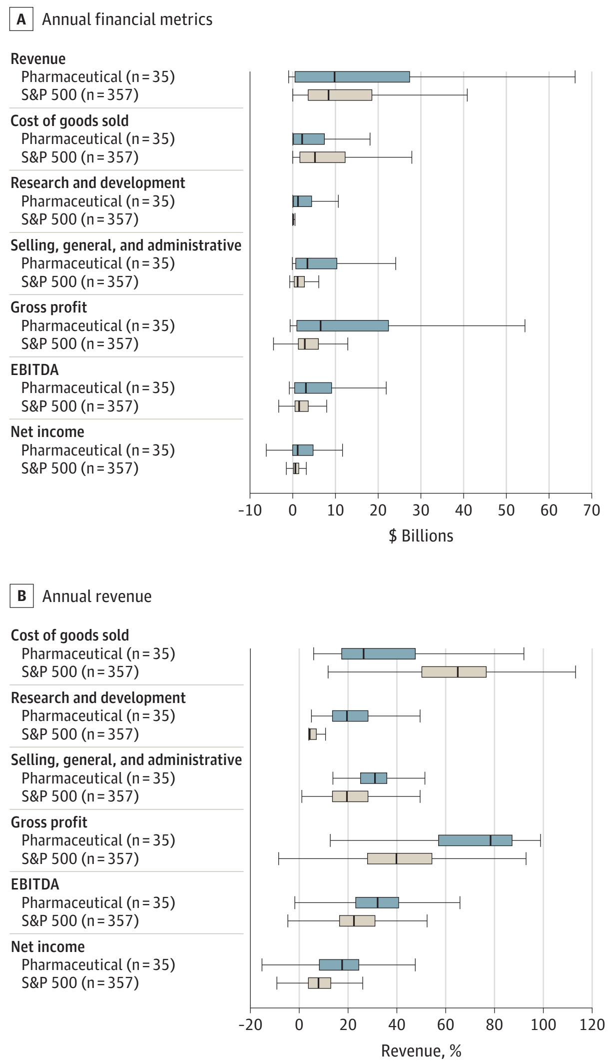
Comparison of Pharmaceutical and S&P 500 Profits

Figure 1A shows the distribution of annual financial metrics for companies in the pharmaceutical and S&P 500 data sets. There was no significant difference between the median annual revenue of pharmaceutical and S&P 500 companies ($10.6 billion vs $8.4 billion; median difference, −$289 million [95% CI, −$971 million to $569 million]; $P = .47$). However, pharmaceutical companies were significantly larger than S&P 500 companies as measured by median market capitalization ($36.1 billion vs $12.2 billion; median difference, $15.6 billion [95% CI, $12.0 billion to $19.7 billion]; $P < .001$) (**Table 1**).

Figure 1B shows the distribution of annual expenses and profit metrics as a fraction of annual revenue. Pharmaceutical companies had significantly lower median cost of goods sold as a fraction of revenues than S&P 500 companies (23.5% vs 62.6%; median difference, -32.6% [95% CI, −34.5% to −30.6%]; $P < .001$), but significantly higher median research and development expense as a fraction of revenue (16.2% vs 0%; median difference, 14.5% [95% CI, 14.0%-14.9%]; $P < .001$) and median sales, general, and administrative expense as a fraction of revenue (28.2% vs 16.6%; median difference, 10.7% [95% CI, 9.8%-11.5%]; $P < .001$) (Table 1). Distributions of these data are illustrated in eFigure 1 in the Supplement.

Pharmaceutical companies had significantly higher annual profit margins than S&P 500 companies for the 3 primary outcome measures of gross profit, EBITDA, and net income ($P < .001$) (Table 1). These results were confirmed using bivariable median regression (**Table 2**). For pharmaceutical companies, the median gross profit margin was 76.5% (95% CI, 70.3%-82.7%), the median EBITDA margin was 29.4% (95% CI, 26.3%-32.5%), and the median net income margin was 13.8% (95% CI, 10.2%-17.4%). For S&P 500 companies, the median gross profit margin was 37.4% (95% CI, 35.2%-39.6%), the median EBITDA margin was 19% (95% CI, 17.8%-20.3%), and the median net income margin was 7.7% (95% CI, 7.2%-8.2%) (Table 2). In bivariable median regression, the difference in median gross profit margin was 39.1% ([95% CI, 32.5%-45.7%]; $P < .001$), the difference in EBITDA margin was 10.4% ([95% CI, 7.1%-13.7%]; $P < .001$), and the difference in net income margin was 6.1% ([95% CI, 2.5%-9.7%]; $P < .001$).

