Global Health Governance: Analysis and Lessons Learned from the Ebola Virus Disease Outbreak and the Identification of Future Response Options

Group 6

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1. Background and Purpose of This Paper

1.1 Ebola Virus Disease Outbreak Across National Boundaries

The number of deaths from Ebola hemorrhagic fever, or Ebola virus disease, which spread mainly throughout three countries in West Africa (Guinea, Sierra Leone and Liberia), has reached 11,299, and the number of those infected with the virus (including suspected cases) has totaled 28,598 as of November 2015[1]. Since 1976 when the Ebola virus disease was first discovered, the recent outbreak has proven to be the most serious and complex[2].

Early on, Médecins Sans Frontières (MSF) issued warnings, stating that the "geographical expansion (of Ebola) was unprecedented" (March 2014) and "uncontrollable" (June 2014)[3]. However, insufficient attention was paid to these warnings at the 67th World Health Organization (WHO) World Health Assembly held that same year, and an international response was not developed. More specifically, it was not until August that the outbreak was recognized as a "public health emergency of international concern (PHEIC)" as prescribed by the International Health Regulations (IHR)[4]. However, by the time a PHEIC was declared, it was already impossible for the WHO to coordinate countries' efforts to control the epidemic.

Faced with such a situation, the United Nations Secretary-General initiated a response. In September, the UN Mission for Ebola Emergency Response (UNMEER) was established in accordance with General Assembly Resolution 69/1 and Security Council Resolution 2177 (2014), which would be the first mission ever to respond to a global health threat, surpassing responses executed under previous frameworks. Based on the UNMEER appeal, the United Nations, concerned international organizations, NGOs, and other partners came together to meet in Accra in October to determine how roles and operations should be divided between them. This process put in place a structure for an international response with UNMEER at the core. Previous individually-deployed responses and information were consolidated and the necessary resources secured and reallocated. Subsequently, the number of people infected decreased dramatically.

The end of the Ebola outbreak was declared on May 9, 2015 for Liberia, but a renewed outbreak was reported in November. In Sierra Leone, an end to the outbreak was declared on November 7. In Guinea, although there were reports of infected persons, numbers have stayed low.

UNMEER was closed at the end of July 2015 as its mission had ended[5]. Authority for overall management was subsequently handed over to the WHO. Currently, the international community's interest has moved on to a phase where the lessons learned from the response in the three countries are taken into account in reviewing issues that need to be addressed in how a response should be executed in future emergency situations involving health crises as well as the building of sustainable healthcare systems.

1.2 Review of Prior Research

A variety of analyses and proposals have been undertaken regarding issues brought to light in the Ebola outbreak crisis response, and how global health governance should be structured. Some of the issues that the Ebola crisis brought to the forefront are also issues that had previously been repeatedly debated about global health governance, and that were once again demonstrated tangibly. For instance, as pointed out by Frenk and Moon (2013), the inherent tension between national sovereignty and international response, the challenge posed by cross-sectoral interdependence, and the issue of the accountability of intergovernmental organizations and non-state actors were seen in this international Ebola emergency response, as well as the issue of governance deficit (Fidler, 2010)[6] as a consequence of the regime complex (Raustiala and Victor, 2004). In addition, the global delay in responding to the Ebola outbreak has also been discussed at great length, particularly in the context of the IHR recognition of a PHEIC and the issue of financing for the building of core capacities, which may be attributed to IHR's defects as have been discussed previously (Fidler and Gostin (2006), Baker and Fidler (2006), WHO (2009)).

On the other hand, this case has brought to the forefront new and unique issues. These include the importance of treating healthcare horizontally as a system, and that communicable diseases may have consequences in a variety of fields, including security.

A variety of actors are currently debating the Ebola response and reviewing the global health governance precipitated by the outbreak[7]. The has WHO set up an independent panel on the Ebola response, and the report of the WHO Ebola Interim Assessment Panel ,was released in July 2015, setting forth recommendations. Based on these proposals, various reforms have already begun being initiated (WHO Secretariat, 2015). First, concerning WHO's internal reforms, (1) the WHO presented a "A Roadmap for Action" in September 2015 (WHO, 2015c), (2) the emergency response has been discussed by the Advisory Group in order to reform the WHO's work in outbreaks and emergencies with health and humanitarian consequences, under the leadership of the WHO Secretariat Director-General and chaired by Dr. David Nabarro who is the United Nations Secretary-General's Special Envoy on Ebola (WHO Advisory Group, 2015), and (3) the effectiveness of the IHR in facilitating the Ebola response is now being assessed and debated by the Review Committee on the Role of the International Health Regulations (2005) in the Ebola Outbreak and Response.

In addition, the UN Secretary-General has established a high-level panel for the purpose of conducting a review that is not limited to the Ebola outbreak response, but that also considers global and national health governance more comprehensively. In addition, research institutions, universities, and international NGOs have conducted reviews from their own perspectives. These include a review by the National Academy of Medicine (NAM)[8], a joint initiative by Harvard University and the London School of Hygiene and Tropical Medicine (Moon et al, 2015), a review by an independent panel set up by the Bill and Melinda Gates Foundation, a review by MSF (2015), and others.

1.3 Purpose and Organization of This Paper

This study provides a broad analysis of the process of the response to the Ebola outbreak. In doing so, it identifies points that need to be addressed for global health governance reform while maintaining an awareness of what has been debated and what has not. The purpose of this study is to (1) analyze the process and issues of the Ebola response at the national and international levels, and (2) set forth lessons to be learned and present options for responding to potential future outbreaks, providing implications about the way in which global health governance should be structured. In so doing, the paper presents proposals to feed into the G7,Summit agenda, whose role in global health has continued to increase (Kirton and Mannell-G8 Research Group, 2005).

The research methods employed are principally studies of documents (primary documents,

secondary documents, academic papers, etc.) and interviews conducted both inside and outside Japan. As far as research performed overseas, interviews were conducted in July and November 2015 with relevant departments of the WHO, relevant organizations of the United Nations (UN Secretariat, UNMEER, OCHA, UNDP, UNICEF, UNFPA, etc.), the World Bank, research institutes (NAM), think tanks (Council on Foreign Relations, Center for Strategic and International Studies), the Bill and Melinda Gates Foundation, and others.

2. Analysis of the Process of the Response to the Ebola Virus Disease Outbreak

As stated at the beginning of this paper, MSF and other organizations issued several warnings early on about the spread of the Ebola virus disease. WHO could not have been unaware of these warnings (Farrar and Piot, 2014). Much criticism has been leveled at the delay in declaring a PHEIC[9], the lack of leadership (WHO Ebola Interim Assessment Panel, 2015), and other shortcomings of WHO responses[10]. As will be discussed below, issues were identified at different levels of the WHO (level of relationships among departments within the Headquarters, and level of relationships between the Headquarters and regional offices). In addition to issues pertaining to the WHO, there are also issues concerning the affected countries themselves as well as issues in the lack of utilization of UN frameworks for coordination, which are already embedded at the international and national levels. In other words, the fact is that the Ebola outbreak was the product of complicated issues intertwined among a variety of factors in a complex matter.

The subsequent analysis is from two perspectives; (1) from a spatial perspective (local and national levels, as well as regional and international levels), and (2) from a temporal perspective (the phase until a decision is made on a response, and stage of implementation of the decision made). Responses at the local and national levels are analyzed in section 2.1, and those at the regional and international levels in section 2.2. For each part, both the stage up to when a decision was rendered and the implementation stage are discussed.

2.1 Responses and Issues at the Local and National Levels

Important factors, which are related to the delays in country responses to the Ebola virus disease outbreak, include insufficient collection of information in the field and prioritization of political, economic, and social considerations over the need to respond to the health crisis. Governments worried about negative repercussions (travel restrictions, impact on trade, etc.) if they reported on the actual state of the infection and a PHEIC was subsequently declared by the WHO. The acquisition of accurate information is essential for deciding on measures to counter an infectious disease, but, as MSF found in its review, the governments of Guinea and Sierra Leone in particular were very reluctant to cooperate initially (MSF, 2015, p. 8). It has also been reported that, despite the infection having crossed the border and shifted to Sierra Leone in March, the government of Guinea did not communicate such information (Garrett, 2015).

Although there were a number of intentional factors, a fundamental major factor was the fragile health systems of the most affected countries, which were the result of not having thoroughly systematized IHR core capacity items as discussed later. Local governments and communities lacked surveillance capabilities and laboratory services. They were also deficient in terms of personnel, knowledge, and experience, and it was difficult for them to ascertain the true state of the situation. For example, the number of physicians particularly in Liberia and Sierra Leone was extremely low. According to the WHO data of density of physicians[11], for every 1000 people Liberia had only 0.014 physicians (in 2008), Sierra Leone had only 0.022 (in 2010), Guinea only 1 (in 2005), while the US and Japan had 2.452 (in 2011) and 2.297 (2010) respectively.

At the stage when the response was executed, many of the already insufficient numbers of

health workers had fallen victim to the infection, which made the response even more difficult. The spread of this disease led to 881 people becoming infected and 513 dying in three countries in West Africa (as of September 2015). Also, the lack of laboratories within these countries held up prompt determination of the infectious disease and also hindered efforts to trace people who had come into contact with the infection. It has also been pointed out that because the initial contact tracing for Guinea was insufficient, it allowed further spread of the infection (Briand et al, 2014). Furthermore, what made the response even more difficult during the implementation stage was a lack of active cooperation at the local level, a scope that encompasses local governments and communities. The continuation of civil war had developed a strong distrust of the government (Piot, 2014), and that hindered the engagement of local communities, which the government as well as international institutions—MSF and other outside aid organizations—were attempting to promote. Moreover, aid organizations in some cases were even frequently attacked.

UN Country Teams (UNCT), which were in each country, could have strengthened the response at the national level. In fact, the UN as One framework was not completely absent. Within the United Nations Development Assistance Framework (UNDAF), under the overall lead coordination of the Resident Coordinator, it would have been possible to coordinate the health sector to strengthen a response under WHO leadership. Coordination was also considered using the health cluster led by the WHO under the overall coordination of the Humanitarian Coordinator of OCHA, which has a responsibility within the framework of the Inter-Agency Standing Committee (IASC) for coordinating emergency assistance regarding international humanitarian issues resulting from natural disaster and conflict[12]. Nevertheless a sufficient response was unable to be meted out through these frameworks.

The main factors were the small WHO presence in such frameworks, insufficient leadership by Resident Coordinators, absence of any switch from Resident Coordinators to Humanitarian Coordinators, and the failure to develop responses employing liaisons among existing field institutions to form an organic network. Particularly, at the beginning, there was also a lack of awareness within the humanitarian community. The number of people infected with Ebola virus disease initially, according to the humanitarian community, was not considered to be so large that it could be called a state of emergency (WHO Ebola Interim Assessment Panel, 2015, para.71). Furthermore, Resident Coordinators prioritize issues from the perspective of development, while OCHA and Humanitarian Coordinators from a humanitarian perspective, and an Ebola virus disease response from the perspective of health was not their priority. In addition, it has also been pointed out that the Resident Coordinators in the three countries were not able to make such a determination because sufficient information was not provided by the countries or by the WHO.

2.2 Responses and Issues at the Regional and International Levels

2.2.1 WHO: Issues Pertaining to the Regional Office for Africa (AFRO), the Relationship Between AFRO and Headquarters, and Factors within Headquarters)

The factors that led to the delay in the WHO's international response include problems with the Regional Office for Africa (AFRO), insufficient coordination between AFRO and WHO Headquarters, and factors within the WHO Headquarters itself.

(1) Issues Concerning AFRO Capacity and Insufficient Coordination between AFRO and Headquarters

When one considers that the Western Pacific Regional Office (WPRO) played a significant role during the SARS epidemic (Omi, 2011), the role played by AFRO in failing to contain the infection in the region cannot be ignored. Among the factors cited as contributing to AFRO's malfunction are a shortage of human resources and budgetary limitations. There were not even

10 personnel in AFRO's department handling emergency responses at the time and it had also been limited by budget cuts in recent years. It has been pointed out that AFRO's functions for surveillance and support of countries where outbreaks of infectious diseases occur did not function adequately (WHO Ebola Interim Assessment Panel, 2015, para.45). Furthermore, roughly 80% of the staff had been hired from within the African region[13], and the majority were technicians employed in the field known as national professional officers (NPO), so they maintained a cohesive and closed structure with the governments of their home countries.

In addition, the insufficient working relationship among the affected countries, AFRO, and WHO Headquarters was presumed to be one of the factors that delayed the response. It has long been pointed out that insufficient coordination between the Headquarters and regional offices has hindered the WHO's effectiveness (Lee 2009, p.33)[14]. Regional offices are highly independent and operate based on rules under an organizational structure that is unique to their respective regions.

