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Assessment of laboratory specimen referral and transport in 17 CDC partner countries: measuring progress in Global Health Security Agenda implementation

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An abstract of

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Abstract

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By Jordan Barker

This thesis examines the relationship between the laboratory specimen referral and transport indicator and other indicators within the biosafety and biosecurity, national laboratory systems, real time surveillance, reporting, emergency response operations, and workforce development technical areas of the World Health Organization's Joint External Evaluation (JEE) Tool version 1.0 among 17 US Centers for Disease Control and Prevention (CDC) partner countries between October 2016 and September 2019. This time frame was studied because the JEE version 1.0 was used during this time, and some indicators changed in the JEE version 2.0 beginning in October 2019. Data were collected from the US government Global Health Security Agenda interagency progress reports, which are used by the CDC, US Agency for International Development, and the US Department of State to assess a country's capacity in several technical areas. Countries are required to complete these interagency reports twice per fiscal year. Descriptive and multivariate models were assessed using linear regression. After obtaining a final multivariate model, collinearity and interaction assessments were analyzed. Our results showed that two indicators, effective modern point of care and laboratory-based diagnostics and reporting network and protocols in country, were significantly associated with the outcome variable ($p=0.05$ and 0.04, respectively), the laboratory specimen referral and transport indicator. The interaction assessments yielded a non-statistically significant p-value of 0.19 with our outcome variable. Although this assessment did not include country-specific information for each indicator, this analysis can be beneficial to countries by allowing them to make informed decisions for any outcome indicator by including additional country-specific data into the model. By including this other information, a country will also have the ability to determine relationships between indicators within other technical areas.

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INTRODUCTION

Now more than ever, global health security has become an imperative issue across the world as infectious disease threats are capable of spreading to multiple continents in under 48 hours, as seen with the current coronavirus disease 2019 (COVID-19) pandemic (1-2). As a result of globalization and emerging and re-emerging infectious diseases, the International Health Regulations (IHR) were originally developed in the 1960s by the World Health Organization (WHO) to outline responsibilities of member States to identify and report public health emergencies, in addition to assisting other countries in responding to these threats (3-4). The IHR are an international, legally-binding treaty and were updated in 2005 (5). Evolving public health concerns, such as severe acute respiratory syndrome (SARS) of the early 2000s, along with the need for cohesive communication and prevention strategies worldwide, were some of the drivers for the revision of the original IHR (4).

The Global Health Security Agenda (GHSA) was created in 2014 through a collaboration between countries and organizations with the commitment to "prevent, detect, and respond" to public health emergencies, while adhering to the standards set by the IHR (2005) (5, p.S9, 6). With the IHR (2005) as a basis, the GHSA aims to strengthen a country's health system to provide security from emerging and re-emerging disease threats worldwide (7). The GHSA includes 11 Action Packages (also known as technical areas) (Table A) aligned with the three overarching goals of prevent, detect and respond (Tappero et al., 2017; Fitzmaurice et al., 2017). The US Centers for Disease Control and Prevention (CDC) established a partnership with 17 countries (Figure 1), which received

funding and technical support from the CDC to assist in capacity building across the GHSA technical areas (5, 8).

Strengthening a country's public health system, including surveillance and national laboratory systems, is pivotal to creating a healthier and safer environment for its citizens by detecting infectious disease threats at their source and preventing them from spreading to other countries and becoming pandemics. However, the quality of laboratory systems varies across countries. Within a nation's laboratory system, the presence of a specimen referral and transport system plays a principal role in the rapid detection and diagnosis of diseases (9-10). Some of CDC's 17 GHSA partner countries only recently implemented a specimen referral and transport system or have created a pilot program to improve their current system, using the national postal service (9-11). Despite the implementation and/or development of these laboratory systems, several challenges have been identified, such as the lack of a robust laboratory specimen referral and transport system. Without these systems and services being in place or conducted in a timely manner, a health system can miss or have delays in detecting positive cases of an infectious disease (12). Additionally, the laboratory specimen referral system may exclude a portion of the population due to lack of services provided in a particular region of the country (13). In this analysis, we assessed how other JEE indicators may impact the laboratory specimen referral and transport systems (indicator) in the 17 CDC partner countries.

