Changes in performance of the research-based pharmaceutical industry with regard to access to essential medicines in 103 low- and middle-income countries

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Abstract

Background: Every two years since 2008, the Access to Medicine Index has ranked the top-20 pharmaceutical companies based on their efforts to promote access to priority medicines in developing countries. However, absolute progress over time has never been assessed.

Objectives: To measure changes in company performance with regard to access to medicines and technologies for 33 relevant diseases in 103 low- and middle-income countries.

Methods: A meta-analysis of 16 Access to Medicine indicators from 2010 and 2012 that record company policies, transparency, activities and innovation in six technical areas.

Findings: 17/20 companies show progress in their overall Access to Medicine scores. The mean value of six selected representative Access to Medicine indicators rose from 1.45 to 2.67 (scale 0-5). Relevant research and development efforts by the companies more than doubled. Considerable differences in absolute performance and progress were found between companies.

Interpretation: There is progress in company performance in the areas covered by the selected Access to Medicine indicators. In absolute terms, the highest scores were obtained for access management and corporate philanthropy, and the lowest scores for patent policies and data exclusivity. Several companies with higher relative Access to Medicine rankings in 2012 also show progress in absolute terms. This analysis adds a dynamic perspective to the biennial Access to Medicine ranking and can serve as a baseline for the future.

Introduction

Despite many efforts and real progress in many countries, about one third of the world's population remains without regular access to essential medicines. Most of the "bottom billion" living on less than a dollar per day are found in sub-Saharan Africa, India and other emerging economies.[1] Such people face many barriers to obtaining necessary medications. Lack of access may simply be due to high prices and lack of funds, but physical access to health facilities, poor quality of the product, deficient distribution systems, social and cultural barriers and irrational prescribing also play a role. In some cases, the necessary essential medicines do not exist, such as heat-stable insulin for patients without refrigerators in tropical climates, or paediatric combination syrups for treatment of HIV in young children. The responsibility for resolving these problems lies with many actors, one of which is the pharmaceutical industry.

Since 2008, the Access to Medicine Index has ranked the world's 20 largest research-based pharmaceutical companies according to their commitments and actions to make relevant products more available, affordable, and accessible in developing countries.[II III] The aim of the Index, which is published every two years, is to make companies aware of what can be done to improve access to medicine, and to stimulate them to do more by illuminating best practices among their peers and showing specific areas for improvement and leadership.

Full details of the 2012 methodology have been reported elsewhere.[IV] In summary, the ranking is based on companies' efforts to bring medicines, vaccines and diagnostic tests to people in 103 low- and middle-income "Index" countries, focusing on 33 communicable, non-communicable and neglected tropical

diseases, and a range of maternal and neonatal conditions, which account for the highest burden of disease. Information requested and received from the companies is cross-checked with other sources, and peer reviewed by experts. The Index uses a framework that evaluates company commitments and activities on 101 indicators, divided into seven technical areas: overall organization and management of access programs (10% of the final score); conduct of relationships with policymakers, competitors, customers, and the general public (10%); research and development aimed at relevant products (20%); pricing policies and practices, quality of manufacturing and distribution (25%); patent and licensing policies and practices (15%); capacity building in developing countries (10%); and product donations and philanthropic activities (10%). Within each of these technical areas, four important aspects of action are measured: level of commitment by the company (25%); transparency about its policies and activities (25%); actual activities and performance (40%); and the innovative nature of the activities (10%).

Since its inception, the Access to Medicine Index ranking has obtained increasing attention from the pharmaceutical industry, the media, global health experts and several large institutional investors. However, innovative and interesting as the Index is, its publication is not a goal in itself. The ultimate objective of the Access to Medicine Foundation is to promote positive change in the practices of the industry, leading to increased access to priority medicines in developing countries. In order to assess progress in this regard, an independent assessment of absolute, and not only relative, company performance over time is needed. The present study makes a first attempt in this direction.

The objectives of the study are therefore to develop a method to measure absolute progress in industry performance with regard to access to essential medicines in low- and middle-income countries (besides the two-yearly Access to Medicine ranking); to use this method to assess and quantify the development of industry performance; and to create a baseline for future trend analyses.