On July 24, 2014, the Sub-regional Ebola Operation Coordination Centre (SEOCC) was established with AFRO at the core to serve as a platform supporting countries in West Africa where the infection had developed. This was a framework in which not just the WHO, but also OCHA, WFP, UNICEF, the Centers for Disease Control (CDC), and other organizations participated. However, in mid-August, an initiative at the UN Headquarters in New York was launched, and the SEOCC with AFRO at its core no longer played a central role. The SEOCC was consequently closed down with the establishment of UNMEER (WHO Ebola Interim Assessment Panel, 2015, para.80, 81).

(2) Issues of Coordination and Gaps in Information and Recognition Inside the WHO's Geneva Headquarters

The following points have been indicated as factors causing a delay in the initial response as well as a delay in PHEIC declaration by the WHO Headquarters in Geneva.

First, information was insufficiently communicated due to insufficient implementation of IHR monitoring on account of a lack of human and budgetary resources. The budget for IHR implementation was reduced by approximately 50% following worldwide economic stagnation resulting from the 2008 financial collapse[15]. It has been pointed out that at the end of April when figures of infection temporarily trended downward, foreign aid was withdrawn based on a mistaken understanding by the CDC that the situation was under control (Garrett, 2015), but this might have been prevented if there had been more robust surveillance systems at the local and national levels.

Second is the gap between the role as perceived by the WHO Director-General, and the role that the international community demanded of WHO, as well as the lack of leadership exercised during the emergency. As symbolized by the criticism (Gostin, 2014 and others) of the WHO Director-General's statements that the "WHO is a technical agency" and "governments have the primary responsibility" (New York Times, 2015), there was a discrepancy between the role that the international community expected of the WHO and the WHO's own perception of its role. Clearly, even though it is correct that the countries should have primary responsibility, there was room for the WHO to exercise leadership based on information provided by third parties such as MSF. At the Global Outbreak Alert & Response Network (GOARN) meeting held in July, MSF pleaded for an immediate international response, but it was not taken seriously (MSF, 2015, p.8)[16]. This delayed the timing for convening an IHR committee meeting and declaring a PHEIC.

Third, there was a negative perception of the declaring of a PHEIC within the WHO. Specifically, issuing a PHEIC was (1) considered a last resort (Garrett, 2015) because there was concern that it would impose de facto restrictions on the target country[17], (2) there were concerns that intervention would be seen as interference in the domestic affairs of a sovereign state,, and, moreover, (3) there was hesitation on account of criticism that had been leveled in the past about the H1N1 response[18], which was the first PHEIC case, that it was an overreaction

by WHO. Such factors were present in the background and are thought to have delayed the PHEIC declaration. In addition, the fact that there were no intermediate means for adopting a full-scale international response prior to invoking a PHEIC is considered to have significantly contributed to the delayed response.

One issue in terms of internal coordination within WHO Headquarters during the implementation stage is the coordination exercised among different departments. As the WHO itself has also acknowledged, the systems which handled health security and humanitarian issues operated separately (WHO Secretariat, 2015, para.17). Actually, coordination between the department for health security (IHR, GOARN), department for humanitarian and emergency responses (polio, FMT[19]), and department responsible for the long-term building of health systems did not function well initially.

Specifically, there were two broad frameworks for physicians active in the field: (1) GOARN and (2) FMT (Foreign Medical Team). Within the WHO, the departments handling these teams were different. GOARN has been set up for the main purpose of responding to infectious diseases and the WHO serves as its secretariat. It is a network of partner organizations. Many of the staff dispatched are technical personnel and they have been effective in responding to SARS and other outbreaks in the past (Mackenzie et al (2014)). It was set up in the Department of Global Capacities Alert and Response (GCR). On the other hand, FMTs have been established in the Emergency Risk Management and Humanitarian Response Department that mainly deals with trauma-related disasters due to natural or human-induced factors (Burkle, 2014). The reason why collaboration was difficult between these departments within the WHO needs to be further explored, however, it is conceivable that the heads of the respective departments did not communicate or that there were delays made in issuing decisions and instructions by supervisors in both departments. In order to solve the above problems, in recent organizational restructuring, these two departments were merged into one cluster.

2.2.2 Coordination within the UN Family

There was initially a search for the possibility of utilizing existing frameworks to coordinate in the field when a response began to be considered by the UN Secretariat.

If a response had been initiated earlier, it might have been possible for Humanitarian Coordinators supported by OCHA to be dispatched under the IASC framework. However, because intervention was called for after the situation had acutely worsened, and because the Ebola virus was disease that the humanitarian community was unfamiliar with the handling, it was determined that a response would be difficult using the cluster approach with OCHA at the core. In addition, rapid access to a large amount of funding was imperative at that time, but that would have been difficult using OCHA's usual funding process. It was also considered that more time would be required to form a consensus to agree to use the Central Emergency Response Fund (CERF) for the Ebola virus disease response, which is a use that is different from ordinary natural disasters and armed conflict.

In the ultimate response to this situation (that is to say, September 2015), a recognition was broadly shared that the establishment of UNMEER could be justified based on the UN Secretary-General's initiative to mobilize resources, procure funding, and coordinate UN organizations in a top-down manner over a short period of time[20].

However, this is not to say that there were no issues to be addressed in the UNMEER response. More specifically, (1) the construction of a new organization gave rise to problems such as coherence and overlapping issues with the aforementioned existing frameworks (overlapping with OCHA and the UN Development Group coordination frameworks present at the international level, as well as with Ebola response frameworks established by national governments, etc.). (2) Initially, because the operation was conducted in a top-down manner and emphasized military-like logistics, there was also confusion from the field (comments were voiced that cultural factors in the field should also have been emphasized). (3) Although UNMEER made it possible to take swift action with a clear division of labor, time was also

needed until the process began to operate substantively (it was in October when the Accra meeting was held that the division of responsibilities among international organizations was completed and substantive deployments initiated).

The above analysis shows that the factors resulting in the delayed response to the Ebola virus disease, leading to a more serious situation, were issues pertaining to coordination and issues involving gaps in information and perception among a variety of actors at a variety of levels intertwined in a complex manner.

3. Response Options for Global Health Governance

Taking into account the above analysis of the process of responding to the Ebola outbreak, the following response options along two broad topics are proposed. One is strengthening the capability to respond during an emergency and the other is strengthening health systems during ordinary times. The success of emergency responses depends on the health system, which ensures that information is collected and responses implemented during ordinary times. The systematic infrastructure for collecting information for an emergency response as well as for responding to it can be also utilized during ordinary times. In addition, increasing the efficiency of emergency responses spares resources and allows for expanded access to be secured within a health system during ordinary times. In that sense, these two topics are closely related. Below, response options related to these two topics from three perspectives are presented: (1) strengthening organizational capabilities (improving capacity), (2) strengthening coordination among organizations, and (3) strengthening frameworks for procuring funding.

3.1 Strengthening Response Capabilities During an Emergency

3.1.1 Strengthening Organizational Capability

(1) Construction of Frameworks Enabling Progressive Stages of Response and Systems for Collecting Information

As indicated in section 2.2.1, one factor leading to a delay in the response was that there was no intermediate stage between ordinary times and a PHEIC. PHEIC determination was a clear choice between two alternatives, and there was no framework allowing for progressive stages of response. In order to execute progressive stages of response, (1) the construction of a framework for making progressive determinations about the situation, and (2) strengthened capabilities to gather information to support such judgments are required.

With regard to (1), multiple stages need to be established to allow for progressive stages of response between the current PHEIC and non-PHEIC situations[21]. In the IHR, there is a provision (Article 8) that consultations with the WHO on appropriate measures may be conducted through the National IHR Focal Point even for information not required to be reported, particularly for events for which there is insufficient information available to complete a decision on whether it constitutes a PHIEC. Such a provision should be utilized to build an operational framework for collecting a broad range of information and making stage-based situational determinations. It is also important to strengthen the WHO's risk assessment capability and staffing to allow for the operation of such framework. However, care needs to be taken so that the criteria for judgments can operate with some flexibility.

With regard to (2), the IHR (2005) allows for the use and analysis of information sourced not only from countries, but also from other sources (Article 9.1) including international institutions, non-state actors, and a variety of entities. This was the strategy to overcome two potential limitations of surveillance under the IHR (1969): inadequate capacities at the local and national levels to fulfil surveillance, and government reluctance to comply for fear of the adverse consequences of reporting (Baker and Fidler, 2006, p.1062). However, such WHO authority and capabilities are not sufficiently utilized. Pursuant to this provision, the WHO

should consider the development of a mechanism for collecting a broader range of information to adopt necessary measures, including in cases where there may not be a clear indication of a PHEI and also from a variety of sources that are active at the grassroots level, such as MSF.

In all of the above-mentioned judgment stages, it is also fundamental to acknowledge that the governments and leaders of the countries concerned have the primary responsibility and should play a leading role. Such an awareness must be sought to be improved.

(2) Strengthening Organizational Capability to Respond to Diverse Situations: Provision of Flexible and Integrated Programs

In this response to the Ebola virus disease outbreak, operations were deployed on a large scale in both the emergency disaster and humanitarian community, and the health security community. However, unlike in the case of the Polio response in which both communities collaborate on a daily basis, there were no routine procedures and protocols for the Ebola response. Cultural and organizational differences between the two surfaced, rendering cooperation difficult. A system is needed that allows for stage-based and flexible collaboration in responding to a variety of situations as has been discussed above.

The need for an integrated program for emergencies was recognized and a decision was made to establish such a program at the 68th WHO General Assembly in 2015. The proposal of an Advisory Group on Reform of WHO's Work in Outbreaks and Emergencies is in line with this direction (WHO Advisory Group, 2015)[22]. The WHO appears to have adopted the direction of organizationally bringing together humanitarian and health security communities. In many review reports, differences between humanitarian and health security communities have been highlighted and there has been much debate calling for strengthened coordination and merging of the two (for example, the WHO Ebola Interim Assessment Panel, 2015). The WHO secretariat is now reviewing a variety of framework liaisons such as GOARN and FMT, which have previously been handled by separate departments, to be merged into one cluster. It may be worthwhile to note that at the regional office level, for example in the case of WPRO, both humanitarian and health security departments are dealt with under the Division of Health Security and Emergencies.

However, whether or not organizational merging of two different departments by itself constitutes a sufficient solution requires further analysis. Cooperation and coordination among departments is of course important, but it is also true that each has their own legitimate purpose and functions. The issue is to operate in such a manner that collaboration can be carried out in response to circumstances in a way that makes use of their respective merits. It is important that a variety of tools be available during times of emergency. Training and something along the lines of a set of protocols and manuals for interaction are needed to enhance the ability to collaborate and coordinate.

3.1.2 Ensuring Cross-Sectoral Coordination and Cooperation Among International Organizations According to Situational Categories

Every emergency occurs under different conditions, and coordination and cooperation are required based on each circumstance. As a result, the coordination and cooperation necessary differs depending on the type of situation. A "switch function," which enables the change of the lead agency of coordination and cooperation in response to a situation is critical in the utilization of situation and stage-based framework.

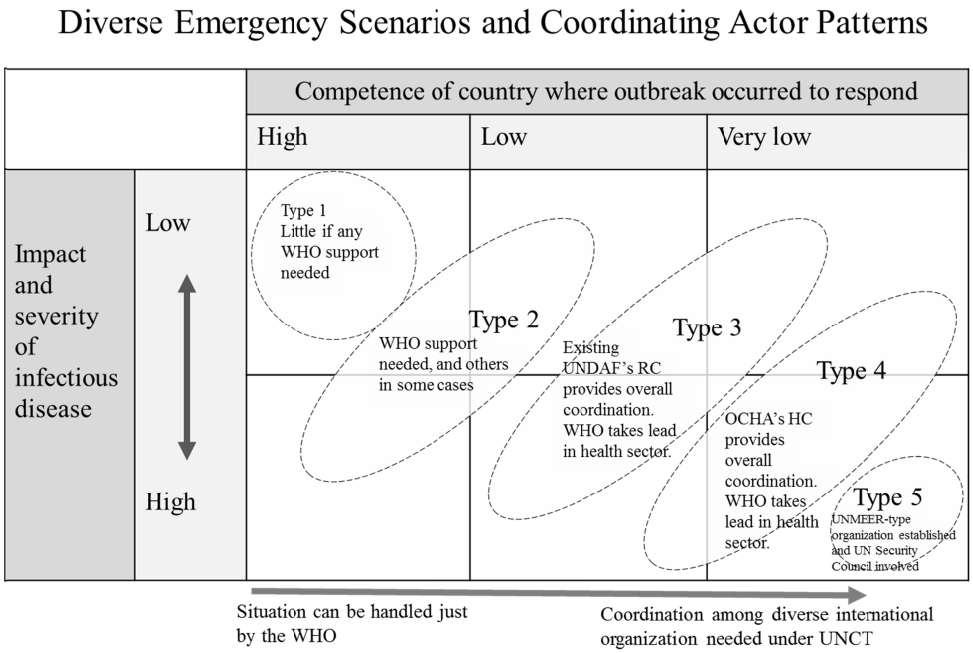
(1) Diverse Situational Categories for Emergencies and Patterns of Coordination and Cooperation

As seen in section 2.2.2, there is a clear necessity for developing situation-based flexible partnerships for coordination and cooperation among international institutions (relationships

between WHO and the humanitarian community in the field, development community, security community, etc.). Clearly, the WHO is the only actor that can perform the central leading role in providing technical and medical recommendations concerning a health crisis, and there is no doubt about this. However, as was evident in the lessons learned from the Ebola outbreak, health crises often entail situations that cannot be dealt with by just providing technical knowledge, guidelines, and a limited deployment of technical and medical experts. Consequently, diverse international emergency situations need to be anticipated and diverse patterns for coordination and cooperation among international institutions for each situation need to be prepared.