METHODS

We conducted a longitudinal, retrospective study to assess the laboratory specimen referral and transport system in 17 CDC partner countries from October 2016

to September 2019 and determine which WHO Joint External Evaluation (JEE) indicators potentially are affecting the laboratory specimen referral and transport system JEE indicator. The primary data source was the US Government (USG) GHSA interagency progress reports. CDC Country Office staff complete these interagency reports twice per year based on their assessment of the countries' capacities in 19 technical areas; USG templates developed by the National Security Council, US Department of State, and CDC are sent to countries in or around April and October and are typically completed in May and November, respectively, each year. The reports are then reviewed by experts across CDC, and CDC's GHSA Technical Working Groups, for clarity and further understanding on the progress of the JEE scores. The reports are then maintained and stored within CDC's Office of the Director, Division of Global Health, Center for Global Health.

To assess a country's progress in developing capacity across these technical areas, the GHSA and WHO IHR (2005) created a monitoring and evaluation framework-- the WHO Joint External Evaluation (JEE) Tool-- in early 2016 (14). The WHO JEE version 1.0 was expanded from the original 11 technical areas formed by the GHSA to cover 19 technical areas and more than 40 indicators, as referenced in Table A (15). Of the 19 technical areas outlined within the JEE version 1.0, the national laboratory systems technical area is of primary interest in this thesis due to its impact on surveillance systems and reporting and ability to be an alert or warning signal for a potential outbreak.

We examined the three-year fiscal period of October 2016 to September 2019 because the JEE version 1.0 was used during this time period. After September 2019, the

WHO transitioned to the JEE version 2.0, which included some indicators that do not directly align with JEE version 1.0.

For this assessment, there were a total of seven (7) data points that were used, including: official baseline JEE capacity level scores for each indicator for each country and two (2) data points per fiscal year over three years (October 2016 - September 2017; October 2017 – September 2018; and October 2018 – September 2019). (The official baseline JEE was conducted by external reviewers coming to the country and rating the country's capacities, using the JEE scores, compared to the other six data points, which use the USG GHSA interagency progress reports and are from the perspective of the CDC's Country Office). Of the 48 indicators within the WHO JEE Tool version 1.0, there are 15 indicators of interest for this analysis (in bold and starred in Table A). These indicators were selected based on existing literature regarding their association with laboratory specimen transport and referral networks (Best and Sakande, 2016), in addition to discussions with laboratory system subject matter experts at CDC (16-19).

Scores for each indicator in the JEE and of interest in this analysis range from 1-5 with a scoring and color system. A JEE score of "1" is labeled red and represents no capacity; a score of "2" or "3" are labeled in yellow and represent limited capacity and developed capacity, respectively. A score of "4" or "5" are labeled in green and represent demonstrated capacity and sustainable capacity, respectively (14-15).

Data analysis was conducted using SAS software version 9.4 (20). Prior to an exploratory analysis, it was determined that the preparedness technical area and its two indicators would be excluded in this analysis, as there were no reported data for the time frame of October 2016 – September 2019. Descriptive statistics, including the JEE score

over time, the number of observations for each variable, beta estimates, standard errors, and p-values for the 14 explanatory variables using the "laboratory specimen referral and transport system" as the outcome variable were obtained utilizing a simple linear regression with PROC SURVEYREG, and parameter estimates for each indicator were obtained. Linear regression using PROC SURVEYREG was chosen in order to take into account the lack of independence of scores at the country level. Each variable included scores from all 17 CDC partner countries. Missing observations were excluded from the crude models. All variables with a p-value <0.10 were retained for consideration within the multivariate model. For each model in this assessment, the scores for every indicator have been combined and were not stratified by country or by time point. During exploratory analysis, we considered using a time series model to stratify by time points and by country, but further assessments indicated that there was no variability on the country level or by time point. Therefore, a multiple linear regression approach was chosen.

