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## **Short Communication**

# Globalization of pharmaceutical trade and healthcare coverage of the Millennium Development Goals

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## **Abstract**

**Objective** This study intends to empirically examine the influence of globalization of pharmaceutical trade on healthcare coverage of the Millennium Development Goals (MDGs; i.e. the measles immunization and antiretroviral therapy coverage).

Method This study uses the matched data set from World Bank and WHO during 2000-2014. The heterogeneity robust panel regression method and the fixed-effect estimation method are used to analyse the relation between globalization of pharmaceutical trade and healthcare coverage of the MDGs.

**Key findings** This study identifies the positive relations between globalization of pharmaceutical trade and the measles immunization coverage/ antiretroviral therapy coverage. Conclusion The globalization of pharmaceutical trade can help achieve healthcare coverage of the MDGs, especially for countries under the resource-constrained condition.

Keywords antiretroviral therapy coverage; globalization; immunization coverage; Millennium Development Goals; pharmaceutical trade

## Introduction

The role of pharmaceutical trade in improving healthcare coverage is practically contentious. On the one side, the pharmaceutical trade may to some extent alleviate the plight of developing countries who have no capability to provide access to effective pharmaceuticals, by making the introduction of essential and generic drugs possible. [1] On the other side, the pharmaceutical trade is not guaranteed to solve the problem of affordability<sup>[2]</sup> and thus may not meet the needs of large populations.

For most of the countries with weaker industrial foundation for local pharmaceutical production, the pharmaceutical trade is regarded as the most feasible solution to achieve health targets of the Millennium Development Goals (MDGs). [3,4] To prioritize the public health benefits over business purpose in the pharmaceutical trade, the World Trade Organization (WTO) and other health-related international organizations are striving to keep a balance between encouraging the pharmaceutical R&D with profitable market prospects and preventing the pharmaceutical trade from being a pure tool of grabbing benefits from less developed economies. [5] For this purpose, some exemptions are granted by WTO members to prevent the strict patent regulation from being an obstacle to improving public health in the global pharmaceutical trade, such as allowing a compulsory licence for third parties to produce or sell drugs without patent holders' permission when the supply is insufficient (Agreement on Trade-Related Aspects of Intellectual Property Rights, TRIPS.).<sup>[6]</sup> Although with good intentions to maximize the influence of pharmaceutical trade on healthcare coverage, such exemptions are rarely and discreetly authorized even in sub-Saharan countries who lack sufficient pharmaceutical supply. This may partially constrain the influence of pharmaceutical trade. [7,8]

Accordingly, it remains uncertain whether the pharmaceutical trade can effectively improve healthcare coverage. This study tries to provide an empirical exploration of this issue. By using multi-source data of trade and public health, this study intends to fill this research gap and enrich the relevant empirical evidence.

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**Table 1** The overview of country-level variables (2000–2014)

Variables	Description	Mean	SD	Min	Max	Number of observations
Immunization coverage, measles	Immunization, measles (% of children aged 12–23 months)	85.0798	14.8284	28.0000	99.0000	1003
Antiretroviral therapy coverage	Antiretroviral therapy coverage (% of people living with HIV)	22.8989	22.5399	0.0000	89.0000	870
Globalization of pharmaceutical trade	The number of destinations per exporter, mean	3.4106	1.9853	2.0000	13.7392	511
Share of total health expenditure in gross domestic product (GDP)	Current health expenditure (CHE) as percentage of GDP (%)	6.1597	2.1835	1.0000	13.1000	993
Market competition of pharmaceutical trade (exporter number)	The number of entrants divided by the number of exiters	1.2223	0.9941	0.0000	17.1484	451
Market competition of pharmaceutical trade (in value)	Export value per entrant (mean) divided by export value per exiter (mean)	2.4598	10.1903	0.0035	190.2099	437
Growth of pharmaceutical trade	Growth of incumbents, mean	0.1823	1.3860	-5.0553	9.9428	431
New destination extension of pharmaceutical trade	Share of new destinations in total export value of incumbents, mean	0.5035	0.3307	0.0000	2.0000	432