Figure 1. Annual Financial Metrics of 35 Large Pharmaceutical and 357 Companies From the S&P 500, 2000-2018



Box plot lines represent the 25th percentile, median, and 75th percentile. Whiskers are 1.5 times the interquartile ranges. Financial terms are defined in the Box. A, Annual financial metrics in millions of US dollars inflation adjusted to 2016. B, Annual financial metrics as a percentage of annual revenue. Gross profit; earnings before interest, taxes, depreciation, and amortization (EBITDA); and net income expressed as a percent of revenues represent gross profit margin, EBITDA margin, and net income margin, respectively.

Controls and Subset Analysis

The difference in annual profit margins for pharmaceutical and S&P 500 companies was estimated with controls for company size (market capitalization) and time trends (year fixed effects) using median multivariable regression (Table 2). Complete results of the regression analyses are available in eTable 7

Table 1. Financial Metrics for Large Pharmaceutical and S&P 500 Companies From 2000 to 2018

Financial Metric[a]	Median Amount, $[b]			Median Revenue, %[c]		
	Pharmaceutical (35 companies; 631 fiscal years[d])	S&P 500 (357 companies; 6258 fiscal years[d])	Difference (95% CI)[e]	Pharmaceutical (35 companies; 631 fiscal years[d])	S&P 500 (357 companies; 6258 fiscal years[d])	Difference (95% CI)[e]
Market capitalization	36 103	12 159	15 562 (12 024 to 19 737)	NA	NA	NA
Revenues	10 564	8426	−289 (−971 to 569)	NA	NA	NA
Expense metrics						
Cost of goods sold	2276	5265	−2147 (−2558 to −1733)	23.5	62.6	−32.6 (−34.5 to −30.6)
Research and development	1247	0	982 (861 to 1141)	16.2	0.00	14.5 (14.0 to 14.9)
Selling, general, and administrative	3528	1216	1589 (1232 to 1969)	28.2	16.6	10.7 (9.8 to 11.5)
Profit metrics						
Gross profit	6556	2885	2528 (1755 to 3440)	76.5	37.4	32.6 (30.6 to 34.5)
EBITDA	3152	1535	886 (562 to 1257)	29.4	19.0	8.8 (7.7 to 9.9)
Net income	1147	574	420 (256 to 612)	13.8	7.7	4.5 (3.6 to 5.4)

Abbreviations: EBITDA, earnings before interest, tax, depreciation, and amortization; NA, not applicable.

[a] For definitions of financial metrics, see the Box or the eAppendix in the Supplement.

[b] Value in US dollars inflation adjusted to 2016.

[c] Profit metrics expressed as percentage of annual revenue represent profit margins.

[d] One fiscal year represents 1 observation in the statistical analysis.

[e] Median difference between pharmaceutical and S&P 500 data sets, with 95% CI calculated as Hodges-Lehman estimator. This value is calculated as the median of differences between all pairs of observations from the pharmaceutical and S&P 500 data set and may not be equivalent to the simple difference between medians or to the differential profit margins calculated using multivariable regression models with controls.

in the Supplement. With these controls, pharmaceutical companies were significantly more profitable, although there was less of a difference between pharmaceutical and S&P 500 companies. The difference in gross profit margin was 34.6% ([95% CI, 25.3%-44.0%]; $P < .001$), the difference in EBITDA margin was 8.6% ([95% CI, 4.7%-12.5%]; $P < .001$), and the difference in net income margin was 4.1% ([95% CI, 0.6%-7.5%]; $P = .02$) (Table 2).