After obtaining the parameter estimates for the crude analyses, a backwards elimination approach was used to form the final multivariate model using PROC SURVEYREG. Missing observations for each variable were excluded from the analysis. After backwards elimination methods were completed, variables with p-values <0.10 were retained in the final multiple linear regression model. Collinearity assessments were analyzed, including variance inflation factors (VIFs) assessments. Interactions within the final model were analyzed.

RESULTS

Six (40%) of the 15 indicators in the crude analyses were statistically significant ($p < 0.10$). These six indicators were: Laboratory testing for detection of priority diseases (JEE indicator D.1.1); Effective modern point of care and laboratory-based diagnostics (JEE indicator D.1.3); Syndromic surveillance systems (JEE indicator D.2.4); System for efficient reporting to WHO, Food and Agriculture Organization (FAO) and World Organization for Animal Health (OIE) (JEE indicator D.3.1); Reporting network and protocols in country (JEE indicator D.3.2); and, Biosafety and biosecurity training and practices (JEE indicator P.6.2) (Table 1). Of these six variables, effective modern point of care and laboratory-based diagnostics had the highest β (Beta) estimate, or association, with the outcome variable (JEE indicator D.1.2) at 0.56, and the lowest β was laboratory testing for detection of priority diseases with an estimate of 0.23.

The two remaining JEE Indicators in the multivariate model were statistically significantly associated with specimen referral and transport networks ($p <0.10$). The variables within the final full multivariate model include: Effective modern point of care and laboratory-based diagnostics (JEE indicator D.1.3) and Reporting network and protocols in country (JEE indicator D.3.2) (Table 2). The final regression equation is shown below:

- Specimen transport and referral system (D.1.2) = 1.16 + 0.32 (Effective modern point of care and laboratory-based diagnostics, D.1.3) + 0.27 (Reporting network and protocols in country, D.3.2) + Ɛ.

The adjusted R^2 for the final multivariate model was 0.25 and included 102 observations. The effective modern point of care and laboratory-based diagnostics variable had the largest β at 0.32 and a design effect of 1.89.

DISCUSSION

In this longitudinal, retrospective study, we examined the importance of a national laboratory specimen referral and transport system for 17 CDC partner countries and investigated potential variables that could influence these systems. First, effective modern point-of-care and lab-based diagnostics play a critical role in a laboratory specimen referral and transport system, having the highest Beta estimate within the multivariate model. Secondly, reporting network and protocols in country are also very important for the detection, reporting, and response to a public health emergency.

Our finding that an effective modern point-of-care and lab-based diagnostic system is crucial to the overall success of a specimen transport and referral system ($p = 0.05$, Table 3) is consistent with multiple studies (21-22). A 2017 study indicated the necessity for adequate point-of-care testing to quickly diagnose and treat patients, especially during a public health emergency, such as the 2014-2016 West Africa Ebola outbreak (21). Furthermore, a study conducted in South Africa outlines the advantages that point-of-care testing would bring to rural and urban areas alike, such as the decrease in turnaround time after transporting specimens to clinics and laboratories; however, healthcare workforce availability at these sites is also vital to decreasing the delays in results (22). Because this particular JEE indicator (D.1.3) is also in the national laboratory systems technical area and directly related to a specimen referral and transport system, the results of our analyses are aligned with our initial objectives for the study.

However, given the results of the referenced qualitative study on point-of-care testing in South Africa, it would be beneficial to explore the associations between urban and rural point-of-care testing with other variables, such as healthcare workforce availability, to further determine how a laboratory specimen referral and transport system network may be affected.

The existence of a reporting network and protocols in countries have also been shown to positively affect the progress of a specimen referral and transport system ($\beta = 0.27$; $p = 0.04$). A 2016 study outlined the importance and endorsement of a centralized national information management system that will improve accessibility to and reporting disease surveillance information, along with assisting with the process of specimen referral and transport through paper trails, such as emails and facsimile (19). Similarly, authors of another study suggested the need for expanding access of the District Health Information Software 2 (DHIS2) reporting platforms to every laboratory within a network, rather than retaining this information in a centralized location (23). This expansion would allow disease surveillance data to become widely available, while also potentially adding the benefit of being cost effective for the laboratory system (23). Furthermore, standardized guidelines for the training of healthcare and laboratory personnel on handling, packaging, shipping and storing specimens should be implemented and a dearth of proper training can result in invalid specimens (10-11, 24-25). The aforementioned existing literature on reporting networks and specimen referral and transport systems offer information that is consistent with our findings, but we must also take into account internal and external barriers (e.g., funding or resources) that are potentially affecting countries with lower JEE scores for this variable.