The patterns of coordination and cooperation differ depending on the competency of the affected country and the type of infectious disease. Therefore, as to the question of who should develop what sort of initiative at the international level, the following options can be considered depending on situational categories which are based on (1) the capability of the country where an infectious disease outbreak has occurred requiring the response, and (2) the type of infectious disease (scope of impact and magnitude of severity).

Table. Coordination Patterns by Situation-based Typology



Type 1 cases, in which the country where the outbreak has occurred maintains a high response competency and the degree of severity of the infectious disease and the scope of its impact are low, responses may be handled by the country concerned with minimal support from the WHO. In Type 2 cases, the country and the WHO are central in handling the situation, and support from organizations other than the WHO may also be necessary in some situations. In Type 3 cases, under the existing UNDAF framework, the Resident Coordinator provides overall coordination, within which the WHO leads the health sector and a response is extended while obtaining the cooperation of a variety of international organizations of the UNCT. In Type 4 cases, there is a greater sense of urgency and more humanitarian elements are required than afforded by development frameworks for ordinary times. In these cases, a framework is implemented in which OCHA deals with the humanitarian crisis, and the Humanitarian Coordinator exercises overall coordination under an IASC framework where the WHO plays a central role in leading the health cluster. Lastly, Type 5 cases are those where it is determined that a response is beyond OCHA or other existing frameworks' capabilities and are handled by

establishing a new organization through the strong political initiative of the UN Secretary-General to serve as a measure to counter the infectious disease, such as UNMEER in the case of the Ebola virus disease. Moreover, in cases where serious crises are dealt with, it is also conceivable that a UN peacekeeping operation (PKO), military, or other security maintenance organization in the security community may also be utilized. In the present case, a resolution was passed by UN Security Council to endorse the establishment of UNMEER, and it had the advantage of being effective in heightening awareness of the international community because of its binding power and high political importance. If the approach (top-down logistical approach that restricts state sovereignty to a certain extent) taken by the Department of Field Support (DFS), which is in charge of PKOs, is implemented successfully, a quick and efficient response may be executed. However there are also elements that place the operation in a tense relationship from the perspective of democracy. Outbreaks classified as Type 5 are extraordinary cases and the establishment of a new permanent organization is not desirable. It is important that cases be dealt with using organizations for limited periods with clear mandates. It should be noted that UNMEER, which was responsible for the Ebola response, was disbanded after having achieved its mission, and the subsequent authority to coordinate the overall response has been handed over to the WHO Director-General.

(2) Coordination and Cooperation Issues to be Considered and the Person Responsible for the "Switch Function"

The following two points must be emphasized. First, an issue in terms of operation in the cases of outbreak types 3, 4, and 5 is that coordination and cooperation between the health security community and the humanitarian community are important because the objectives, subjects, and organizational culture differ for each community. The issue of coordination between the humanitarian and health security communities is present not just within the WHO, but also in relationships between the WHO and other organizations within the UN system, working together in the health sector or in clusters.

Second, because circumstances may change, the necessary patterns of coordination and cooperation need to be continuously reassessed based on changing situational categories. For example, there is continuity in changes of circumstance that necessitate a switch from Type 3 to Type 4 (switching includes personnel from ordinary times to emergency mode). Accordingly, it is important that there be a "switch" that alters the patterns of coordination and cooperation discontinuously by taking into account ongoing circumstances. Particularly in cases where a coordinating entity is already present under an existing framework such as a UNCT Resident Coordinator, it is necessary to allow for honorable replacement with a Humanitarian Coordinator or a new coordinating entity such as UNMEER. For this reason, it may also be necessary to prepare in advance a protocol that enables smooth switches. Ultimately, the person responsible for the "switch function" should be the UN Secretary-General under the leadership of the UN headquarters based on a comprehensive determination.

3.1.3 Building Financing Mechanisms for Procurement During Times of Emergency

In order to make timely responses, it is necessary to have in place a financial mechanism that is readily available. However, the absence of any framework for procuring funds to be used immediately during an emergency in the health sector contributed to the delayed response. Existing organizations such as OCHA depend on voluntary contributions, so budgeting takes time, and the delayed response was also one of the reasons for establishing UNMEER to be led by the UN Secretary-General following resolutions of the Security Council and the General Assembly.

Such problems in responding to the Ebola outbreak were taken up at the 68th WHO General Assembly in 2015 where it was agreed that a USD100 million Contingency Fund for

Emergencies (CFE) would be set up within WHO. The disbursement of CFE funds is at the discretion of the WHO Director-General, and the building of a fund that can be immediately mobilized is indispensable for timely responses during emergencies[23]. However, this was designed for only three months worth of expenses required for deploying WHO staff. In addition, the possibility has also been pointed out that this amount may not even be sufficiently secured from member countries. Accordingly, other funding frameworks and tools need to be prepared.

As a mechanism for supplementing the CFE, the discussion led by the World Bank to establish a Pandemic Emergency Facility (PEF) underway is important, as it is a financing mechanism including the involvement of private insurance. The budget scale of the PEF is still under discussion at the World Bank, but it is estimated to be approximately USD 500 million. In its actual design, there is the issue of the trigger parameters, which are the criteria for providing funding. More specifically, (1) there is the issue of timing for PEF intervention and (2) the issue of the criteria for disbursement (for private insurance to get involved, criteria based on quantifiable data is a prerequisite, but such data is not always available particularly in the early stages of health crises). First, concerning (1), the issue is that if the payment is to take place too early, then there is an increased likelihood that multiple payments may have to be made, which makes the insurance rate higher; but if the payment is to be made too late, then the payment amounts increase while the insurance rate might become lower. Second, concerning (2), in case where data is unavailable for private insurance payouts, a pool of funding by donors may be needed where a certain degree of discretion is permissible under the World Bank, separate from the amount afforded by private insurance. In addition to the CFE and PEF, OCHA's CERF may also be utilized if the situation is determined to be a humanitarian issue. So, in addition to the relationship between CFE and PEF, the interrelationship between these and the CERF also needs to be considered.

Furthermore, there is the issue of how to build a financing mechanism for researching and development, for example vaccines during times of emergency. As the case of the recent Ebola virus disease outbreak showed, when responding to infectious diseases, existing vaccines and other such technology need to be dispersed throughout society, but research and development on new technologies, such as new vaccines was also needed. This point has also been recognized in the WHO's Roadmap for Action (WHO, 2015c). An option for the future is to have such research and development make use of the vitality of the private sector and have more diverse public-private partnerships (PPP) constructed[24]. For example, the Global Health Innovative Technology Fund (GHIT Fund) is one such effort in the upstream stage of development. A framework is needed to connect such upstream research and development funding with downstream activities such as the broad distribution of existing vaccines.

In Alignment with such diverse funding frameworks, as discussed in sections 3.1.1 and 3.1.2, a financing mechanism should be built that allows for rapid and timely disbursement without any gaps or discontinuities so that funds may be provided that will enable situation and stage-based responses during times of emergency.

3.2 Strengthening Health Systems During Ordinary Times

It is important that health system strengthening during ordinary times be supported so that an early warning may be signaled to prevent outbreaks before they happen. Also, information collection and systematic infrastructure for responding during emergencies to specific infectious diseases can be utilized by the health system during ordinary times as well in a cross-sectional manner to address diseases. Therefore, it is important that the governance structure and design of response measures in times of emergencies be closely linked to reinforcing the health system during ordinary times.

3.2.1 Strengthening IHR Core Capacities

(1) Strengthening IHR Implementation at the Country Level

In order to respond to infectious diseases, it is necessary that the IHR core capacities be built up in countries when strengthening a health system. Currently, in AFRO, not one country has completed implementation of building the minimum core capacities for IHR (WHO AFRO, 2015). Of the eight IHR core capacities[25], it is particularly essential that surveillance, human resources, and laboratory services be strengthened and built so that stage-based decisions may be made about situations. Along with a framework seamlessly linking a variety of levels (communities⇒local governments⇒countries⇒regions⇒international), partnerships also need to be created with the private sector to strengthen surveillance, laboratory services, and human resources. It is necessary that the range of information to be reported be expanded (a surveillance system needs to be reconsidered so that not just cases where there is concern about PHEIC, but also events spanning a variety of alert levels, are ascertained).

(2) Strengthening Responses at the Regional and International Levels for IHR Implementation in Countries

In order to strengthen IHR implementation at the country level, responses at the following such regional levels must be enhanced. First, there is the need for the augmentation of WHO regional offices. In order to build up staffing, as WPRO has done, it is important that "truly international" staff be employed based on an ability to ensure diversity and capabilities. To achieve this, reforms may be necessary, for example, that impose an obligation on all regional agencies to hire on the basis of ability a certain percentage of their staff from outside the region. However, this does not mean that the independence per se of regional offices is bad (during the SARS response, WPRO's discretion enabled early containment). Also, verification of effectiveness of strategic frameworks, for example WPRO's Asia Pacific Strategy for Emerging Diseases (APSED) and AFRO's Integrated Diseases Surveillance and Response (IDSR) in IHR implementation, which have already been launched by regional agencies, also appears to be needed.

Second, regional monitoring must be strengthened (for example, the establishment of a version of the CDC for the Africa Union (AU)[26]). These activities need to be linked with actors other than those in the public sector. Public-private partnerships (PPP) are particularly important for the utilization of information (challenges include how to effectively absorb information from activities conducted by MSF and others at the regional and grassroots level) and for strengthening preparedness at the local level (training on responding to disasters)[27].

At the international level, departments within the WHO concerned with health security need to be strengthened. Current debate is focused on coordination between departments involved with emergencies and humanitarian issues, and those concerned with health security, but if continuity between times of emergency and ordinary times is taken into consideration, then it is also important to rank the strengthening of IHR core capacities as one element of strengthening health systems in so as to ensure coordination between health security departments and health system departments.

3.2.2 Coordination Among Diverse Organizations Laterally Supporting IHR Enhancement

It is considered necessary to build a cooperative framework such that organizations and frameworks besides the health sector directly and indirectly support IHR enhancement.

As a condition for building a cooperative framework, it is necessary to recognize that the IHR is based on an "all hazard" approach. The commitment of organizations in a variety of fields, such as development, trade, disaster prevention, and security, are needed for an all hazard

response. To ensure such a commitment from a diverse range of organizations, it is necessary to have commitment not just at the level of the health minister, but also from the top national level.

As WHO presence at the country level is not necessarily sufficient, it is difficult for the WHO to play a direct role in the enhancement and monitoring of IHR implementation in all countries. It is important that international organizations active in the field such as UNDP and UNICEF acknowledge that the building up of IHR core capacities contributes to overall strengthening of the health systems of developing countries, and play the role of monitoring whether the IHR requirements of core capacities are met.

In addition, there is the issue of what to do about measures involving unnecessary trade restrictions that may potentially be adopted by neighboring countries when a certain country reports information that may constitute a PHEIC. With regard to this, a framework may be strengthened to check the appropriateness of measures under the IHR, and coordination may be pursued with actors in other sectors such as World Trade Organization (WTO)[28]. The WTO's Sanitary and Phytosanitary (SPS) Agreement states that when national standards are adopted that are stricter than international standards, the national standards must be scientifically justified. For example, in the case where Europe instituted trade restrictions during a cholera outbreak in Africa, the WTO's SPS Committee deliberated the restrictions including a scientific debate on the risk these measures pose to public health, which resulted in the trade restrictions being lifted (WHO and WTO Secretariat, 2002).