## Materials and method

The data used in this study combine the Exporter Dynamics Database, MDGs database accessed from World Bank, and the Health Financing data set published by the World Health Organization (WHO). The combined data set covers the time period from the year 2000 to 2014. The Exporter Dynamics Database (HS-2-digit) provides indicators at the 'country-product-year' level, and the indicators are calculated based on exporter-level customs data for each country. Two major indicators - measles immunization and antiretroviral therapy coverage in MDGs - serve as dependent variables in this study. The globalization of pharmaceutical trade as the independent variable is proxied by the number of destinations per exporter. The effects of the share of total health expenditure in gross domestic product, market competition in pharmaceutical trade, growth of pharmaceutical trade and new destination extension in pharmaceutical trade are also controlled in this study. This combined data set contains 55 countries, and the list of matched countries covers both low-middle-income and high-income countries among which the developing countries are in the majority. More details about variables are shown in Table 1, and the list of matched countries is shown in Table 2.

For robustness, the heterogeneity robust panel regression (also called feasible generalized least square, FGLS) and the fixed-effect estimation are respectively performed in this study to control the potential heterogeneity of countries. These two estimation methods can effectively deal with the potential heterogeneity problem in different ways. The former takes the disturbance term of each country as the country-specific heterogeneity. The latter uses the individually varying intercept term to capture the heterogeneity of each country, and takes the disturbance term to be independent identically distributed (i.i.d.). The STATA (13.0) is used for analysis. The regression equations are shown below.

Table 2 The list of matched country.

Albania	Denmark	Kyrgyz Republic	Romania
Bangladesh	Dominican Republic	Lebanon	Rwanda
Belgium	Ecuador	Madagascar	Senegal
Bolivia	Egypt, Arab Rep.	Malawi	South Africa
Botswana	El Salvador	Mauritius	Spain
Bulgaria	Estonia	Mexico	Sweden
Burkina Faso	Ethiopia	Morocco	Thailand
Cambodia	Georgia	Nepal	Turkey
Cameroon	Germany	Nicaragua	Uganda
Chile	Guatemala	Norway	Tanzania
Colombia	Iran, Islamic Rep.	Pakistan	Uruguay
Costa Rica	Jordan	Paraguay	Yemen, Rep.
Cote d'Ivoire	Kenya	Peru	Zambia
Croatia	Kuwait	Portugal	

Notes: The matched list contains 55 countries for which the values of the dependent variable (immunization coverage, measles), independent variable (globalization of pharmaceutical trade) and control variables are all non-missing in the same year, and thus, such country-year observation is valid in the regression analysis.

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Table 3 The influence of globalization of pharmaceutical trade on healthcare coverage of MDGs