Methods

Selection of core indicators for detailed longitudinal analysis

In order to determine which indicators in the Access to Medicine Indices from 2010 and 2012 were suitable for a detailed longitudinal analysis, the following selection process was used, starting with the 101 indicators used in 2012. First, indicators that had no comparable equivalents between the 2010 Index and 2012 Index were excluded. Secondly, for indicator data to allow for objective comparison between 2010 and 2012, the nature and quality of the data provided by the companies had to be adequate, consistent and verifiable, with a comparable level of detail. Thirdly, the data should be comparable quantitatively, either in absolute terms or by rescoring the raw data from 2010 according to the scoring methods of 2012. Finally, a correlation analysis was performed on the remaining indicators whereby, within each technical area of the Access to Medicine Index, the most representative and predicative indicator was selected (see below).

Correlation analysis

For each of the provisionally selected indicators and for each of the 20 companies, the Pearson correlation coefficients were calculated between the longitudinal indicator value of 2012 and the total score for the relevant technical area in 2012 (r_1); and between the indicator value of 2012 and the overall Access to Medicine score in 2012 (r_2). The level of significance was examined at both the 99% (p<0.01) and the 95% (p<0.05) levels, which resulted in critical r values of 0.561 and 0.444 respectively.

Statistical analysis

For the crude longitudinal analysis, the absolute values of the overall Access to Medicine rankings in 2010 and 2012 were compared for the 20 companies. Value changes for each company were calculated, as well as the mean change.

The numbers of rising, stable and falling scores (n=20) between 2010 and 2012 for each of the six core scored indicators were compared using a simple sign test and by calculating the 95% confidence limits (CL) of the percentages of rising and falling scores.

Absolute changes in score-based longitudinal indicators were calculated with mean and median values. For six number-based research indicators, the mean percentage change of the 20 companies was calculated; the median value of the six mean percentages was used as a measure of change.

Transparency and anonymity
Company scores for individual indicators are not published in the Access to Medicine Index reports and remain confidential. In this study, company names are only mentioned if the data underlying the analysis have already been published in Access to Medicine Indices. New data (e.g., Table 4) are presented anonymously.

Results

Selection of core indicators for longitudinal analysis
Of 101 indicators in the Access to Medicine Index, ten indicators fulfilled all selection criteria for the detailed longitudinal analysis (Table 1). Unfortunately, no indicator in the technical area of pricing fulfilled all criteria. The six "core scored indicators" (one for each of the remaining six technical areas) with the highest correlation with overall Access to Medicine scores reflect overall industry performance in the most balanced way and were therefore used for the detailed longitudinal analysis. Four additional scored indicators and six number-based research indicators were used for additional comparisons.

Crude analysis of change between 2010 and 2012
The crude analysis of change in overall company Access to Medicine scores is presented in Figure 1. The mean score increases from 1.95 in 2010 to 2.30 in 2012 (*n.s.*). There are 17 companies with rising overall Access to Medicine scores, and three with a decrease. The difference between 17/20 risers and 3/20 fallers is significant ($p < 0.05$).

Detailed longitudinal analysis
The results of the detailed longitudinal analysis are shown in Table 2 and Figure 2. Between 2010 and 2012, the mean value of the six most representative ("core") indicators increased from 1.45 to 2.67 (scale 0 – 5), representing an increase of 84%. The mean score for all ten scored indicators increased from 1.73 to 2.75 (59%). The median increase in research-based activities is 132% (Table 3).

For each of the companies, the number of rising and falling scores of the scored indicators is shown in Table 4, in which each line represents one company. For all indicators except A.I.1 (governance structure) and G.II.3 (philanthropy disclosure), the number of companies with a rising score is significantly higher than those with falling score ($p < 0.05$).