While pharmaceutical companies reported research and development expense in every year from 2000 to 2018, S&P 500 companies reported research and development expense in less than half of those years (Table 1). Considering a subset of data with nonzero research and development expense and controls for company size and time trends, pharmaceutical companies were significantly more profitable than S&P 500 companies, although the difference in net income margin was reduced. In this analysis, the difference in gross profit margin was 30.5% ([95% CI, 20.9%-40.1%]; $P < .001$), the difference in EBITDA margin was 9.2% ([95% CI, 5.2%-13.2%]; $P < .001$), and the difference in net income margin was 3.6% ([95% CI, 0.01%-7.2%]; $P = .05$) (Table 2). These estimates of the differential profit were not outside the 95% CI for the complete data set.

Both the pharmaceutical and S&P 500 data sets included data from companies such as Incyte, Gilead, Vertex, Amazon, Salesforce, and Twitter in the years before they were listed in the S&P 500 Index. To assess whether the inclusion of data from these years biased estimates of differential profit, the profits of pharmaceutical and S&P 500 companies were compared using a subset of data comprising years that companies were listed in the S&P 500 Index along with controls for company size and time trends. In this analysis, the difference in gross profit margin was 37.2% ([95% CI, 25.4%-49.0%]; $P < .001$); EBITDA margin, 11.1% ([95% CI, 5.4%-16.8%]; $P < .001$); and net income margin, 6.8% ([95% CI, 3.5%-10.1%]; $P < .001$) (Table 2). While these estimates of the differential profit were higher than those calculated with the complete data set, they were not outside the 95% CI of the complete data set.

The profit margins of pharmaceutical and S&P 500 companies over the past 5 years were compared using a subset of data from 2014 to 2018 with controls for company size and time trends. Over this interval, the median gross profit and EBITDA margins of pharmaceutical companies were significantly higher than S&P 500 companies, but there was no significant difference in the median net income margin. The difference in gross profit margin was 35.8% ([95% CI, 28.3%-43.4%]; $P < .001$); EBITDA margin, 9.0% ([95% CI, 2.9%-15.1%]; $P = .004$); and net income margin, 2.3% ([95% CI, −1.0% to 5.6%]; $P = .17$) (Table 2).

Comparison of Pharmaceutical Companies and S&P 500 Sectors

The profit margins of pharmaceutical companies and companies in 10 sectors of the S&P 500 (eTable 3 in the Supplement) were compared. Medians and interquartile ranges are shown in **Figure 2**A and median regression with controls for company size and time trends is shown in **Table 3**. Complete results of regression analysis are available in eTable 8 in the Supplement. In this analysis, the median gross profit margin of pharmaceutical companies was significantly higher than that of companies in each of the S&P 500

Table 2. Differential Profit Margins of Pharmaceutical and S&P 500 Companies

Profit Margin[a]	Sample Period	No. of Companies	No. of Fiscal Years[b]	Reference Profit Margin (95% CI), % Revenue[c]	Differential Profit Margin of Pharmaceutical Companies Relative to S&P 500 Companies (95% CI), % Revenue[d]	Pseudo R^2
Gross profit margin						
Bivariable[e]	2000-2018	392	6889	37.4 (35.2 to 39.6)	39.1 (32.5 to 45.7)	.06
Multivariable[f]	2000-2018	392	6889	32.1 (28.8 to 35.4)	34.6 (25.3 to 44.0)	.07
Multivariable (R&D >0)[g]	2000-2018	219	3553	37.6 (33.1 to 42.0)	30.5 (20.9 to 40.1)	.08
Multivariable (S&P 500)[h]	2000-2018	378	5087	30.9 (27.6 to 34.2)	37.2 (25.4 to 49.0)	.09
Multivariable (2014-2018)[i]	2014-2018	392	1918	37.5 (35.6 to 39.5)	35.8 (28.3 to 43.4)	.11
EBITDA margin						
Bivariable[e]	2000-2018	392	6889	19.0 (17.8 to 20.3)	10.4 (7.1 to 13.7)	.01
Multivariable[f]	2000-2018	392	6889	15.9 (14.5 to 17.4)	8.6 (4.7 to 12.5)	.02
Multivariable (R&D >0)[g]	2000-2018	219	3553	15.3 (13.7 to 16.9)	9.2 (5.2 to 13.2)	.04
Multivariable (S&P 500)[h]	2000-2018	378	5087	17.2 (15.4 to 19.0)	11.1 (5.4 to 16.8)	.06
Multivariable (2014-2018)[i]	2014-2018	392	1918	19.7 (18.6 to 20.7)	9.0 (2.9 to 15.1)	.04
Net income margin						
Bivariable[e]	2000-2018	392	6889	7.7 (7.2 to 8.2)	6.1 (2.5 to 9.7)	.003
Multivariable[f]	2000-2018	392	6889	5.4 (4.7 to 6.2)	4.1 (0.6 to 7.5)	.01
Multivariable (R&D >0)[g]	2000-2018	219	3553	6.1 (4.9 to 7.3)	3.6 (1.1×10^{-2} to 7.2)	.02
Multivariable (S&P 500)[h]	2000-2018	378	5087	5.9 (5.0 to 6.8)	6.8 (3.5 to 10.1)	.05
Multivariable (2014-2018)[i]	2014-2018	392	1918	8.0 (7.3 to 8.8)	2.3 (-1.0 to 5.6)	.02