	Panel A. Regressions without control variables	ıt control variables			
	Immunization coverage, measles	asles		Immunization coverage, measles	Se
	FGLS estimation	Fixed effect estimation	imation	FGLS estimation	Fixed effect estimation
Independent variable	9 9	9 9		an an	d
Globalization of Pharmaceutical trade	0.7123	1.9333**		4.1009	3.9573**
	(0.0773)	(0.5460)		(0.0905)	(1.6277)
	[0.5608, 0.8638]	[0.8601, 3.0064]		[3.9235, 4.2783]	[0.7584, 7.1562]
Intercept	87.7687**	$81.3594^{**}$		9.8831**	$11.3975^*$
	(0.4210)	(1.8760)		(0.5375)	(5.2166)
	[86.9436, 88.5938]	[77.6726, 85.0462]	62]	[8.8296, 10.9365]	[1.1414, 21.6536]
Wald statistics	84.90	ND		2052.15	ND
[P-value]	[0.0000]	ND		[0.0000]	ND
F statistics	ND	12.54		ND	5.92
[P-value]	ND	[0.0004]		ND	[0.0155]
Number of observations	511	511		444	444
Number of countries	61	61		53	53
Period	2000–2014	2000–2014		2000–2014	2000–2014
	Panel B. 1	Panel B. Regressions with control variables	ariables		
	Immuniza	Immunization coverage, measles		Immunization coverage, measles	easles
	FGLS estimation	timation	FGLS estimation	FGLS estimation	FGLS estimation
Independent variable					
Globalization of Pharmaceutical trade	0.2686***		2.2541**	2.4364**	3.9132*
	(0.0856)		(0.6268)	(0.3138)	(1.9321)
	[0.1009, 0.4362]		[1.0215, 3.4867]	[1.8213, 3.0514]	[0.1113, 7.7151]
Control variables	:			:	:
Share of total health expenditure in GDP	0.5560**		-0.6981	5.0662**	3.3966**
	(0.1695)	· .	(0.3960)	(0.3021)	(0.8927)
Moderate commentations of advances continued (version)	[0.2277, 0.8922]	1	[-1.4/69, 0.0806]	[4.4/41, 5.6583] 0.1622	[1.6405, 5.1528]
Market compension of pharmaceutical name (exponer number)			0.0000	0.1972	0.2450
	[-1.4694, 0.4334]		[-0.5156, 0.5168]	[-1.2687, 1.6632]	[-0.8835, 1.3747]
Market competition of pharmaceutical trade (in value)	0.0588		-0.0532	-0.4701*	-0.2409
•	(0.0364)		(0.0544)	(0.2182)	(0.2382)
	[-0.1301, 0.0124]		-0.1602, 0.0538	[-0.8977, 0.0425]	[-0.7096, 0.2278]
Growth of pharmaceutical trade	0.3985		$0.5839^{**}$	-0.3776	$0.3600^{**}$
	(0.2984)		(0.2174)	(0.4182)	(0.4782)
	[-0.1863, 0.9833]		[0.1563, 1.0114]	[-1.1871, 0.4420]	[-0.5809, 1.3010]
New destination extension of pharmaceutical trade	-4.45/1 (1.2352)		-0.9851	-0.9/86	-2.2792
	(1.2332)	-2.03611	(0.9790) [-2.9105, 0.9404]	(1.8270) [-4.5594, 2.6023]	(2.1020) [-6.5345, 1.9762]

Immunization coverage, measles   FGLS estimation   89.5360** (1.2993)   [86.9894, 92.0826]   77.03   (0.0000)	estimation FGLS estimation  **  **  **  **  **  **  **  **  **	Immunization coverage, measles  FGLS estimation  -16.3464** (2.1154)	
FGLS estimation 89.5360** (1.2993) [86,9894, 92.0826] 77.03 [0.0000]	imation :	FGLS estimation -16.3464** (2.1154)	FGLS estimation -8.2237***
89,5360*** (1.2993) [86,9894, 92.0826] 77.03 [0.0000]	2.0826]	-16.3464*** (2.1154)	
(1.2993) [86.9894, 92.0826] 77.03 [0.0000]	2.0826]	(2.1154)	(00000)
[86,9894, 92.0826] 77.03 [0.0000]			(8.2420)
[0.0000]		[-20.4925, -12.2004]	[-24.4419, 7.9945]
[0.0000]	QN	755.38	ND
	ND	[0.0000]	ND
QN	3.75	ND	3.65
[P-value] ND (0.0	[0.0013]	ND	[0.0016]
417	417	360	360
Number of countries 55 55	55	48	48
Period 2000–2014 200	14 2000–2014	2000–2014	2000–2014