Discussion

This is the first study to assess, in a standardized manner, progress in the policies and practices of the top-20 research-based pharmaceutical companies in promoting access to essential medicines in low- and middle-income countries. The **limitations** of the study are the following. First, only 16/101 (16%) of the Access to Medicine indicators allowed for a proper longitudinal analysis, as all other indicators had been added, removed or changed in between the 2008, 2010 and 2012 Index reports. In fact, none of the indicators used in the 2008 report could be included in the analysis, due to significant changes in the Index methodology and scope between 2008 and 2010. The current analysis therefore had to be limited to the period from 2010 to 2012. Secondly, the potential longitudinal indicators are not proportionately divided between the seven technical areas; the important area of pricing, manufacturing and distribution could not be represented at all. A simple mean value of the 16 longitudinal indicators would imply a moderate overrepresentation of scores in the technical areas of management, capacity building and donations, and a serious over-representation of the area of research and development. For this reason, six core indicators were identified, which allowed each of remaining six technical areas to be represented by their most representative and predictive indicator. A longitudinal analysis of progress in the area of pricing will have to wait till the Index results of 2014 have become available.

The normal Access to Medicine ranking does not allow for an assessment of absolute change because the rankings of the companies are only relative to each other. Yet a very rough comparison of the company scores underlying these rankings in 2010 and 2012 allows for a **crude longitudinal analysis** (Figure 1). This analysis does not take into account the many changes in the types of indicators between 2010 and 2012, and the stricter scoring guidelines in some. This latter consideration in particular may explain why some company scores decreased: the same level of performance in 2010 could give a lower score in 2012. On the basis of this crude analysis, we can only conclude that 17/20 companies seem to move in the right direction. Only a detailed analysis of indicators that have remained unchanged over time can give a realistic picture of development.

Changes in the ten **score-based longitudinal indicators** reflect the development of company policies and practices in absolute terms, without changing the standards

in between the two measurements (Table 3). Within this group, the six core indicators best reflect overall change. Their 84% increase from 1.45 to 2.67 on a scale of 0 – 5 is the best quantitative estimate of the change in industry performance between 2010 and 2012. While this increase is considerable and to be welcomed we should not forget that the 2012 score implies a mean industry performance of only 53 – 55% of the maximum score currently possible. In other words, much progress is still possible.

The overall change in the six indicators in the area of **research and development** can be quantified by looking at the underlying figures. The mean numbers underlying all these indicators are rising, and the median value of the average percentage increases is 132% (Table 4). If we accept this percentage as a meaningful expression of change, we are able to conclude that research and development activities in Access to Medicine Index diseases have more than doubled between 2010 and 2012.

Mean values for the industry as a whole mask the many differences that exist between individual indicators, and between companies. Figure 2 visualizes the large **differences between the six core indicators** in current level and rate of progression. All these core indicators show a strong correlation with the score of their technical area as a whole (Table 1) and we can therefore conclude that the industry is well advanced in the areas of governance (A.I.1) and donations (G.I.2) which both score around 75% of the current maximum, with 13/20 (65%) of companies scoring a 4 or 5. On the other hand, industry still has a long way to go in issues of data exclusivity (B.I.3) and patents (E.II.2), where industry averages stand at less than 35% of the current maximum (Figure 2). It can be seen from the figure that the dynamics in these two technical areas are different. Half the companies are improving their score on patents (Table 4) but from a very low baseline (0.125) to a slightly less low level (1.625). On the other hand, little improvement can be observed in the area of data exclusivity, with only six companies showing an improvement (Table 4). Medium performance and good progress are seen in the areas of research (C.III.4) and capacity building (F.III.1).

The mean scores also mask the fact that there are large **differences between companies** in performance and progress (Figure 1, Table 4). Confidentiality agreements preclude the publication of indicator data of individual companies, but it will be no surprise to the reader that the four strongest risers in Figure 1 also occupy the

first four lines in Table 4. This provides further support for our conclusion that changes in the selected indicators, and especially the six core indicators, represent changes in the Access to Medicine Index as a whole.