Limitations

There are a number of limitations to our study. First, the results of these analyses may not be generalizable, as we are only including specific data from three fiscal years (October 2016 – September 2019), and only data that have been collected through the use of the WHO JEE version 1.0 have been included in this study. After September 2019, the WHO JEE version 2.0 is being used for monitoring and evaluation, and some indicators within this version do not directly align with those within the WHO JEE version 1.0. An evaluation of the similarities and differences between JEE version 1.0 and 2.0 and its impact in measuring countries' capacities is currently underway at CDC.

Secondly, there are several missing observations for each country, which may reduce the overall power of our study and induce bias within our results, as each variable is not truly represented. Third, due to the lack of variability at the country level, we were unable to assess each country individually and instead ran regression models with all country data combined. In doing this, we also did not assign specific weights to each variable, as these data were not available to us during the time of analyses. These variable weights for each indicator may vary by country, and may also vary by other factors, such as available funding and resources (i.e., staff and time) available and money invested for each JEE indicator.

We also did not include any confounding factors within our analyses that may affect the progress of developing and maintaining a laboratory specimen referral and transport system. These factors include, but are not limited to: pathogen type; type of test for the specimen; the time that the specimen was collected, tested, processed, and reported; costs associated with the packaging, handling, and transport of the specimen;

how the specimen was collected (i.e., may not even be a viable specimen at time of collection or time of processing); and the specifics (e.g., distance to destination) of referral and transport of the specimens to local, regional, or national laboratories or referring laboratories, which may be out the country. These variables were not included within our analyses, as we did not have access to this information at the time of this evaluation.

Conclusion

The formation of the JEE Tool and the GHSA has provided countries the ability to consistently improve their health security through measuring progress in various technical areas, using a variety of monitoring and evaluation tools and indicators. Our findings suggest that these JEE indicators are associated with one another, and the progress of one indicator may affect the performance of other indicators. The status of a country's laboratory specimen referral and transport system can be an asset or a hinderance in the detection, reporting, and response to a public health emergency. While it is important to evaluate the progress of this system on a continuous basis, it is imperative to understand that internal and external factors will affect the performance of a laboratory specimen referral and transport system and should be taken into consideration for future studies.

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TABLES

Table A: Joint External Evaluation (JEE) Indicators by Global Health Security Agenda (GHSA) Core Area and Action Packages (also known as Technical Areas)

Core Area	Technical Area	Indicator
Prevention	National Legislation, Policy and Financing	P.1.1 Legislation, laws, regulation administrative requirements, policies or other government instruments in place are sufficient for implementation of IHR
		P.1.2 The state can demonstrate that it has adjusted and aligned its domestic legislation, policies and administrative arrangements to enable compliance with the IHR (2005)
	IHR Coordination, Communication and Advocacy	P.2.1 A functional mechanism is established for the coordination and integration of relevant sectors in the implementation of IHR
	Antimicrobial Resistance (AMR)[1]	P.3.1 Antimicrobial resistance (AMR) detection
		P.3.2 Surveillance of infections caused by AMR pathogens
		P.3.3 Healthcare associated infection (HCAI) prevention and control programs
		P.3.4 Antimicrobial stewardship activities
	Zoonotic Disease[1]	P.4.1 Surveillance systems in place for priority zoonotic diseases/pathogens
		P.4.2 Veterinary or Animal Health Workforce
		P.4.3 Mechanisms for responding to infectious zoonoses and potential zoonoses are established and functional