[a] For definitions of financial metrics, see the Box or eAppendix in the Supplement.

[b] Each fiscal year represents 1 observation in the statistical analysis.

[c] The reference profit margin is the intercept of the median regression models. In the bivariable model, the intercept represents the median profit margins of S&P 500 companies. In the multivariable model, the intercept represents the median profit margin of S&P 500 companies when all year indicator variables and the company size variable are set equal to zero.

[d] The differential profit margin of pharmaceutical companies relative to the S&P 500 is the coefficient of the PHARMA indicator variable. The coefficient value represents the differential profit margin for pharmaceutical companies compared with S&P 500 companies (after controlling for size and year in the multivariable model).

[e] The bivariable median regression model included an indicator variable (PHARMA) set equal to 1 for pharmaceutical companies. The bivariable model does not include terms for company size (market capitalization) or year (year fixed effects).

[f] The multivariable median regression model included an indicator variable (PHARMA) set equal to 1 for pharmaceutical companies, a variable to control for company size (market capitalization), and an indicator variable for each year to control for time trends.

[g] Estimates of differential profit by multivariable median regression on data only from fiscal years with nonzero research and development (R&D) expense. All pharmaceutical companies had nonzero R&D expense for all years in the study. This model compares the profitability of pharmaceutical companies to only those S&P 500 companies with nonzero R&D expense in a given year.

[h] Estimates of differential profit by multivariable median regression on data only from fiscal years during which a company was included in the S&P 500 Index. This excludes data from companies in the years before they were included in the S&P 500 Index.