The question remains whether progress in Access to Medicine Index scores, as reported here on the basis of selected longitudinal indicators, reflects real progress in company commitment, transparency, performance and innovation, or just better reporting. It is known that some fast-rising companies have developed clear strategies to increase their performance across all or many areas measured by the Access to Medicine Index. It can safely be assumed that these companies have both strengthened their access-related activities and improved the management of access initiatives and thus are able to report better on the impact of these activities. On the other hand, most of the Access to Medicine Index indicators, and especially the longitudinal indicators used in this report, have been chosen on the basis of their robustness and their potential for verification. In other words, progress in the scores for these indicators is likely to represent real progress.

Conclusion

This longitudinal analysis of the Access to Medicine Index scores between 2010 and 2012 allows, for the first time, an objective assessment of absolute progress by the top-20 R&D-based pharmaceutical companies in promoting access to essential medicines in low- and middle-income countries. As Access to Medicine Index scores reflect policies and practices that are in the interest of public health, we conclude that the research-based pharmaceutical industry as a whole is moving in the right direction, albeit with large differences in performance and progress between individual companies. This adds a dynamic perspective to the biennial Access to Medicine ranking and can serve as a baseline for the future.

Table 1

Score-based longitudinal indicators, and correlation coefficient with overall score of the relevant technical area (r_1) and with overall Access to Medicine Index score (r_2) in 2012.

Core score-based indicators[a]	r_1	r_2
Industry commitment		
■ A.I.1 The company has a governance system that includes direct board-level responsibility and accountability for its access to medicine initiatives	0.70**	0.69**
■ B.I.3 The company refrains from pursuing data exclusivity	0.71**	0.51*
■ G.I.2 The company commits to ensuring that donated products are administered to patients	0.78**	0.70**
Transparency		
■ E.II.2 The company discloses the patent status of its products	0.51*	0.67**
Industry activities and performance		
■ C.III.4 Research and product development partnerships in which the company has been involved, with the aim of developing products or new formulations for Index Diseases specifically targeting Index Countries' needs (adjusted for the number of the molecules in the company's research pipeline)	0.81**	0.77**
■ F.III.1 Is there evidence that the company assists local Index Country manufacturers or in-house manufacturing facilities to achieve international good manufacturing standards* in the Index Countries?	0.73**	0.76**

Other score-based indicators[a]		
Transparency		
■ A.II.2 The company discloses quantitative and qualitative performance measures and targets for its access to medicine practices	0.75**	0.68**
■ G.II.3 The company discloses the amount of resources dedicated to and achievements resulting from its philanthropic activities	0.31	0.20
Industry activities and performance		
■ F.III.2 Evidence that company takes part in local research training partnerships	0.74**	0.71**
■ F.III.4 The company is actively engaged in developing and implementing national pharmacovigilance-related programmes	0.87**	0.72**

Number-based research indicators[a]		
■ C.III.1 Proportion of financial R&D investments dedicated to index diseases	0.76**	0.76**
■ C.III.2 Share of R&D pipeline and number of new molecules for index diseases	0.47*	0.35
■ C.III.3 Share of R&D pipeline and number of products registered reflecting adapted molecules or new technologies for index diseases	0.72**	0.76**
■ C.III.4 Number of R&D partnerships for products for index diseases	0.81**	0.77**

* $p < 0.05$

** $p < 0.01$

a   Numbers refer to the indicator classification of the Access to Medicine Index 2012

Table 2
Detailed longitudinal analysis of ten scored indicators, 2010-2012 (scores 0 – 5).

Data analysis was only possible where the quality of data from companies was comparable between 2010 and 2012.