	Food Safety	P.5.1 Mechanisms are established and functioning for detecting and responding to foodborne disease and food contamination
	Biosafety and Biosecurity[1]	P.6.1 Whole-of-government biosafety and biosecurity system is in place for human, animal, and agriculture facilities
		P.6.2 Biosafety and biosecurity training and practices*
	Immunization[1]	P.7.1 Vaccine coverage (measles) as part of national program
		P.7.2 National vaccine access and delivery
Detection	National Laboratory System[1]	**D.1.1 Laboratory testing for detection of priority diseases***
		D.1.2 Specimen referral and transport system *
		D.1.3 Effective modern point of care and laboratory-based diagnostics*
		D.1.4 Laboratory quality system*
	Real Time Surveillance[1]	**D.2.1 Indicator and event-based surveillance systems***
		D.2.2 Interoperable, interconnected, electronic real-time reporting system*
		D.2.3 Analysis of surveillance data*
		D.2.4 Syndromic surveillance systems*
	Reporting[1]	**D.3.1 System for efficient reporting to WHO, FAO and OIE***
		D.3.2 Reporting network and protocols in country*

	Workforce Development[1]	**D.4.1 Human resources are available to implement IHR core capacity requirements***
		D.4.2 Applied epidemiology training program in place such as FETP*
		D.4.3 Workforce strategy*
Respond	Preparedness	R.1.1 Multi-hazard national public health emergency preparedness and response plan is developed and implemented
		R.1.2 Priority public health risks and resources are mapped and utilized
	Emergency Response Operations[1]	**R.2.1 Capacity to Activate Emergency Operations***
		R.2.2 Emergency Operations Centre Operating Procedures and Plans
		R.2.3 Emergency Operations Program
		R.2.4 Case management procedures are implemented for IHR relevant hazards
	Linking Public Health and Security Authorities[1]	R.3.1 Public Health and Security Authorities, (e.g., Law Enforcement, Border Control, Customs) are linked during a suspect or confirmed biological event
	Medical Countermeasures and Personnel Deployment[1]	R.4.1 System is in place for sending and receiving medical countermeasures during a public health emergency
		R.4.2 System is in place for sending and receiving health personnel during a public health emergency
		R.5.1 Risk Communication Systems (plans, mechanisms, etc.)
		R.5.2 Internal and Partner Communication and Coordination

	Risk Communication	R.5.3 Public Communication
		R.5.4 Communication Engagement with Affected Communities
		R.5.5 Dynamic Listening and Rumour Management
Other IHR and PoE	Points of Entry (PoE)	PoE.1 Routine capacities are established at PoE
		PoE.2 Effective Public Health Response at Points of Entry
	Chemical Events	CE.1 Mechanisms are established and functioning for detecting and responding to chemical events or emergencies
		CE.2 Enabling environment is in place for management of chemical Events
	Radiation Emergencies	RE.1 Mechanisms are established and functioning for detecting and responding to radiological and nuclear emergencies
		RE.2 Enabling environment is in place for management of Radiation Emergencies

(Information in Table A adapted from World Health Organization, 2016)

Table A. Summary of the WHO JEE indicators. WHO= World Health Organization; FAO= Food and Agriculture Organization; OIE= World Organization for Animal Health; FETP= Field Epidemiology Training Program; IHR = International Health Regulations; PoE = Point of Entry.

[1]Represents the GHSA Action Packages (n=11)

∗**and bolded** represents the variables of interest for this analysis (n=15)

Table 1. Crude Analyses between Explanatory JEE Indicators (Variables) and the Laboratory Specimen Referral and Transport System (JEE D.1.2) Indicator for 17 CDC Partner Countries, October 2016 - September 2019

Variable (JEE Indicator)	**No. of Variables**	**Beta Estimate**	**Standard Error**	**T-value**	**Design Effect**	**P-value**
D.1.1	116	.23	.11	2.03	1.30	**.06**
D.1.3	112	.56	.17	3.24	2.71	**.01**
D.1.4	116	.11	.10	1.11	1.41	.28
D.2.1	116	.16	.22	0.75	3.59	.47
D.2.2	114	.16	.11	1.43	1.40	.17
D.2.3	114	.03	.15	0.23	2.46	.82
D.2.4	113	.34	.13	2.61	1.24	**.02**
D.3.1	104	.37	.16	2.26	2.43	**.04**
D.3.2	104	.36	.11	3.26	2.35	**.00**
D.4.1	112	.21	.21	1.02	4.64	.32
D.4.2	116	.15	.16	0.93	1.47	.36
D.4.3	113	.15	.17	0.88	2.62	.39
P.6.2	114	.38	.20	1.87	3.16	**.08**
R.2.1	114	.15	.10	1.66	2.56	.11