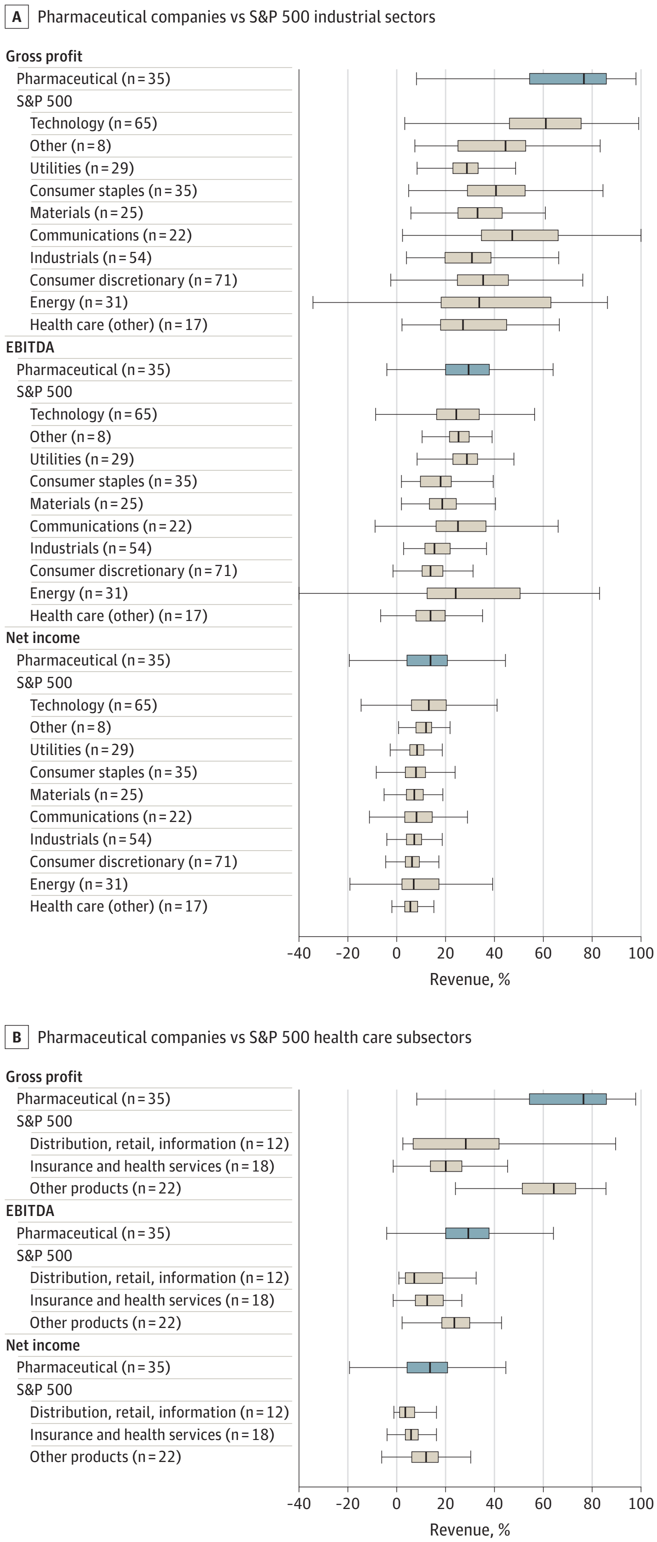
[i] Estimates of differential profit by multivariable median regression on data only from 2014 to 2018.

sectors. The median EBITDA margin of pharmaceutical companies was significantly greater than that of companies in the consumer staples, materials, industrials, consumer discretionary, and health care sectors, but not companies in the technology, other, utilities, communications, or energy sectors. The net income margin of pharmaceutical companies was higher than that of companies in each sector except for technology and other, although the difference was only significant for the consumer discretionary and health care sectors.

Considering 4 of the largest S&P 500 companies, Amazon, Alphabet (Google), Apple, and Microsoft, the median annual gross profit margins of Alphabet (65.8%) and Microsoft (83.1%) were similar to those of pharmaceutical companies, while those of Apple (40.8%) and Amazon (26.8%) were lower. The median annual EBITDA margin of Apple was 29.0%; Alphabet, 33.0%; Microsoft, 41.7%; and Amazon, 6.0%. The median annual net income margin of Apple was 19.2%; Alphabet, 21.9%; Microsoft, 27.6%; and Amazon, 1.7% (eTable 4 in the Supplement).

The profit margins of pharmaceutical companies were compared with 3 other subsectors of the health care data set (Figure 2B and eTable 5 in the Supplement). Pharmaceutical companies had significantly higher median gross profit margins and EBITDA margins than companies in other health

Figure 2. Annual Profit Margins of Pharmaceutical Companies Compared With Other Industrial Sectors



Box plot lines represent the 25th percentile, median, and 75th percentile. Whiskers are 1.5 times the interquartile ranges. Financial terms are defined in the Box. Annual profit margins are expressed as a percentage of annual revenue. A, Comparison of pharmaceutical companies with 10 industrial sectors in the S&P 500 data set. B, Comparison of pharmaceutical companies with 3 other subsectors of the health care data set. EBITDA indicates earnings before interest, taxes, depreciation, and amortization.

care sectors. Pharmaceutical companies also had significantly higher median net income margins than companies in distribution, retail, and information and insurance and health services ($P < .001$), but not higher than other product companies (median difference, −1.6% [95% CI, −3.1% to −0.1%]; $P = .035$) (eTable 6 in the Supplement).