Moreover, it is possible to embed functions supporting IHR core capacity construction into new systematic frameworks for emergency responses. For example, with the PEF, imposing IHR implementation as an insurance term can promote domestic implementation of IHR and necessitates an evaluation of IHR implementation by third-party assessment for insurance premiums, thereby ensuring transparency in implementation and incentivizing IHR implementation in developing countries. However, because the payment of funds is contingent on damage, there remain concerns that moral hazards may arise in which the weaker a country is (with insufficient IHR implementation), the easier it will be to receive funds in the end.

In addition, it is also important that there be coordination among frameworks for aid and cooperation from the perspective of security, which has been developed bilaterally and multilaterally. Collaboration with initiatives such as the Global Health Security Agenda (GHSA) is also possible. The GHSA is a multilateral framework led by the United States, which has stated that it will achieve its goals in a minimum of 30 countries over the next five years, and has declared that it will invest USD1 billion in 17 countries toward this effort. The United States has called for donor countries to participate in the GHSA, and at the G7 Summit in 2015, it was agreed that aid would be provided to 60 countries overall, including countries in West Africa[29]. Although the countries targeted are limited, this initiative can contribute to rapid build-up of IHR core capacities. The merit of this kind of initiative is that it has a strong political commitment from the perspective of security and is useful for bridging the gap with issues that are not able to be carried out under existing frameworks. However, on the other hand, the demerits include dependence on political momentum, and the challenge of institutionalization to extend such efforts sustainably.

3.2.3 Building a Comprehensive Funding Framework for Health Systems

It is also important that the World Bank coordinate not only with emergency response frameworks such as the PEF, but also with aid frameworks for ordinary times implemented by the International Development Association (IDA). Funding frameworks that mainly specialize in specific infectious diseases, such as the Global Fund to Fight AIDS, Tuberculosis and Malaria (GFATM) and Gavi,-the Vaccine Alliance, may also be utilized. For example, although GFATM's targets are limited, one-third of its expenditures support comprehensive and horizontal elements such as the strengthening of health systems(GFATM 2015), and it is also conceivable that such allocations may be extended through links with funding frameworks that support health systems through other horizontal elements.

There are multiple options for actors to lead initiatives pertaining to strengthening systems for comprehensive funding frameworks. Such efforts may be addressed by the World Bank or led by the GFATM, which currently has a large amount of funding designated for specific infectious diseases. Or, these efforts may be undertaken by the UNDP, which has a significant presence in the field in developing countries, and divisions may also be established concerning health systems mainly for strengthening IHR core capacities in frameworks for health aid collaboration such as the International Health Partnerships (IHP)+, which aims to coordinate aid in the health sector for the purpose of coordinating a variety of initiatives. It is also possible to strengthen coordination with security policies.

4. Future Challenges

This paper presented issues to be addressed and lessons learned based on analysis of the process of the response to the Ebola virus disease outbreak, and proposed options for addressing global health governance.

Currently, international interests and assessments appear to be focused on improving organizational coordination between health security and humanitarian aid, which is necessary for responding to infectious diseases such as Ebola, and on the necessity for the general strengthening of health systems. However, the focus on improvement of organizational coordination has been narrowed down to mainly improvements within the WHO, and consideration needs to be given to issues related to organizational coordination across the entire UN system, including OCHA and UNDG members.

Also, it is important that responses to such specific infectious diseases are positioned within cross-sectional and comprehensive reinforcement of health systems, which makes such monitoring possible, and are linked to strengthening health systems in countries as well as to universal health coverage (UHC). Generally speaking, an emergency response depends on the health system employed during ordinary times, which provides the systematic infrastructure for information collection and response. On the other hand, the systematic infrastructure for information collection and response that is developed for use in emergency response can also be able utilized during ordinary times. Furthermore, improving the efficiency of emergency responses allows for resources to be secured to expand access to health systems during ordinary times. However, the paths for undertaking such linkages differ depending on the country. On this point, Japan is able to play a significant role on account of its experience in realizing UHC in responding to a variety of infectious diseases, such as tuberculosis.

In addition, the debate over funding is currently focused on vertical funding mechanisms in the sense of being for emergencies and specific infectious disease. However, if the issue of global health governance is understood from a long-term perspective, what is important is how to construct a comprehensive and horizontal funding mechanism. For example, the GFATM maintains a set allocation for responding to specific infectious diseases, but it has begun to expand that scope by strengthening horizontal aid for health systems. It is necessary to promote such moves encouraging vertical funding mechanisms to employ horizontal funding elements.

Although it has been discussed in the debate over PHEIC, a point that has not been sufficiently delved into is the issue of constructing mechanisms for collecting information about events that occur at levels below PHEICs and how to control the unnecessary restrictions on trade or in other areas. With regard to these, further research is necessary as to whether the IHR needs to be revised, whether it needs to be adapted in terms of operation, or whether considerations are needed with other systems such as funding frameworks or the WTO. In addition, the importance of the UN Secretary-General and the Chief of Staff at the UN Headquarters as the people responsible for the “switch function” from ordinary times to emergencies that involves a change in leadership roles where an event develops past a certain stage was recognized, but the remaining issue is how to institutionalize such mechanisms at the international level.

Furthermore, responses must also be considered in line with specific scenarios in cases where an outbreak occurs not in a vulnerable country such as where the Ebola outbreak spread, but, for instance, in big countries in Asia such as China and India, where pandemics develop due to a different infectious diseases (airborne diseases or something more contagious). The table in section 3.1.2 needs to be utilized to review a variety of stage-based response modes in keeping with the terms of global health governance by conducting reviews on the capacity to respond to specific infectious diseases at multiple levels (national, regional and international) in coordination with the situational categories based on the competence of the country (high or low) where the outbreak has occurred and the type of infectious disease.

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Public-Private Partnerships for Strengthening Global Health

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Overview - Challenges in Global Health Governance

Based on lessons from the responses to the Ebola outbreak, group 6 will assess the global health governance landscape in order to identify major challenges that require new thinking and reform in the governance structure. Authors will analyze recent trends and propose areas of reform needed to respond to changing needs and priorities in global health and health security, with a focus on the role of Japan and the G7.

Major questions

- What are the recent trends of public sector involvement and public-private partnerships (PPPs) in the area of global health?
- What are the lessons learned to effectively respond to disasters and how can global health incorporate them in order to create a resilient governance structure?
- How can the private sector contribute to develop a strengthened governance structure in the area of global health?

Additional questions

- What are the options for PPPs for R&D during an emergency (the Partnership)?
  - Structure : What is an ideal structure for the Partnership? How will the Partnership work with WHO and its internal reform?
  - Style: What kind of leadership is needed for the Partnership?
  - Skill: What kind of core competencies is needed for the Partnership?
  - Staff: What are the motivations and incentives for the Partnership members?
  - Shared value : What should be the vision and mission of the Partnership?
  - Strategy: How does the Partnership prioritize R&D issues? What does the Partnership develop strategies?
  - System: How does the Partnership share the materials (pathogens, etc) and results of the R&D outcomes?
  - Size: What is an ideal level of funding that the Partnership manage - is US$ billion enough or not? If not, why and what is an ideal level?

1. Introduction

1.1 Drastic changes in the global health community

Over the last few decades, the landscape of the global community has changed dramatically.

The range of issues has become more diverse, particularly with the proposed transition from 8 Millennium Development Goals (MDGs) to 17 Sustainable Development Goals (SDGs). The number and variety of players has increased to include not only the United Nations (UN), recipient and donor governments, and civil societies, but also emerging governments and the private sector, including business. The level of funding for all areas of development has increased sharply, from US $58.5 billion in 1990 to US $150.4 billion in 2013 [1], and development assistance for health (DAH) has quintupled in the same period [2]. Finally, approaches to tackling health problems have also become diversified – from traditional funding, to innovative financing mechanisms such as IFFIm and World Bank Green Bonds, to various initiatives like PEPFAR, the Muskoka Initiative, and Malaria No More.

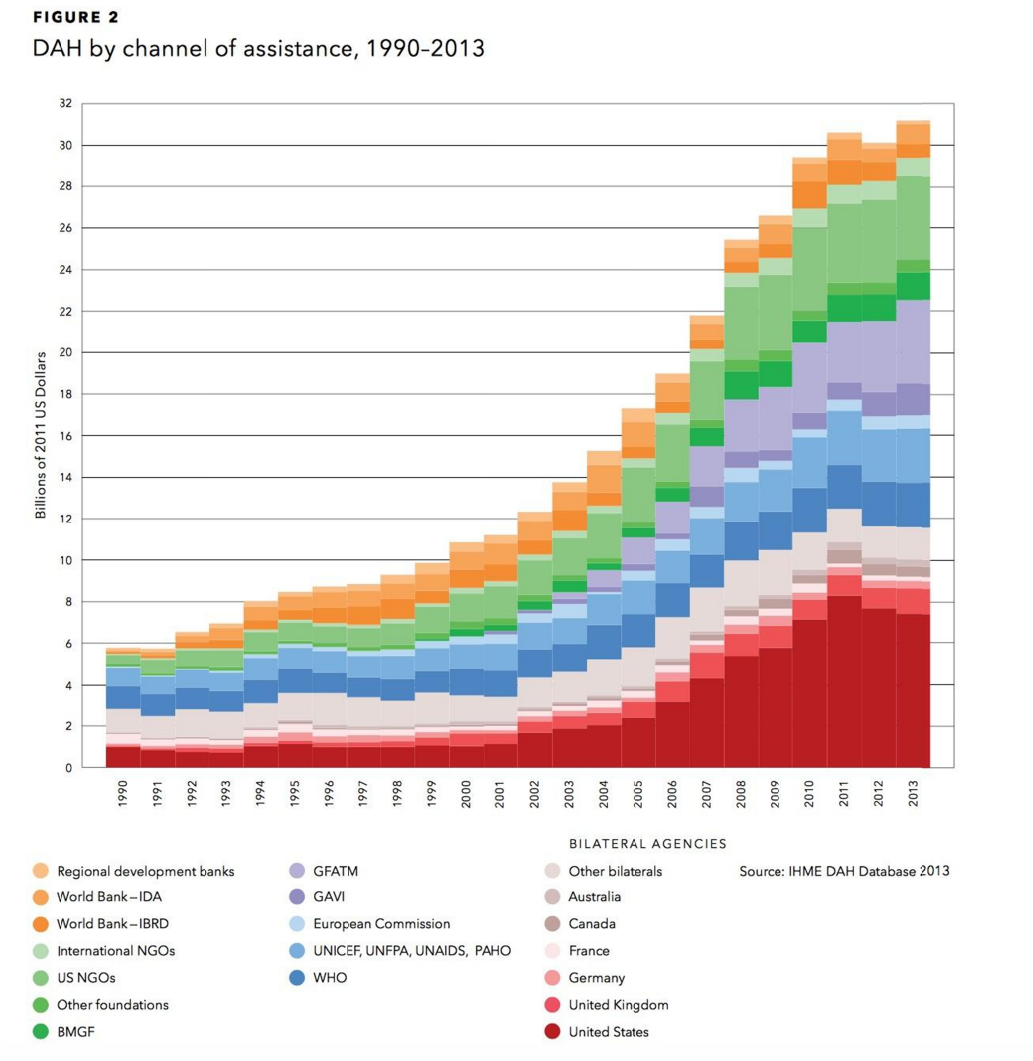
The recent Ebola outbreak reminds us, however, that such an eclectic environment does not always provide more effective solutions. We must also consider the importance of strengthened governance and management at global, regional, national and community levels.

1.2 The rise of public-private partnerships

In recent years, many public-private partnerships (PPPs) have arisen in the field of development assistance for health. Just a few decades ago, such collaborations were quite rare. Prior to the 1980s, what few public-private collaborations existed were often marked by distrust and conflict [3]. However, changing attitudes – neoliberalism; increasing dissatisfaction with the UN; recognition of global health market failures, the interdependence of public and private actors, and the broad nature of emerging health threats – opened the door to new partnerships with NGOs in the ‘80s, and with private for-profit corporations in the ‘90s [3].

Today, these partnerships occupy a major position on the global health stage. Two major PPPs – Gavi, the Vaccine Alliance (GAVI); and The Global Fund to Fight AIDS, Tuberculosis, and Malaria (Global Fund) – provided 17.8 percent of all DAH in 2013, for a combined total of US $5.5 billion [2]. Meanwhile, private sector involvement in global health has grown in other ways too, with NGOs and private US foundations providing another US $6.9 billion in DAH in 2013, or 21.9% of worldwide totals [2]. Going forward, private actors and partnerships will have an integral role to play in strong global health governance system.