*Note: P-values in bold indicate variables that are statistically significant at $p < 0.10$.
Exact language for each JEE indicator is in Table A.
JEE = Joint External Evaluation

Table 1A. Full Multivariate Model between Explanatory JEE Indicators (Variables) and the Specimen Referral and Transport (JEE D.1.2) Indicator for 17 CDC Partner Countries, October 2016 - September 2019

Variable (JEE Indicator)	**Beta**	**Std Error**	**Design Effect**	**T-value**	**P-value**
Model	0.17	0.72	2.04	0.24	0.82
D.1.1	0.07	0.14	1.93	0.52	0.61
D.1.3	0.22	0.17	1.77	1.29	0.21
D.2.4	0.26	0.17	2.13	1.51	0.15
D.3.1	-0.09	0.24	3.10	-0.35	**0.72**
D.3.2	0.21	0.12	1.63	1.75	0.09
P.6.2	0.18	0.27	3.85	0.66	0.52
N	=100				
Adjusted R^2	=0.26				

*Note: The p-value in bold indicates the highest p-value for this model and was omitted to re-run the model. D.3.1 had the largest p-value at 0.72. Exact language for each JEE indicator is in Table A.
JEE = Joint External Evaluation

Table 1B. Backwards Elimination Results for Final Multivariate Model between Explanatory Variables and the Specimen Referral and Transport (JEE D.1.2) Indicator for 17 CDC Partner Countries, October 2016 - September 2019

Variable (JEE Indicator)	**Beta**	**Std Error**	**Design Effect**	**T-value**	**P-value**
Model	0.15	0.69	1.95	0.22	0.83
D.1.1	0.06	0.14	1.91	0.43	**0.67**
D.1.3	0.21	0.17	1.89	1.21	0.24
D.2.4	0.24	0.14	1.62	1.67	0.11
D.3.2	0.19	0.12	2.08	1.53	0.12
P.6.2	0.18	0.27	3.99	0.67	0.51
N	=101				
Adjusted R^2	=0.27				

*Note: The p-value in bold indicates the highest p-value for this model, and this variable was omitted to re-run the model. D.1.1 had the largest p-value at 0.67. Exact language for each JEE indicator is in Table A.
JEE = Joint External Evaluation

Table 1C. Backwards Elimination Results for Final Multivariate Model between Explanatory Variables and the Specimen Referral and Transport (JEE D.1.2) Indicator for 17 CDC Partner Countries, October 2016 - September 2019

Variable (JEE Indicator)	**Beta**	**Std Error**	**Design Effect**	**T-value**	**P-value**
Model	0.24	0.64	1.90	0.38	0.70
P.6.2	0.19	0.25	3.69	0.74	**0.46**
D.1.3	0.22	0.16	1.81	1.37	0.18
D.2.4	0.25	0.14	1.68	1.71	0.10
D.3.2	0.19	0.12	2.10	1.57	0.13
N	=101				
Adjusted R^2	=0.27				

*Note: The p-value in bold indicates the highest p-value for this model, and this variable was omitted to re-run the model. P.6.2 had the largest p-value at 0.46. Exact language for each JEE indicator is in Table A.
JEE = Joint External Evaluation

Table 1D. Backwards Elimination Results for Final Multivariate Model between Explanatory Variables and the Specimen Referral and Transport (JEE D.1.2) Indicator for 17 CDC Partner Countries, October 2016 - September 2019

Variable (JEE Indicator)	**Beta**	**Std Error**	**Design Effect**	**T-value**	**P-value**
Model	0.48	0.59	1.86	0.81	0.43
D.3.2	0.23	0.11	2.02	2.05	0.06
D.1.3	0.30	0.16	1.97	1.92	0.07
D.2.4	0.23	0.16	1.99	1.44	**0.17**
N	=101				
Adjusted R^2	= 0.27				