Table 3. Differential Profit Margins of Pharmaceutical Companies and Sectors Within the S&P 500[a]

Sector	Differential Gross Profit Margin (95% CI), % Revenue[b]	Differential EBITDA Margin (95% CI), % Revenue[b]	Differential Net Income Margin (95% CI), % Revenue[b]
Pharmaceutical reference)[c]	70.3 (61.1 to 79.5)	25.2 (21.3 to 29.2)	10.2 (6.6 to 13.8)
Sector within S&P 500[d]			
Technology	−14.4 (−24.0 to −4.9)	−3.2 (−7.9 to 1.4)	0.9 (−2.9 to 4.7)
Other[d]	−32.2 (−49.3 to −15.1)	−1.4 (−7.8 to 5.1)	0.3 (−4.8 to 5.3)
Utilities	−45.9 (−54.7 to −37.1)	1.6 (−2.5 to 5.8)	−3.3 (−6.9 to 0.3)
Consumer staples	−33.6 (−43.9 to −23.3)	−10.1 (−14.9 to −5.2)	−3.9 (−7.7 to 0.0)
Materials	−40.3 (−51.0 to −29.7)	−8.5 (−13.5 to −3.6)	−4.3 (−8.1 to −0.6)
Communications	−27.5 (−40.9 to −14.0)	−4.2 (−10.5 to 2.0)	−4.6 (−8.1 to −1.0)
Industrials	−43.7 (−53.0 to −34.4)	−12.0 (−16.1 to −7.8)	−4.9 (−8.4 to −1.4)
Consumer discretionary	−39.4 (−49.0 to −29.9)	−13.1 (−17.1 to −9.0)	−5.4 (−9.0 to −1.8)
Energy	−40.4 (−54.1 to −26.8)	−4.0 (−15.9 to 8.0)	−5.7 (−9.9 to −1.5)
Health care (other)	−48.3 (−64.5 to −32.0)	−12.3 (−18.7 to −5.9)	−5.8 (−9.7 to −1.9)
Pseudo R^2	.17	.06	.02

[a] Differential profit was estimated using the multivariable median regression model including an indicator variable for each sector, a control for company size (market capitalization), and indicator variables for each year (year fixed effects) to control for time trends. Regressions were performed with 6889 fiscal years (observations) for the years 2000 to 2018, representing the combined pharmaceutical and S&P 500 data sets. For definitions of profit metrics, see the Box or eAppendix in the Supplement.

[b] The differential profit margin of companies in each of the S&P 500 sectors relative to pharmaceutical companies was estimated as the coefficient on the indicator variable for that sector. This represents the differential profit margin between companies in that sector and pharmaceutical companies after controlling for size and year. Negative values indicate that the profit margins of pharmaceutical companies were larger than those for that sector.

[c] The reference profit margin is the intercept of the median multivariable regression model. In these multivariable models, the reference profit margin reflects the median profit margin of pharmaceutical companies when all year indicator variables and the company size variable are set equal to zero.

[d] Companies in the S&P 500 data set were classified by the Bloomberg Industry Classification System. Health care (other) comprised companies classified as *health care*, excluding pharmaceutical companies. *Other* comprised primarily companies in the financial services and real estate sectors that were not excluded from the S&P 500 data set under initial sample criteria. Sectors are ordered by the differential net income margin of the sector relative to pharmaceuticals.

Discussion

In this study, the profitability of a set of large, fully integrated pharmaceutical companies, which generate revenue primarily from the sale of pharmaceutical products, was shown to be significantly greater than that of other large, nonpharmaceutical companies in the S&P 500 Index from 2000 to 2018. Three metrics for profitability were examined.

The greatest difference between pharmaceutical and S&P 500 companies was in the gross profit margin, a measure of the difference between the cost of goods sold and total revenue. This profit measure does not take into account expenses related to research and development or the costs of selling a product or managing the company. Pharmaceutical companies also had a significantly greater EBITDA margin, a measure of pretax profits from the company's core operations, which does not consider nonoperational expenses, including interest, taxes, or the accounting expense associated with reductions, in the value of company assets over time (depreciation or amortization). In addition, pharmaceutical companies had significantly greater net income margin, a measure of posttax profit accounting for all revenue and expenses. Net income, also called *earnings*, represents a company's "bottom line" and is used to calculate earnings per share, an important measure of profit for shareholders.