Figure 1: DAH by channel of assistance, 1990-2013 [2]



2. The role of public-private partnerships in global health today

Despite the proliferation of PPPs in global health today, the term “public-private partnership” is still a relatively ambiguous term encompassing a variety of arrangements. It is beyond the scope of this paper to rigorously define a framework for understanding which global health partnerships do or do not constitute “true” PPPs. However, in the interests of providing clarity while still allowing for the wide range of partnerships operating in global health today, we will adopt the broad guidelines proposed by Reich: a global health PPP should 1) include at least one for-profit and one not-for-profit organization, 2) distribute efforts and benefits among core partners, and 3) commit to creating social value in the form of improved health [4].

2.1 Types of global health PPPs

PPPs for global health engage in a wide variety of different ventures (Figure 2). Possible objectives include (but are by no means limited to) product development, distribution of donated or subsidized products, or strengthening health services [5].

Figure 2: Variety of PPPs in Global Health

Objective	Example of Partnership
Product development partnerships (PDPs)	PATH Malaria Vaccine Initiative
Distribution of donated or subsidized products	Mectizan Donation Program
Strengthening health services	Gates Foundation and Merck's Botswana Comprehensive HIV/AIDS Partnership

2.1a Vertical and horizontal partnerships

In the early 2000s, most global health PPPs arose as narrowly focused vertical programs, with very specific disease targets or technical specialties [6]. GAVI, for example, has worked to improve immunization rates since 2000, while the Global Fund has fought AIDS, TB, and malaria since 2002. The Gates Foundation, a strong supporter of both of these initiatives and many others, has long favored such a technocratic approach to solving global health problems [6-7].

These large vertical partnerships have demonstrated the benefits of the model, with substantial successes in their scope of action. GAVI estimates that its efforts have supported the immunization of 539 million children and helped avert 7.1 million future deaths as of 2014 [8]; the Global fund supports programs that have provided 8.1 million AIDS patients with antiretroviral therapy, have treated and tested 13.2 million TB patients, and have distributed 548 million insecticide-treated nets as of July 2015 [9]. Both have been rated highly by the UK Department for International Development (DFID) on measures of value for money within their areas of expertise [10].

However, the vertical approach is not without its drawbacks. Some critics warn that partnerships with too narrow a focus run the risk of creating "islands of excellence in seas of underprovision" [11], while others suggest that even "excellence" might be too strong a word, and perhaps "sufficiency" would be more appropriate [12]. Semantics aside, there is a range of evidence indicating that the benefits of vertical efforts can often be to the detriment of local health systems more broadly. Reviews of specific initiatives indicate positive effects on service delivery for those services targeted by PPPs, but also a number of external negative effects including distortion of national priorities, additional burdens on inadequate national capacity, inefficiency through duplication and parallel services, imbalances in the utilization of the health workforce, and interruption of routine services [13-15].

Over the last decade, many organizations have shown increasing interest in moving towards horizontal models, with broader goals of health systems strengthening (HSS). The 2007 WHO framework for action on health systems cites HSS as an agenda item of utmost importance [16]. It is generally recognized that to achieve large-scale health goals, such as the health-related MDGs or SDGs, attention to HSS must be a priority area for global health actors. Indeed, building strong health systems will be a vital first step in working towards Japan and world goals of worldwide universal health coverage (UHC). Even some staunchly vertical organizations, including GAVI and the Global Fund, have opened windows to HSS support, recognizing that better systems are needed to effectively deliver their disease-specific interventions [17-18].

However, in their current state most HSS initiatives are still underdeveloped. Many partnerships

have struggled to define the scope of activities that fall under "health systems strengthening." The WHO health systems framework provides a starting point, but it is broad and open to a variety of interpretations. Critics have suggested that, in too many cases, so-called HSS activities have been little more than a means for partnerships to achieve their own specific, narrow health targets, rather than a truly comprehensive attempt to improve health systems [13]. However, going too far in the opposite direction may also be problematic: for example, early HSS attempts by the Global Fund have been described as "'messy' and 'inconsistent,'" with substantial financial support for activities that were "diffuse and difficult to define" [19]. This tension – between maintaining expertise in a narrow mandate, and expanding to a comprehensive HSS platform – has plagued major HSS initiatives from both GAVI and the Global Fund since their inception [6-7].

GAVI's current HSS initiatives provide a useful encapsulation of much of the current debate around HSS. The GAVI HSS window offers a suite of grant options for prospective applicants, categorized under the six building blocks of the WHO framework [17]. Proponents of the system cite a "'niche focus on eliminating health system bottlenecks'" impeding immunization coverage [19] with sufficient flexibility to have impacts beyond that narrow mandate [13,20], and a commitment to the principles of aid effectiveness outlined in the Paris Declaration, including national ownership, alignment, and harmonization [20]. But critics suggest that despite GAVI's rhetoric about holistic HSS support, its activities continue to skew the global HSS agenda unfairly in favor of the technocratic "Gates approach" [7].

2.1b Product development partnerships

Product development partnerships (PDPs) represent an important subset of the global health PPP landscape, distinguished from other partnerships by a focus on research and development of new medicines for neglected diseases [21]. Data from the G-FINDER Public Search Tool recognizes 16 major PDPs active as of 2013, receiving total funding in that year amounting to US $482 million [22]. While this is a drop in the bucket relative to total global pharmaceutical R&D spending – for example, Pharmaceutical Research and Manufacturers of America members report spending US $51.6 billion on R&D in 2013 [23] – results from many PDPs have so far been positive.

PDPs have been and continue to be integral in bringing private-sector innovation to bear on neglected diseases. The public health community has long recognized that pharmaceutical R&D is strongly biased in favor of products targeting affluent markets in high-income countries, leading to a market and policy failure that ignores diseases of poverty despite the massive worldwide burden of such diseases [24]. By linking pharmaceutical companies with government and nonprofit organizations invested in global public health, PDPs offer incentives to align private-sector resources and capacity with public-sector interests. Several new products have come to market over the past decade, such as combination therapies for various diseases from the Drugs for Neglected Diseases Initiative (DNDi) [25], or a new meningitis vaccine from the PATH Meningitis Vaccine Project (see Box 1).

However, the PDP model is not without limitations. Observers have noted the need for diversified funding sources - from 2007 to 2013, for example, the Gates Foundation has provided approximately half of all funding to PDPs each year [22]. Diverse and unrestricted funding is necessary to ensure that PDPs can operate flexibly without being tied to a single donor's strategy [26]. Moreover, while PDPs have succeeded in bringing private-sector attention to neglected diseases on a partnership-by-partnership basis, they offer only a limited resolution to the fundamental flaws in the pharmaceutical incentive structure, which still broadly preclude the development of affordable treatments for diseases of poverty [27]. A serious attempt to restructure these incentives could bolster the development of such vital products even further.

In Japan, the Global Health Innovative Technology (GHIT) Fund operates on a business model intended to alleviate this problem. Founded in 2013, the GHIT Fund utilizes an investment strategy based on sustainably engaging the private sector in Japan and worldwide, while ensuring product accessibility once developed [28]. The Fund's commitment to encouraging partnerships around the world for a range of high-impact products signals a move to expand the scope of private sector engagement with global health R&D, and the Fund portfolio already supports a range of new projects.

Moreover, Incentives for Global Health has for several years advocated for a global Health Impact Fund (HIF), another innovative solution to pharmaceutical incentive problem. Pharmaceutical companies who partner with HIF would commit to selling a product at cost worldwide, as well as provide free licenses after a 10-year reward period; in return, HIF would pay partner companies from a reward pool, in proportion to the actual measured health impact of their product [29]. Such a financial apparatus could both encourage private interest in neglected diseases and ensure that the products developed reach their intended markets, thus promoting even further PDP collaboration in the future. In particular, the market realities in middle-income countries often make it difficult for PDPs to reconcile the profit interests of commercial partners with the affordable provision of products in these areas; the HIF could greatly mitigate this problem [30].

Box 1: PATH Meningitis Vaccine Project (MVP)

Despite the high need for group A meningococcal meningitis vaccinations in Africa, for many years no manufacturers stepped up to develop an affordable solution. Recognizing the unmet need, PATH and the WHO collaborated on the Meningitis Vaccine Project (MVP), a public-private partnership for the development, testing, and licensing of a new meningitis vaccine.

While the components and technology existed prior to the MVP, the challenge lay in finding partners willing to take the economic risk of developing a product for an impoverished market [31]. With the support of a ten-year grant from the Bill & Melinda Gates Foundation, PATH located three such partners: SynCo Bio Partners BV, the Serum Institute of India Limited (SIIL), and the U.S. Food and Drug Administration's (FDA's) Center for Biologics Evaluation and Research. Each partner contributed something unique and vital to the development process: key vaccine components, production capacity, and conjugating technology, respectively [31].

The partnership involved an exchange of nonexclusive, sublicensable licenses for key technologies between PATH, the FDA, and SIIL, an unusual arrangement in vaccine manufacturing [32]. The final product, MenAfriVac, launched in late 2010 at a cost of less than US $0.50 per dose, and within a few months mass vaccination campaigns reached over 19 million people in three countries [33]. The results demonstrate that the MVP succeeded in bridging the gap between a critical public health need and the commercial interests of the pharmaceutical companies involved.

2.2 Keys to a successful partnership

Several essential factors underlying PPP success or failure are well understood. At the most basic level, strong partnerships should have a clear and mutually agreed-upon goal, a pre-defined division of labor, and a sharing of both benefits and risks acceptable to all partners [34]. Multiple commentators have specifically emphasized the importance of transparency, accountability, and clarity in common understandings between partners [34-35]. Moreover, good PPPs are not static structures – the best work to actively maintain and adjust their partnerships in order to achieve maximum impact [35-36].

Attempting to coordinate public and private sector entities presents its own unique set of

opportunities and challenges. The complexity of many global health problems demands a range of skills and competencies that neither the public nor private sector can individually provide [4]. Thus, strong partnerships can create innovative solutions by offering the best of both worlds: the resources, technical expertise, flexibility, and management skills of the private sector, combined with the legitimacy, legal and regulatory assets, and development experience of the public sector [37]. However, creating such a partnership also necessitates aligning divergent interests, i.e. the public good and corporate bottom lines. As such, partners must actively acknowledge their differences in interest and strive to generate mutual benefit, through programs that improve public health while still offering corporate partners a return on investment or an opportunity to expand business interests [35,37].

Additionally, it is utterly essential that global health PPPs, like other international development agents, adhere closely to the principles of effective aid outlined in the Paris Declaration, particularly ownership, alignment, and harmonization. As outlined in the previous section, too often a myopic focus on a particular program can have negative effects on the broader health system, leading to distorted priorities, burdens on strained capacities, and inefficiencies. By contrast, for example, positive reactions to GAVI's HSS window have highlighted successes in strengthening in-country coordination and producing well-aligned funding proposals [20]. The international community continues to call for placing national plans at the center of aid agendas, moving, in the words of Dr. Paul Farmer, "from 'aid' to 'accompaniment'" [38].

Other recommendations for strong partnerships, drawn from independent evaluations of major PPPs, include focus on a comparative advantage distinct from other global health actors, maintaining a secretariat of the appropriate size and structure, and practicing good performance management with continuous internal assessment [35].

3. The role of the private sector in global health today

While a substantial fraction of private sector engagement in the global health arena occurs through PPPs, these partnerships by no means represent the full extent of private involvement in the field. Nor does "private sector" refer exclusively to for-profit corporations: many other private entities, including NGOs and foundations, are also major suppliers of development assistance for health, and play major roles in a wide variety of PPPs. Each of these entities occupies a different niche in the global health ecosystem.

3.1 For-profit corporations

Perhaps unsurprisingly, even in the modern global health landscape, certain sectors of private industry remain antagonistic to public health progress, such as the tobacco and alcohol industries and segments of the food industry [39]. However, attention to corporate social responsibility (CSR) has become increasingly widespread over the past 20-30 years [40], and in turn many corporations are more attuned to issues of international health and development than ever before.

CSR in the pharmaceutical industry provides a key example, with obvious relevance to global health. Engagement includes targeted research arrangements through PDPs, as discussed in the previous section, but this reflects only one dimension of pharmaceutical CSR activities. A survey of several major pharmaceutical companies found that other common CSR activities included product donation and/or differential pricing, improving local distribution capacities, engaging private or informal healthcare providers, and mobile health (mHealth) initiatives [41]. These activities may involve working with other corporate partners, such as telecommunications companies for mHealth [41]. Some companies also provide personnel: for example, Pfizer's Global Health Fellows Program sends employee volunteers to global partner sites in order to

transfer knowledge and build capacity [42].