	Number of companies with rising score	Number of companies with falling score	Median score 2010	Median score 2012	Increase in median score	Average score 2010	Average score 2012	Increase in average score	% Increase in average score
Core scored indicators									
■ A.I.1 Governance	4	1	3.08	5	1.93	3.08	3.7	0.63	20%
■ B.I.3 Data exclusivity	6	0	0	0	0	0.4	1.65	1.25	313%
■ C.III.4 R&D partnerships	14	0	1	3	2	1.05	2.55	1.5	143%
■ E.II.2 Patent status	10	0	0	2.5	2.5	0.13	1.63	1.5	1200%
■ F.III.1 GMP training	9	1	0	2.5	2.5	1.58	2.88	1.3	83%
■ G.I.2 Donations	7	0	2.5	5	2.5	2.5	3.63	1.13	45%
Average	*8.33*	*0.33*	*1.10*	*3*	*1.90*	*1.45*	*2.67*	*1.22*	*84%*
Median	*8*	*0*	*0.5*	*2.75*	*2.25*	*1.31*	*2.71*	*1.28*	*97%*
Other scored indicators									
■ A.II.3 Performance targets	9	1	2.5	4	1.5	2.65	3.55	0.9	34%
■ F.III.2 R&D training	12	0	2.5	2.5	0	1.85	3.05	1.2	65%
■ F.III.4 Pharmacovigilance	6	0	0	0	0	0.75	1.25	0.5	67%
■ G.II.3 Philanthropy	10	7	4	4	0	3.3	3.65	0.35	11%
Average	*9.25*	*2.00*	*2.25*	*2.63*	*0.38*	*2.14*	*2.88*	*0.74*	*35%*
Median	*9.5*	*0.5*	*2.5*	*3.25*	*0*	*2.25*	*3.30*	*0.7*	*31%*
All scored indicators									
Average	*8.70*	*1*	*1.56*	*2.85*	*1.29*	*1.73*	*2.75*	*1.03*	*59%*
Median	*9*	*0*	*1.75*	*2.75*	*1.71*	*1.71*	*2.96*	*1.16*	*68%*

Table 3
Detailed longitudinal analysis of six number-based research indicators, 2010-2012.

Data analysis was only possible where the quality of data from companies was comparable between
2010 and 2012.

Research indicators	Number of companies with rising score	Number of companies with falling score	Median score 2010	Median score 2012	Increase in median score	Average score 2010	Average score 2012	Increase in average score	% Increase in average score
▪ C.III.1 R&D investment*	4	0	31.4	36	4.6	73	327	254	348%
▪ C.III.2 New molecules **	11	5	1	3	2	2.4	4.6	2.2	92%
▪ C.III.2 New pipeline***	11	6	1	1	0	6.4	15.1	8.7	136%
▪ C.III.3 Adapted molecules**	11	3	1.5	2	0.5	1.55	3.7	2.15	139%
▪ C.III.3 Adapted pipeline***	13	4	3	6	3	6.2	9.25	3.05	49%
▪ C.III.4 R&D partnerships	16	0	1	6	5	2.65	6.05	3.4	128%
Average	*11*	*3*							*149%*
Median	*11*	*3.5*							*132%*

Medians and averages are expressed in the following units:

*   In US$ millions

**   Number of molecules

*** Percentage of total pipeline

Table 4

Rising (⊞), stable or falling (⊟) score-based indicators for each of 20 companies, 2010–2012*.

Data analysis was only possible where the quality of data from companies was comparable between 2010 and 2012.

| Core score-based indicators						Other score-based indicators			
A.I.1	B.I.3	C.III.4	E.II.2	F.III.1	G.I.2	A.II.2	F.III.2	F.III.4	G.II.3
+	+	+	+	+	+	+	+	+	+
	+	+	+	+	+	+	+	+	
	+	+		+	+				+
+		+		+	+			+	+
	+	+	+	+		−	+		+
		+	+		+	+			+
		+	N/A	+	+	+	+	+	+
		+	+	+		+			
	+	+	+				+	+	−
		+	+	+			+		
−		+	+	+		+			−
+		+		+		+			+
		+	+	−			+		
	+	+	N/A				+		−
		+	+			+	+		+
		+						+	−
+							+		+
						+			+
							+		−
							+		−
4 ⊞	**6** ⊞	**16** ⊞	**10** ⊞	**9** ⊞	**7** ⊞	**9** ⊞	**12** ⊞	**6** ⊞	**10** ⊞
1 ⊟	**0** ⊟	**0** ⊟	**0** ⊟	**1** ⊟	**0** ⊟	**1** ⊟	**0** ⊟	**0** ⊟	**6** ⊟
n.s.	*p<0.05*	*p<0.05*	*p<0.05*	*p<0.05*	*p<0.05*	*p<0.05*	*p<0.05*	*p<0.05*	*n.s.*

* Each line in the table represents one company. Company names are not
   disclosed in view of the confidential nature of the information

Figure 1

Crude comparison of total Access to Medicine Index score, 2010-2012 (score 0 - 5) with company names following the 2012 ATM Index.