*Note: The p-value in bold indicates the highest p-value for this model, and this variable was omitted to re-run the model. D.2.4 had the largest p-value at 0.17. Exact language for each JEE indicator is in Table A.
JEE = Joint External Evaluation

Table 2. Results of Multiple Regression Analysis Between Explanatory Variables and the Specimen Referral and Transport (JEE D.1.2) Indicator for 17 CDC Partner Countries, October 2016 - September 2019

Variable (JEE Indicator)	**Beta Estimate**	**Standard Error**	**T-value**	**Design Effect**	**P-value**
Model	1.16	.44	2.63	2.27	.02
D.1.3	.32	.15	2.11	1.89	.05
D.3.2	.27	.12	2.26	2.38	.04
N	= 102				
Adjusted R^2	= .25				

*Note: Exact language for each JEE indicator is in Table A.
JEE = Joint External Evaluation

Table 3. Collinearity Assessment Results for Final Multivariable Model between Explanatory Variables and the Specimen Referral and Transport (JEE D.1.2) Indicator for 17 CDC Partner Countries, October 2016 - September 2019

Variable (JEE Indicator)	**Beta Estimate**	**Standard Error**	**Tolerance**	**P-value**	**VIF**
Model	1.16	.30		.0001	0
D.1.3	.32	.11	.83	.005	1.21
D.3.2	.27	.07	.83	.0007	1.21
N	= 102				
Adjusted R^2	= .25				

*Note: Exact language for each JEE indicator is in Table A.
JEE = Joint External Evaluation; VIF = Variance Inflation Factor

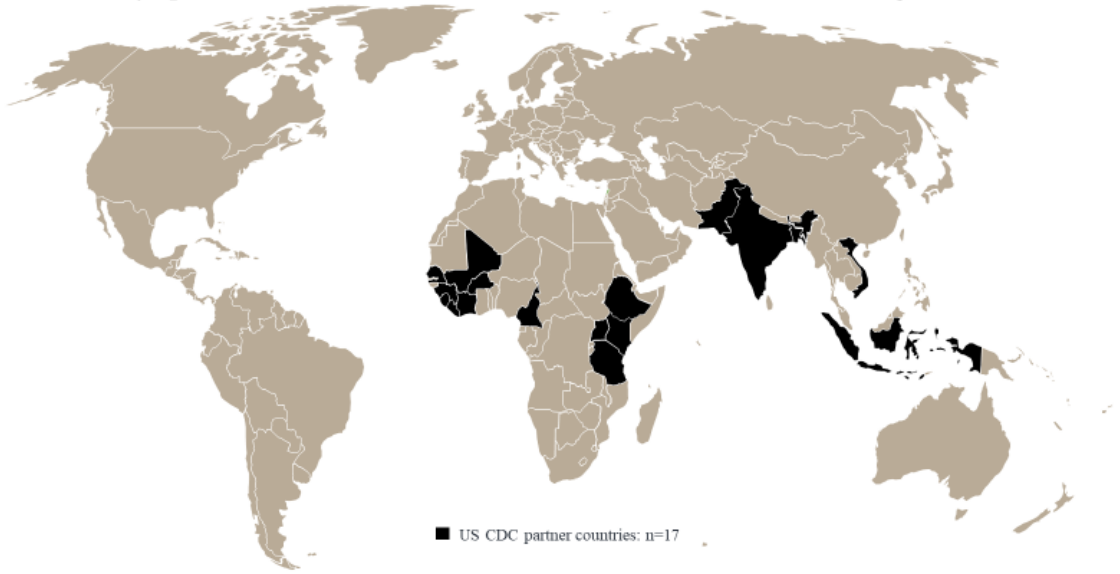
Table 4. Interaction Assessment Results for Final Multivariate Model between Explanatory Variables and the Specimen Referral and Transport (JEE D.1.2) Indicator for 17 CDC Partner Countries, October 2016 - September 2019