Some other companies outside the health sector have also mounted initiatives contributing to global health. For example, Google.org, the charitable arm of Google, provides funding to a variety of global health actors, and also manages programs such as Google Crisis Response and, previously, Google Flu and Dengue Trends. Moreover, the advent of the sustainable development era has brought new corporate initiatives to the playing field, such as Impact 2030, a business-led collaboration intended to encourage corporate volunteerism in service of the SDGs. However, various observers have cautioned that better evidence is needed to understand the efficacy of CSR initiatives, particularly in the global health context [41,43-44].

3.2 NGOs

Non-governmental organizations, or NGOs, comprise a hugely diverse spectrum of private groups outside of traditional for-profit corporations (Figure 3). Within global health, these groups operate in numerous different capacities, with various objectives.

Figure 3: Variety of NGOs in Global Health [45]

Type of NGO	Example
Humanitarian aid	Doctors Without Borders (MSF)
Philanthropic foundation	Bill and Melinda Gates Foundation
Membership organization	Global Health Council
Consulting	John Snow, Inc.
Academic research	Johns Hopkins Center for Global Health

Historically, the position of NGOs in the global health landscape was initially somewhat contentious, with some derogatory commentators referring to NGOs as “pressure groups” [3]. Criticisms of NGOs working in global health remain today, including accusations of bypassing governments or undermining democracy, limited accountability and transparency, or poor relationships with national health systems and community organizations [46]. Yet the presence of NGOs has grown into an undeniable force in the global health arena.

In addition to their individual activities, NGOs have played a major role in many important global health partnerships. For example, PATH engages in a range of different PDPs, and both Rotary International and the Gates Foundation have been important partners with Japan and other national and international bodies in the fight to eradicate polio. The significant funding power of the Gates Foundation, in particular, has arguably been a driving factor behind the proliferation of vertical global health initiatives in the past 15 years [7].

An interesting and increasingly important function of NGOs in global health is in disease surveillance. Analyses have indicated improvements in outbreak discovery and public communication over the past 20 years, though gains vary regionally [47]. NGOs have advanced disease surveillance through innovative initiatives, such as the internet-based reporting systems HealthMap and the International Society for Infectious Diseases’ ProMED, and through efforts to coordinate independent surveillance programs in a “network of networks,” such as the Nuclear Threat Initiative’s CORDS program. NGOs have also provided on-the-ground intelligence in emerging situations, as Doctors Without Borders did in the wake of the 2010 Haiti earthquake [48] and in the current Ebola crisis [49].

4. Partnerships and private-sector responses to global health emergencies: lessons from the Ebola crisis

The international response to the ongoing Ebola outbreak, particularly the response of the WHO, has been widely criticized by both outside actors [49] and the WHO itself [50]. Yet a wide variety of private actors stepped in to provide critical support in the emergency response, with at least 150 companies participating in various capacities [51]. Taking explicit steps to coordinate these corporations' resources and expertise could prove invaluable in strengthening preparedness, response capacity, and recovery efforts in the face of future public health emergencies.

4.1 Disaster preparedness

The scale of the current Ebola crisis stems in part from the reality that none of the nations experiencing the brunt of the outbreak were equipped to deal with a disaster of this magnitude. All three are recovering from recent civil wars, leaving their health systems poorly positioned to respond to such a massive emergency [52]. In this sense, the increasing global focus on health systems strengthening activities also represents a long-term investment in preventing future crises. Partnerships should focus on building national capacity to create strong, self-sufficient local health systems [38], which can in turn take the lead in emergency response situations and reduce reliance on international resources.

At the community level, in particular, partnerships focused on local disaster preparedness education can have a valuable impact. Such partnerships have already seen success in other disaster management contexts. For example, communities in West Sumatra, Indonesia, with a disaster preparedness team trained by the partnership P3DM fared better than those without following the 2009 Sumatra earthquake (see Box 2). This strategy should also be applicable to global health emergencies. Disaster preparedness education can provide communities with the tools to mount their own immediate response in an emergency situation, and involving community members directly in the response effort creates important ties to the larger health system [38]. Keeping in mind the rampant mistrust of and hostility towards health workers in the Ebola crisis [52], cultivating these community connections may be an essential facet of effective response preparation.

Another avenue for the improvement of disaster readiness lies in better coordination with pharmaceutical companies for product development. A key failure in the Ebola response has been the dearth of treatments and lack of a vaccination available for the disease. Although Ebola has been known to the scientific and medical communities for nearly 40 years, only the severity of the current situation has brought any serious attention to R&D. Existing partnerships have made efforts to step in and fill this gap, to be sure. For example, Gavi pledged $300 million as of December 2014 to purchase Ebola vaccines for affected nations [53]. Various other new partnerships have also been formed in order to expedite drug and vaccine development [54-56]. But the scramble to create the necessary new arrangements in the midst of a crisis has been inefficient and costly. As one commentator noted, "A crisis is not the time to be exchanging business cards" [51].

Coordinating efforts to facilitate PDPs prior to an outbreak could greatly smooth the development process in the event of an actual emergency [51]. Of course, the underlying incentive issues in the pharmaceutical industry also limit R&D interest in diseases like Ebola until they threaten the developed, not just the developing, world [53]. Restructuring these incentives, through an initiative like the HIF, could bolster preparatory coordination by creating a pre-existing structure to facilitate preemptive or emergency product development in cases of crisis.

Box 2: Public-Private Partnership for Disaster Management in West Sumatra, Indonesia (P3DM)

In the wake of the 2005 earthquake and tsunami in Nias, North Sumatra, the NGO Mercy Corps founded P3DM in September 2008, with the aim of educating local communities in risk management strategies. Mercy Corps, which has actively worked to reduce poverty in Indonesia since 1999, collaborated with Kogami, a tsunami alert community, and other local private sector companies, and received funding from OFDA-USAID and Boeing Corporation for the program [57]. P3DM planned to create local disaster risk reduction in partnership with two local government districts in West Sumatra, and in twelve schools over a two-year period [58].

P3DM also built disaster preparedness teams (DPTs) in each village, and provided recovery, rehabilitation, and reconstruction services [57]. The program was tested unexpectedly by the September 2009 Sumatra earthquake, but a final report says that communities with a DPT were significantly better prepared than others [57].

Through this program, locals were prepared with knowledge of secure locations and appropriate steps to take in an emergency situation. DPTs trained through P3DM, as well as the follow-up program PREPARE SumBar, learned to prepare funding applications, engage in budget discussions, and manage funds. Note, however, the program was not without its difficulties: insufficient government staff, issues with coordination, and challenges securing funding for certain activities all hampered the partnership's efforts [57].

4.2 Response capacity

In the event of an emergency, time is of the essence. Private for-profit companies can often act more efficiently and flexibly than the public sector, due to better management and reduced administrative overhead [59-60]. As such, they are in a prime position to contribute to disaster response efforts, in contrast to the traditional view that disaster management is primarily a public good [60-61].

Private aid contributions in the Ebola crisis reveal a variety of ways for companies to add value to response efforts. For example, in-country operators (i.e. businesses with a local presence in affected areas) were positioned to take on a first-responder role, and contributed resources, training, advocacy, local knowledge, and vital services [51,59]. Other companies offered valuable domain-specific expertise, such as logistics and transportation, communications tech, R&D, or financial services [51]. In a crisis such as this one, where early responders were stretched to the breaking point while the world dragged its collective feet [49], the power of quick local action and expert support to change the course of the outbreak cannot be overstated.

Yet across all levels of private sector involvement, poor coordination has hampered even the best-intentioned response efforts. Previous examinations of successful partnerships stress the importance of clearly defined objectives and responsibilities and effective communication channels [60], as well as strong organizational arrangements to promote mutual coordination [61]. Often, the ad hoc nature of Ebola response partnerships prevented partners from fully realizing these ideals. A lack of communication between the public and private sectors left local responses disjointed, created "solutions" that failed to meet core needs (particularly in technology), and rendered many private actors unsure how to engage at all [51].

To harness the potential of the private sector in a future emergency scenario, the relevant coordinating mechanisms must be put in place before, not during, the crisis. Those players who had an established point of communication with public entities, such as through preexisting UN Clusters or Global Ebola Response Coalition weekly calls, felt they were better equipped to engage effectively and support other responders [51]. Efforts to widen this network and create a well-defined coordinating structure could pay dividends in future emergencies.

Surveillance and information management offer an additional challenge. Private firms' caution regarding employee health hindered efforts to partner for the creation of an efficient real-time information system [59]. In this case, humanitarian NGOs such as Doctors Without Borders may provide a better option for partners in generating on-the-ground intelligence. Of course, effective use of this intelligence requires collaboration with other local partners and rapid action on the information generated, neither of which happened when Doctors Without Borders sounded the alarm in the early days of the Ebola outbreak [49].

4.3 Recovery efforts

Finally, strong disaster management partnerships should focus on "resilience": not just preparedness and response, but recovery in the aftermath [60]. Even with the Ebola outbreak in check, the damage wreaked on local health systems will have an ongoing negative impact on services targeted at other endemic health issues, such as malaria [49]. This is ripe territory for a variety of both vertical and HSS-focused partnerships, who must work quickly to rebuild these vital capacities as soon as possible to prevent the peripheral damage from the crisis from multiplying out of control.

Moreover, the negative effects of the Ebola outbreak extend well beyond pure health system concerns. The World Bank predicts that the three core countries affected by the crisis will forgo a combined US $1.6 billion GDP in 2015, with another US $550 million lost in the rest of sub-Saharan Africa, and significantly more if the disease spreads any further [62]. Additionally, World Food Programme models estimated that the spread of Ebola will have created food insecurity for between 750,000 and 1.4 million people as of March 2015 [63]. A strong recovery will require not only the rebuilding of health systems, but the rebuilding of lives and livelihoods through economic stimulation and provision of basic needs. Here, in-country operators in particular are in a prime position to aid in recovery efforts, by returning to local business and investment activity after the worst of the crisis [51]. Reopening trade flows and resuming stalled projects as soon as possible will encourage a more rapid return to a positive growth trajectory for the region.

5. Options for resilient global R&D framework during an emergency

One of the major lessons learned from the recent Ebola outbreak and its response is the importance of developing an effective and efficient global research and development (R&D) framework during an emergency.

In this paper, we performed an analysis based on the 7-S Framework, which evaluates how well the resilient global R&D framework can be developed to effectively counter infectious disease threats: (1) Structure; (2) Style and Skill; (3) Stakeholders and Staff; (4) Shared value; (5) Strategy; (6) System; and (7) Size. Based on the analysis, we propose four recommendations.

Firstly, the World Health Organization (WHO) should lead in establishing an independent Pandemic Product Development Committee (PPDC), supervised by the Technical Governing Board (TGB) [64]. The PPDC is mainly responsible for oversee global R&D progress, mobilize, prioritize, and allocate R&D resources relating to pandemic threats whereas the TGB is

supervising body to accelerate the PPDC's works by coordinating with and increasing coherence in global health community.

The global community realized during the recent Ebola outbreak that there are no supervising authority that oversees and lead global R&D efforts. Even within the WHO, the clusters are formed according to issues such as Family, Women's and Children's Health (FWC), HIV/AIDS, TB, Malaria and Neglected Tropical Disease (HTM), or Health Systems and Innovation (HIS) apart from administrative offices. Special Programme of Research, Development and Research Training in Human Reproduction (HPR) under the FWC cluster may be the only program that manages R&D issues, but limited to R&D related to FWC and not necessarily pandemic or epidemics [65]. In addition, most of the global R&D efforts are driven by market mechanisms. This resulted in R&D expertise mainly remains in private sector, and in only a few areas of the world, such as North America, Europe, Australia and Japan. In order to globally monitor potential pandemic threats, progress towards R&D according to the threats and effectively response, the WHO should lead the initiative to establish the independent PPDC given its constitutional mandate as well as the nature of pandemic that may affect every human being without distinction of race, religion, political belief, economic or social condition. However, the PPDC should not be established within the WHO, such as under the Outbreaks and Health Emergencies (OHE) cluster but remains independent primarily to promote private-sector involvement. The committee should include public health and R&D experts and representatives from each WHO regions, with a size of less than 15 members respectively. Internationally recognized R&D experts in discovery, development, manufacture, and approval should participate in the committee in a private capacity given its nature of conflict of interest. The committee should also include public specialist who have expertise in distribution of existing and newly available medical products. The TGB should be composed of representatives from the UN Family including WHO, regulatory agencies and industries in order to lead design-institutional arrangements on various regulations for R&D during an emergency, which will be illustrated as follows. To facilitate the linkage, the chair of the PPDC should be a member of the TGB.