Figure 2
Changes in six core Access to Medicine indicators, 2010-2012.
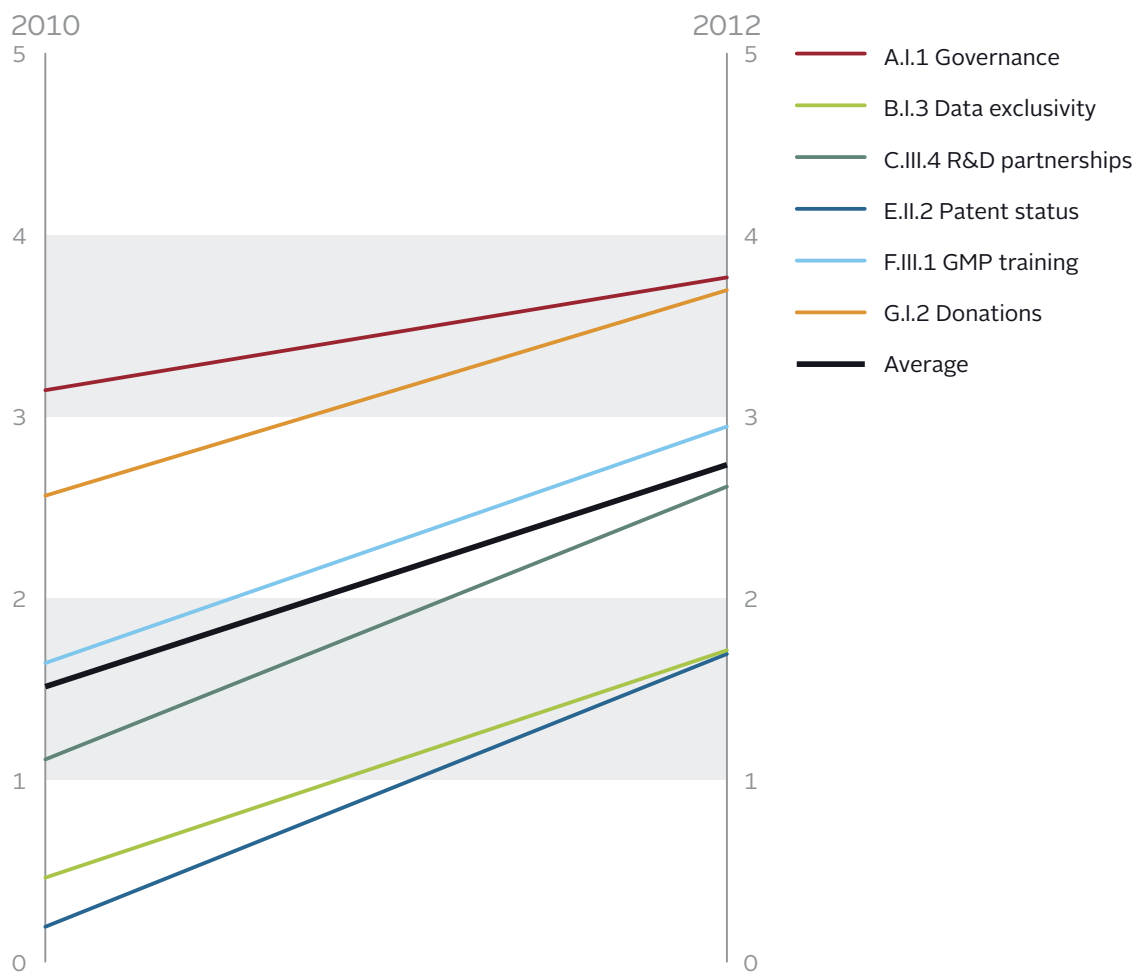
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