Variable	Beta	Std Error	Design Effect	T-value	P-value
Model	-0.09	1.03	1.45	-0.09	0.93
D.3.2	0.80	0.38	1.19	2.09	0.05
D.1.3	0.75	0.37	1.58	2.01	0.06
D.3.2*D.1.3	-0.18	0.13	1.33	-1.34	0.19
N	=102				
Adjusted R^2	=0.26				

*Note: Exact language for each JEE indicator is in Table A.
JEE = Joint External Evaluation

FIGURES

Figure 1. US Centers for Disease Control and Prevention Partner Countries used in Assessment of Laboratory Specimen and Referral Joint External Evaluation Indicator during FY 2017-2019



(Figure adapted from Tappero et al., 2017).
FY = fiscal year
17 CDC Partner Countries: Bangladesh, Burkina Faso, Cameroon, Cote d'Ivorie, Ethiopia, Guinea, India, Indonesia, Kenya, Liberia, Mali, Pakistan, Senegal, Sierra Leone, Tanzania, Uganda, Vietnam

APPENDIX I

After obtaining the parameter estimates for the crude analyses, the backwards elimination results are shown in Tables 1A-1D. Table 2 shows the variables with p-values <0.10 that were retained in the final multiple linear regression model. Table 3 shows the collinearity assessment results, and Table 4 displays the results from the interaction within the final models.

The statistically significant variables from the crude analysis were placed within the full multivariable model for further analysis. The full model is shown below and in Table 1A:

- Specimen transport and referral system (D.1.2) = 0.17 + 0.07 (Laboratory testing for detection of priority diseases, D.1.1) + 0.22 (Effective modern point of care and laboratory-based diagnostics, D.1.3) + 0.26 (Syndromic surveillance systems, D.2.4) – 0.09 (System for efficient reporting to WHO, FAO and OIE, D.3.1) + 0.21 (Reporting network and protocols in country, D.3.2) + 0.18 (Biosafety and biosecurity training and practices, P.6.2) + Ɛ.

Using a backwards elimination approach, p-values were assessed for the full multivariate model. The JEE Indicator D.3.1 (System for efficient reporting to WHO, FAO and OIE) had the largest p-value at 0.72 (Table 1A). This variable was removed from the multivariate model, and the reduced model was then assessed with the remaining five (5) variables. The second multivariate model indicated that the JEE Indicator D.1.1 (Laboratory testing for detection of priority diseases) had the largest p-value at 0.67 (Table 1B). This variable was removed from the multivariate model, and a reduced model

was evaluated with the four (4) remaining variables. A third multivariate model showed that JEE Indicator P.6.2 (Biosafety and biosecurity training and practices) has the largest p-value at 0.46 (Table 1C). This variable was removed from the subsequent model, and re-evaluated. The fourth multivariate model indicated that JEE Indicator D.2.4 (Syndromic surveillance systems) had the largest p-value at 0.17, which is greater than our statistically significant p-value of 0.10 (Table 1D). After removing JEE Indicator D.2.4, a fifth and final multivariate model was assessed.

Collinearity was assessed for the final multivariate model. Table 3 indicates that the variance inflation factors (VIF) for both independent variables are low at 1.21, and tolerance values were estimated at 0.83.

After determining the final multivariate model and running collinearity diagnostics, interactions were assessed for the final two variables (Table 4). The final multivariate model with interaction terms is shown below:

- Specimen transport and referral system (D.1.2) = -0.09 + 0.75 (Effective modern point of care and laboratory-based diagnostics, D.1.3) + 0.80 (Reporting network and protocols in country, D.3.2) -0.18 (Effective modern point of care and laboratory-based diagnostics, D.1.3) *(Reporting network and protocols in country, D.3.2) + Ɛ.

The adjusted R^2 for the full multivariate model was 0.26 (Table 1A), which is the same as the adjusted R^2 for the final multivariate model with interaction terms (Table 4). The β estimate between the interaction of effective modern point of care and laboratory-based diagnostics and reporting network and protocols in country variables was negative, at

-0.18. However, this interaction term was not statistically associated with the specimen referral and transport outcome variable, with a corresponding p-value of 0.19.