Secondly, the PPDC should work to define priorities, map global R&D progress, raise and manage the budget including gap analyses, and draft a pandemic-preparedness plan that illustrates R&D's role, responsibility, and operations during an emergency. Over the last few decades, Product Development Partnerships (PDPs) have accelerated product development for diseases whose solutions lack commercial incentives and which disproportionately affect the poor in developing countries. The PDPs has successfully created 39 products up to now, but most of the targeted diseases are HIV/AIDS, tuberculosis, malaria, NTDs, diarrhea and respiratory diseases [66]. The PPDC should focus primarily on diseases of high pandemic or epidemic potentials including coronaviruses and influenza viruses, prioritize and map global R&D progress according to the list of high-priorities. Prioritization should not confine to potential pandemics among humans but should apply the One Health concept - working locally, nationally, and globally to attain optimal health for people, animals and the environment [67]. Defining priorities should also work along with efforts to strengthening disease surveillance. Although WHO should take a lead on strengthening disease surveillance mechanism in partnership with regional and national focal points, there is also a need to promote non-medical R&D such as implementation of mobile Health or mHealth. Though internet access and mobile phone coverage differs substantially across countries, the number of population who reaches such technologies are certainly increasing even in the rural areas in developing countries [68], and such innovations in information and communications technology (ICTs) will advance surveillance capacities. Raising fund and managing the budget allocation based on the gap analyses of relevant R&D should also led by the PPDC. In addition, the PPDC should draft a pandemic-preparedness plan that illustrates R&D's role, responsibility, and operations during an emergency at least over the next 5 years. This not only provides clear roadmap for various

global R&D stakeholders in government, multi-lateral organizations, academia, regulatory agencies, industry and civil-societies but also accelerates involvement of emerging contributors from education, communication, environment and defense sectors.

Thirdly and the most presumably important, the PPDC should focus to lead design-institutional arrangements on various regulations for R&D during an emergency. Given the fact that it is extremely important to swiftly counter pandemics, it is reasonable to redesign existing protocols and frameworks: especially during clinical trials, manufacture, and approval of medical products as these three phases often require the most time and investment. In practice, there are seven phases where R&D stakeholders can be coordinated and should align. First, during the initial phases of the product development, there's a need to mobilize resources on R&D not only from traditional funders but also from other sectors such as education, communication, environment and defense throughout the different R&D phases. For example, engagement of the locals in the community is indispensable to implement clinical trials during an emergency and long-term education in partnership with education sector is critical. Strengthening local R&D capacities also require long-term investments. Additionally, U.S. Department of Defense (DOD) spending US$70 billion on R&D [69] reflects pandemic threats as a matter of national security. Second, the R&D community should expand its efforts to upstream stage of product development led by the PDPs into high-priority pandemic diseases. Although donor governments supporting PDPs have increased to 21 for now [70], half of the funding comes from the Bill & Melinda Gates Foundation. There remains room to increase other donors involvement both from public and private sectors. Third, R&D community should commit to and agree on new approaches and protocols during clinical trial phase such as introducing adaptive design into clinical trials, ensuring involvement of local government, scientists and communities as well as benefit-share scheme, developing pre-approval for the clinical trial designs and master protocols. Generally, clinical trial is the stage that requires longest period of time and high level of funding, how to effectively and efficiently accelerate product development during this phase is the key to swiftly counter the pandemic threats. Fourth, the R&D community should work to agree on streamlined process for regulatory requirements across countries or regions for approval. Fifth, the R&D community should agree to ensure timely sharing of biomaterials and intellectual property management. The WHO’s Pandemic Influenza Preparedness Framework (PIP Framework), which lays out a streamlined process for the sharing of pathogens with pandemic potential and creates fair benefit-share scheme [71], should be expanded to high-priority pandemic diseases. Sixth, the R&D community should identify manufacture facilities, develop and agree on protection against product liability claims during an emergency. Last, R&D community should plan for access and distribution of available medical products. Even when the products are available, it is highly likely they are often unaffordable or inaccessible for the people most in need. To avoid such cases, pre-agreement on stockpiling and pricing schemes at international level as well as developing effective distribution and administration system at national level are needed.

Lastly, the PPDC should work to secure and deploy a minimum of US $1 billion per year, which is relevant to half of the annual budget for global PDPs, to implement operations described above. The funding source should include donor contribution to the WHO, given there is an equal risk of pandemic threats to the nations worldwide, voluntary contribution from government, outside health sectors, private foundations and business, as well as utilization of innovative financing mechanisms. While prioritization, R&D mapping and gap analysis may not require a large amount of funding, design-institutional arrangements on various regulations for R&D during an emergency may require large amount of funding as well as enormous negotiations, consensus buildings amongst various stakeholders. Therefore, we have to keep in mind that potential pandemics are threats to every human being without distinction of race, religion, political belief, economic or social condition, and we have to have a united effort to fight against them.

6. Strengthening global health governance

Fidler defines global health governance as “the use of formal and informal institutions, rules, and processes by states, intergovernmental organizations, and nonstate actors to deal with challenges to health that require cross-border collective action to address effectively” [72]. The WHO identifies its role in global health governance as “the directing and coordinating authority on international health work” [73]. The expansion and diversity of the global health landscape, then, suggests that a variety of explicit coordinating initiatives may be worthy priorities for the WHO in strengthening governance.

For example, the WHO should take a leading role in setting the global HSS agenda, through a platform to coordinate funding and activities from a variety of global health actors. With respect to the case of HSS, the WHO has outlined a framework for health systems, but there is a weak evidence base for HSS activities and limited agreement on the optimal cost-effective interventions [74-75] . Thus, the framework is interpreted in numerous different ways by a wide variety of global health actors, resulting in diffuse HSS spending and few clear international policy goals. As a leading partner on an umbrella platform, the WHO could put itself in a position to concretely define a health policy research agenda and, in turn, set actionable global HSS priorities. One such platform, the Health Systems Funding Platform, was proposed just a few years ago as a partnership between the World Bank, GAVI, and the Global Fund. However, the proposal ultimately stalled due to the complexities of coordinating the partners’ distinctive funding channels, schedules, business models, and governance structures [76], and perhaps also due to the failure of the World Bank to collaborate effectively with its partners and to actively respect national ownership [77]. The challenges of establishing such a platform are more than evident, but the goal remains admirable, and if past mistakes are heeded a new HSFP-like initiative could turn HSS from an amorphous buzzword to an actionable cornerstone of global health policy.

Innovation in global health represents another area with which the WHO and other governance structures should engage at a high level. The biopharmaceutical research industry clearly has enormous resources at its disposal, but PDPs have only succeeded in leveraging a small fraction of these resources in service of neglected diseases or other global health problems. A broader reform of incentives could help drive R&D for global health on a larger scale. Other initiatives like the GHIT Fund and the proposed HIF already show promise on this front, and they should absolutely earn the backing and investment of the WHO and other major global health agencies. Of course, generating the funds and political will sufficient to create a worldwide impact remains a challenge. Some innovative financing mechanisms indicate investor interest in social good, such as IFFIm vaccine bonds, but such programs have yet to be scaled up or replicated beyond their current, narrow domains [78].

One potential, under-utilized source of public funding might come not from health or development agencies, but from defense agencies. Proposed US federal spending on health security in fiscal year 2016 totals US $13.7 billion, including over $2.5 billion specifically for biodefense and pandemic threats, in addition to funds for multipurpose preparedness [79]. While the actual potential for weaponization of Ebola is probably low [80-81], the threat has been sufficient to drive biodefense spending and research, an important catalyst for the first waves of vaccine development [81]. Indeed, there are past precedents for increases in defense spending following the 2003 SARS outbreak and the 2009 influenza outbreak [82], and for using this funding to engage the private sector [83]. Working to identify diseases that pose potential biosecurity threats, well before they pose an actual biosecurity threat, could contribute to increased funding for vital global health R&D from the defense sector. However, this strategy is limited primarily to pathogens with clear security implications, which may not apply to many neglected diseases (such as the helminthic NTDs).

While outside the scope of this report's discussion, other economic incentives should also be considered to encourage greater participation in global health R&D. For example, perhaps lessons can be taken from tax or trade incentives for environmental protection and applied to create similar incentives for the global health arena.

With respect to global health emergencies, the decentralized bureaucracy of the WHO makes mounting a strong, rapid response very difficult. Their recent report examining the Ebola response recommends the creation of a centralized, command-and-control Center for Emergency Preparedness and Response, but it remains unclear whether this can be achieved while leaving the basic decentralized structure intact [84]. Moreover, the WHO's capacity to respond has been restricted by recent budget cuts, which slashed crisis and outbreak funding in half [85]. In response to criticisms, officials have asserted that the role of the WHO is merely to advise states how to handle crises, rather than direct the response themselves [85]. But while a preference for national ownership is admirable in many aid situations, it is very obviously incompatible with the poor capacity of health systems in nations like Guinea, Liberia, and Sierra Leone. Investing in a stronger network of disaster management partnerships could serve to alleviate both of these issues. Pre-agreement mechanisms with an expanded network of outside responders would connect more private resources to response efforts more quickly, potentially bypassing much of the internal bureaucracy of the WHO. Moreover, these mechanisms should be built first and foremost around local action rather than outside intervention, with external actors primarily supporting in-country operators or even community-based disaster preparedness teams. Making the focus local not only represents a commitment to effective aid, but also permits flexible action attuned to a country's individual needs, and may help bridge the trust gap between communities and the larger health establishments that serve them. With social media increasingly entering the global health toolbox [86-87], more avenues to community engagement are open than ever before for such endeavors.

In its current state, global health governance might be best described as a regime complex, a "'collective of partially overlapping and nonhierarchical regimes'" or regime clusters [72]. The WHO is central to this regime complex, and if it takes its self-proclaimed position as the coordinating authority on international health work seriously, it should invest in developing networks and platforms that helps these varied regime clusters cohere towards coordinated policy objectives. While there are clear problems with the WHO's bureaucracy, political inertia makes radical reform unlikely; instead, as Fidler suggests, efforts should focus on iterative improvements to generate resilience [72]. Strong partnerships and networks can build this resilience by shoring up the weaknesses of the WHO and offering timely access to a greatly expanded pool of resources and expertise, while bringing a wide variety of global health actors under a more unified policy umbrella.

Importantly, Japan has the specific expertise to offer unique contributions in these areas. First, Japan has over 50 years of experience with UHC, and moreover, has achieved this goal at modest levels of health expenditure compared to other developed countries [88-90]. Thus, when considering HSS from the perspective of moving towards UHC, the Japan case may offer some lessons, or at least a starting point from which to develop ideas about how to build strong systems at low cost and target spending effectively. Second, Japan is home to the GHIT Fund, a promising model for encouraging more private sector involvement in innovative global health R&D. The Japanese government's sustained engagement with major pharmaceutical companies in this partnership might serve as a model for sparking broader private engagement worldwide, particularly with increased support from other major global health actors. Third, Japan has already taken a leading role in several major global health issues, including smallpox eradication, DOTS therapy for TB, and the creation of the Global Fund [91], as well as more

recent polio eradication efforts. With this history of leadership under its belt, Japan is positioned once again to bring the pressing issues discussed in this paper to the attention of the world, and set a global health agenda that will garner the international support needed to generate real collective action.

7. Recommendations

Below are the six recommendations to effectively respond to future global health threats based on the public-private partnerships.

- Health systems strengthening will be critical to achieving the SDGs and promoting UHC worldwide. The WHO should develop initiatives, beyond merely proposing a framework, that position it as a leader in this developing field. This will require:
    - Setting a research agenda. HSS needs to be better understood before more effective initiatives can be enacted. The WHO should convene experts and health policy researchers to identify and answer the key questions pertinent to future policy.
    - Coordinating actors. With an increased evidence base, the WHO should develop a platform to synchronize HSS spending in pursuit of optimal policy interventions. Despite the challenges of implementing HSFP, it was an excellent idea, and building a similar platform could be an important step towards smarter HSS spending.
- Innovative global health R&D represents only a small fraction of total biotech research spending, and PDPs are a successful but limited solution. High-level structures to promote better incentives for global health R&D, such as the GHIT Fund or the HIF, should be supported by the WHO and other major global health actors.
    - Gathering significant funding for these initiatives may be challenging, but one possibility beyond traditional sources is defense. Biosecurity is deeply tied to global health, and in some cases, global health R&D could have important security implications. Bringing the two together could open up new sources of funding from worldwide defense departments.
    - Existing innovative financing mechanisms may offer a useful model, if replicated and scaled up. Other tax and trade incentives should also be considered, with lessons taken from areas such as environmental policy.
- The decentralized, bureaucratic structure of the WHO, coupled with recent cuts to disaster response budgets, leaves it in a poor position to respond in a crisis situation. But by creating a network of partners, especially private partners, and establishing pre-agreement mechanisms, it can leverage the resources and flexibility of the private sector to create a faster, stronger response in the future.
    - Actively invest in these connections now! The WHO should snowball its networks through its current points of contact, and organize meetings for interested partners in order to establish communication.
    - Build from the local level. Center national pre-agreement mechanisms on local operators in that country, and get citizens and community groups involved as well. Build locals' capacity to be their own first line of defense, with international resources in a supporting role. Consider community engagement through social media.
- Japan is in a position to contribute specialized expertise to the pursuit of many of these goals. Specifically, this includes:
    - Experience with low-cost UHC, which may guide future explorations of HSS.
    - The GHIT Fund, offering lessons on sustained engagement of the private sector for innovative global health R&D.
    - Global health leadership that can help bring these issues to the attention of the world and hopefully lead to effective action.