The heterogeneity robust regression and fixed effect estimation are performed respectively. Standard errors are reported in the parentheses, 95% confidence intervals are reported in brackets. The intercept term of fixed effect estimation is the average of individually varying intercepts that reflect the heterogeneity of each country. \*\*P < 0.01. \*P < 0.05; Immunization coverage<sub>it</sub> =  $\beta_{0i}$ +  $\beta_1$  Globalization of pharmaceutical trade<sub>it</sub> +  $\beta_2$  Control variables<sub>it</sub> +  $\varepsilon_{it}$ 

Antiretroviral therapy coverage<sub>it</sub> =  $\beta_{0i}$ 

- $+ \beta_1$  Globalization of pharmaceutical trade<sub>it</sub>
- $+ \beta_2$  Control variables<sub>it</sub>  $+ \varepsilon_{it}$

## **Results**

Table 3 demonstrates the effect of globalization of pharmaceutical trade on healthcare coverage. As shown in Table 3, there is a positive and significant relation between globalization of pharmaceutical trade and measles immunization coverage (see the regression coefficient 0.2686, P < 0.01, by using FLGS; 2.2541, P < 0.01, by using fixed-effect estimation), and also a positive and significant relation between globalization of pharmaceutical trade and antiretroviral therapy coverage (2.4364, P < 0.01, by using FLGS; 3.9132, P < 0.01, by using fixed-effect estimation). These empirical results indicate that the globalization of pharmaceutical trade can effectively improve healthcare coverage.

## Discussion and conclusion

The association between pharmaceutical trade and health-care coverage is a considerable concern of researchers. However, there is a lack of relevant empirical evidence for this issue, and thus, it remains contentious. This study provides the empirical exploration and reveals an optimistic picture of this contentious issue with identifying the positive influence of globalization of pharmaceutical trade on health-care coverage of the MDGs (i.e. measles immunization coverage and antiretroviral therapy coverage) during 2000–2014.

This study has several practical implications. First, the findings of this study help ease the concern of international organizations about the influence of globalization of pharmaceutical trade on public health. Although with the criticism of failing to solve the problem of affordability, [9,10] producing new inequality in the trade practice between the developed and developing economies, [6,11–13] and magnifying the counterfeit pharmaceutical problem, [14-17] the globalization of pharmaceutical trade is still found significantly improving healthcare coverage. Second, it is worth noting that the positive relation between the globalization of pharmaceutical trade and healthcare coverage is robust and not disturbed by the policy change or authorized exemption. It can be still identified during the past decade, even though under the circumstance of the rare exemption according to the TRIP clauses authorized by the international organization. As such, in the future, the less developed countries can confidently promote

pharmaceutical trade to improve healthcare coverage, regardless of the long-lasting controversy about the potential disadvantageous status in the trade practice. Third, it is meaningful for less developed countries to utilize the pharmaceutical trade as a tool to cover the shortage of essential or generic drugs, since the authorization of triggering the TRIP clause to increase the pharmaceutical supply is still very discreet in the near future.

This study is also not free of limitations. First, this study cannot exclude the effect of substandard pharmaceuticals from the association between globalization of pharmaceutical trade and healthcare coverage. Previous studies indicate that the pharmaceutical trade can facilitate access to both effective and substandard pharmaceuticals.<sup>[18,19]</sup> The effective influence of globalization of pharmaceutical trade on healthcare coverage may partially be overrated due to the presence of substandard pharmaceuticals. Second, this study just examines two types of healthcare coverage and involves about a quarter of countries in the world. The data availability restricts the efforts to make a more general evaluation. Third, for lack of the data of each specific type of pharmaceuticals in trade, we can only take traded pharmaceuticals as a whole rather than make the detailed evaluation by type.

## **Declarations**

#### **Conflict of interest**

The Author(s) declare(s) that they have no conflicts of interest to disclose.

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#### Authors' contributions

B. Yuan contributes to the study design and data analysis. J. Li contributes to the data collection and writing of original manuscript. Z. Wang contributes to the review and editing of manuscript. All Authors state that they had complete access to the study data that support the publication.

#### **Ethical statement**

This study does not involve human/animal patients or require any ethical approval.

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