These analyses also showed that there was considerable complexity underlying the differential profitability of pharmaceutical companies. The estimated differential profitability of pharmaceutical companies was lower when controlling for company size and time trends, and was even lower when the analysis was restricted to years of data with reported research and development expense. In contrast, the estimated differential profit of pharmaceutical companies was larger when the analysis was restricted to years when companies were listed in the S&P 500 Index. Moreover, sector analysis showed considerable overlap between the EBITDA margins and net income margins of pharmaceutical companies and those in certain other industrial sectors.

The differential profitability of pharmaceutical companies was also markedly lower over the past 5 years (2014 to 2018), and there was no significant difference between the net income margin of pharmaceutical and S&P 500 companies during this interval. Further research is required to assess whether the lower differential net income of pharmaceutical companies over the past 5 years represents a meaningful trend.

The present analysis focused explicitly on accounting metrics based on generally accepted accounting principles. These metrics are designed to promote consistency and comparability in financial statements[16] and represent important benchmarks for corporate performance. However, these metrics do not reflect cash balance or cash flow in any single fiscal year and may not correspond with public conceptions of profitability.[17] Accounting terms have technical definitions that are often not synonymous with colloquial meaning. For example, *expense* is not synonymous with *spending* and does not include long-time capital investments in tangible assets (eg, facilities or equipment), capitalized acquisitions of intellectual property, or distributions of earnings through dividends or stock buybacks.

The median net income margins calculated in this report are lower than the weighted mean net income margins reported by the US Government Accountability Office.[5] The report described a weighted mean net income margin of 20.1% for the 25 largest pharmaceutical companies compared with weighted mean net income margins ranging from 21.7% in 2006 to 13.4% in 2015 for the 25 largest software companies and 8.9% in 2006 to 6.7% in 2015 for the largest S&P 500 companies by revenue.[5] These values are substantially lower than those in a National Academies of Sciences, Engineering, and Medicine report,[1] which quoted an estimate of 25.5% "net margin" from an article in Forbes and a mean 28% margin based on work from University of Southern California's Leonard D. Schaeffer Center for Health Policy and Economics.[8] However, the latter value represents the profit margins of branded products from United States–based activities, not total company profits.

Limitations

This study has several limitations. First, this analysis focused on large, fully integrated pharmaceutical companies that generate revenue and profit primarily from drug sales. It did not consider small or midsized biopharmaceutical companies or biotechnology companies engaged in discovery research or early-stage development, which typically have little revenue and negative profits (losses).[18] As such, the pharmaceutical data set was not representative of the broad biopharmaceutical industry and the results cannot be extrapolated to the industry as a whole.

Second, this analysis did not consider other companies in the layered pharmaceutical distribution system. Thus, these data do not describe the fraction of the sale price ultimately recognized as profit by the health care industry.[8] Such an analysis must take into account not only the profits of pharmaceutical companies, but also those of insurers, pharmacy benefit managers, pharmacies, and wholesalers.[6,8]

Third, this analysis did not consider whether companies in the pharmaceutical data set had excess profit. In accounting and finance, *excess profit* is defined as profit over and above a "normal" return on capital invested in the company—a return that is commonly associated with the risk of the investment. Future research can be directed at examining the relationship between investment risk, returns on capital investments, and reported profits.

Fourth, this analysis focused explicitly on pharmaceutical revenue and profit, which are only indirectly related to drug prices in the United States.[6,8] Pharmaceutical revenues do not reflect the list price of medicines, but the net received from intermediaries in the pharmaceutical distribution system after rebates or discounts.[6,8,19,20] Moreover, while the US market represents 47% of global pharmaceutical sales (2016-2018),[21] it generates a disproportionately larger fraction of pharmaceutical profits.[8] Thus, while understanding pharmaceutical profits is essential to formulating evidence-based policy regarding drug pricing, considerable caution is required in applying these results to policies aimed at controlling drug prices in the United States.

Conclusions

From 2000 to 2018, the profitability of large pharmaceutical companies was significantly greater than other large, public companies, but the difference was less pronounced when considering company size, year, or research and development expense. Data on the profitability of large pharmaceutical companies may be relevant to formulating evidence-based policies to make medicines more affordable.

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