- It bears repeating that all policy measures must adhere to principles of aid effectiveness, particularly *national ownership*. Make coordination with local needs a top priority.
- The global community should invest to develop an effective and efficient global research and development (R&D) framework during an emergency.
    - WHO should lead in establishing an independent Pandemic Product Development Committee (PPDC), supervised by the Technical Governing Board (TGB).
    - PPDC should work to define priorities, map global R&D progress, raise and manage the budget including gap analyses, and draft a pandemic-preparedness plan that illustrates R&D`s role, responsibility, and operations during an emergency.
    - PPDC should focus to lead design-institutional arrangements on various regulations for R&D during an emergency. Given the fact that it is extremely important to swiftly counter pandemics, it is reasonable to redesign existing protocols and frameworks: especially during clinical trials, manufacture, and approval of medical products as these three phases often require the most time and investment.
    - PPDC should work to secure and deploy a minimum of US $1 billion per year, which is relevant to half of the annual budget for global PDPs, to implement operations described above.

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Global Health Working Group
White Paper on Fostering Global Health Innovation

GROUP 7

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Introduction: An Opportunity to Foster Global Health Innovation

The recent outbreak of Ebola hemorrhagic fever in West Africa was tragic for thousands of people and terrifying for millions. The outbreak of this highly infectious diseases also reminded policy makers, global health professionals and scientists[1] about the challenges facing health systems across the world, and the global risks created when these systems are weak or nonexistent.

The recent outbreak of Ebola hemorrhagic fever in West Africa was tragic for thousands of people and terrifying for millions. The outbreak of this highly infectious disease also reminded policy makers, global health professionals and scientists about the challenges facing health systems across the world, and the global risks created when these systems are weak or nonexistent.[2]

While many problems arose in the global response to Ebola, key stakeholders collaborated in successful ways to rapidly develop a new vaccine.[3] This exceptional instance – the innovation of a critically needed new product for global health – highlights an endless global health challenge. How can global health research and development (R&D), the scientific discovery and development of new products to fight neglected diseases, be promoted in the absence of news-making crises?

At Ise-Shima G7 Summit in Japan in May 2016, the G7 governments can review prior successes in global health innovation and put in place new mechanisms to sustain and leverage the impact of recent investments in global health. The Ise-Shima Summit provides an excellent opportunity to build on lessons learned in recent years about successful approaches to fostering global health innovation by making bold commitments of new financial, technical and human resources.[4]

This policy brief argues that increasing the G7's investments in global health innovation is a sound – and necessary – investment that will yield dividends in terms of economic, diplomatic and humanitarian progress. Based on interviews with key leaders in global health, this policy brief concludes that the most significant impediments to global health innovation are:

- *Insufficient funding* invested in research and development of new vaccines, diagnostics and medicines needed for those diseases that disproportionately affect developing countries;

- The *regulatory complexities and systemic redundancies* in licensing new global health products, especially in countries that lack a strong national regulatory framework; and,

- Profound *inefficiencies in global information sharing* and collaboration on innovation processes for global health products.

In response to these challenges, we propose that the G7 countries take three actions to foster

global health innovation:

- *Increase government and philanthropic funding* to support global health innovation processes;
- Advance efforts to *streamline and harmonize national regulatory practices* for new global health products; and,
- Follow through with *support for more effective information/knowledge-sharing systems* in order to promote collaboration in global health innovation.

Despite the medical advances of the past century, the world is still struggling with how to assure that scientific discovery and technological progress benefit all people. In short, how do we assure the fair distribution of investment in the development of new health products, both among and within countries? The three proposals presented in this policy brief will lead to improvements in global health innovation, and thus to progress in global health. Ultimately, the investments in global health innovation proposed here will benefit people, and will strengthen health systems and economies, around the world.

The Need for Technological Innovation in Global Health

Global health is the "study, research, and practice that places a priority on improving health and achieving equity in health for all people worldwide."[5] Global health practice emphasizes interdisciplinary and transnational approaches to understanding the determinants of health, prominent health issues and the implementation of proposed solutions at all levels. Many global health programs focus on infectious diseases, which disproportionately affect people living in developing countries. Increasingly, however, global health programs are addressing heart disease, diabetes, cancers, and other non-communicable and lifestyle diseases that affect all countries.

This policy brief focuses primarily on policies to foster innovation of products to address infectious diseases, because they continue to present major obstacles to economic growth, health security and human development in poor countries. By extension, infectious diseases also have a major impact on global development. However, infectious diseases are increasingly rare in industrialized countries. The infectious diseases that cause a majority of associated death and disability are endemic only in poor countries. (In this paper, the term "endemic diseases" is used to refer to HIV/AIDS, tuberculosis, malaria and the 17 neglected tropical diseases (NTDs) that disproportionately affect people in poor countries.)

The health burden of endemic infectious diseases is immense. Over 25 million people are living with HIV, more than 2 billion people are infected with tuberculosis, and over 500 million people die each year of malaria.[6] Infectious diseases are the leading cause of death in children worldwide.[7] And non-fatal endemic diseases cause considerable disability. The effects of these diseases extend across generations, limiting the ability of individuals, their communities and their nations to thrive.

Despite the global toll of infectious diseases, many of the "tools" (vaccines, diagnostics and medicines) needed to prevent, treat and control them have not been discovered. A few examples of the need for technological innovation for endemic diseases: there is neither a vaccine for HIV nor a cure for AIDS; there is no medicine to treat Dengue fever, chikungunya disease or dracunculiasis; and there are no clinical diagnostic tests available for Buruli Ulcer and Chagas disease, while the diagnostic methods use for tuberculosis are notoriously unreliable. Table 1 shows which of the top 20 endemic diseases have a vaccine, diagnostic, and treatment, and which diseases do not have these technologies

or have only suboptimal options. (Additional information is available in Appendix A.)

In addition to the 20 endemic diseases listed, the world regularly experiences sudden emergent infectious diseases such as Ebola, SARS, avian influenza, and MERS. These outbreaks generate fear around the world, as they threaten not only individuals but also national and economic security, and because existing tools often do not work to fight these new diseases.

Another critical global problem related to infectious diseases is that the effectiveness of existing tools, particularly medicines, is increasingly threatened by the evolution of resistance among the infectious agents. Anti-microbial resistance (AMR) exacerbates the spread of both endemic and emerging infectious diseases by undercutting existing prevention and treatment options.

Widespread resistance to antibiotics among disease-causing organisms is rolling back previously achieved health gains, while no major new antibiotics have been developed in the last 30 years.[8] Resistance problems are occurring with various endemic diseases. For example, after a decade of decreases, malaria deaths increased among African children under age five beginning in the 1970s due to spreading chloroquine resistance in the malaria parasite.[9] Similarly, new strains of multi-drug resistant tuberculosis, streptococci and other diseases are increasingly ubiquitous.

All of these problems – missing tools, tools for emerging new diseases, and new tools to replace those becoming obsolete – urgently require global health innovation. Strengthening global investments in R&D for global health innovation is vitally important.

Table 1: The Need for Innovations for Endemic Diseases: Current Portfolio and Gaps in Key Global Health Tools (Vaccines, Diagnostics, and Medicines)

Disease	Vaccine	Diagnostic	Therapeutic
HIV/AIDS	NO	Yes	Yes
Tuberculosis	NO	SUBOPTIMAL	Yes
Malaria	SUBOPTIMAL	Yes	SUBOPTIMAL
Buruli Ulcer	NO	NO	SUBOPTIMAL
Chagas Disease	NO	NO	SUBOPTIMAL
Dengue and Chikungunya	SUBOPTIMAL	Yes	NO
Dracunculiasis	NO	SUBOPTIMAL	Worm extraction
Echinococcosis	NO	NO	Surgery
Endemic treponematoses	NO	NO	Yes
Foodborne trematodiases	NO	NO	Yes
Human African trypanosomiasis	NO	SUBOPTIMAL	SUBOPTIMAL
Leishmaniasis	NO	Yes	SUBOPTIMAL
Leprosy (Hansen's disease)	NO	NO	Yes
Lymphatic filariasis	NO	SUBOPTIMAL	SUBOPTIMAL
Onchocerciasis	NO	SUBOPTIMAL	Yes
Rabies	Yes	NO	NO
Schistosomiasis	NO	SUBOPTIMAL	Yes
Soil-transmitted helminthiases	NO	SUBOPTIMAL	Yes
Taeniasis/Cysticercosis	NO	NO	SUBOPTIMAL
Trachoma	NO	NO	Yes

Barriers to Global Health Innovation

Significant hurdles exist in improving global health, particularly around the development of new vaccines, drugs, and diagnostics. Yet there is little consensus about how to accelerate investment in global health innovation, especially for products that will primarily benefit people in poorer countries.

Major stakeholders in global health innovation include governments, donors, multilaterals, industry, and non-government organizations. In 2013, more than three quarters of all funding for R&D for global health was provided by seven institutions, including five governments and two philanthropies. In preparing this policy brief, we interviewed representatives in the seven funding institutions. (Details on the methodology and results are in Appendix B.) Key stakeholders from these institutions were asked to identify the major bottlenecks that impede global health R&D for vaccines, diagnostics, and medicines needed to control and eradicate endemic infectious diseases.

The respondents noted that considerable progress has been made in the fight against infectious diseases, thanks in part to economic development, improved health systems and targeted control programs, along with increased access to effective vaccines, diagnostics, and medicines. All of these factors have contributed to reducing the global burden of infectious diseases. But in many areas the rate of decline of infectious diseases has plateaued or fallen short—especially in countries with weak health systems. The respondents were then asked to identify the key obstacles, as well as the most promising strategies, to fostering global health innovation that could address the persistent challenges of endemic infectious diseases. Their responses pinpointed three areas: funding, regulation, and knowledge management.

Strategies for Accelerating Innovation for Global Health

I. Substantially Increase Funding for Global Health Innovation

The Problem

Major, and systemic, funding gaps exist for financing the processes that lead to the introduction of a novel, licensed product for an endemic disease. Further, the sources of funding for global health innovation are different from other areas.

Funding for global health R&D has already increased significantly over the past decade, and the investments are beginning to pay off, leading to new innovations and subsequent formulations. Over the past half century, governments and philanthropic foundations have been the primary funders of research and development of new products targeting infectious diseases of the developing world. Their investment totaled US$3.2 billion in 2013.[10] The pipeline of new products is steadily increasing. For example, by 2011 the Drugs for Neglected Diseases initiative (DND*i*), which was founded in 2003, enabled the development of two antimalarials, a new treatment for visceral leishmaniasis, and pediatric formulations for Chagas disease treatment, among others.

The pharmaceutical industry, on the other hand, spent an aggregate US$400 million on global health research and development in 2013. For-profit companies in the biomedical industry are the primary developers of new vaccines, diagnostics and medicines for developed markets, and they have the infrastructure, professional expertise and other resources needed to bring new products from discovery to market. Yet for-profit companies typically invest only in areas where they see potential for profitable financial return. Market incentives are minimal to encourage for-profit companies to invest in developing new products for endemic infectious diseases that primarily affect poor people in poor countries. The potential returns on investment are viewed as low because of the limited market power of the people who need the products.

These arguments, however, are now being challenged. Recent studies at the national and global levels demonstrate that investment in global health innovation has both economic and social benefits. According to a 2013 report in *The Lancet,* funds invested in global health R&D generate a benefit between 9 and 20 times the cost in the global economy.[11] Likewise, GHPD investments have a significant benefit at the national level. In the U.S.A., for example, approximately 64 cents of every government dollar on global health R&D is invested domestically.[12] In the European Union, 66 cents of every Euro invested in global health R&D is spent within the E.U.[13] Research!America, an advocacy and education alliance made up of over 350 institutions, has examined the issue in depth, and prepared a top-ten list of reasons to invest in global health R&D (see panel).[14]

Public and private donors have often stepped in to fill gaps left by pharmaceutical companies in funding for global health innovation. However, government and other non-industry funding is often directed to basic science, discovery and early product development phases; funding later stage clinical trials, for example, is far less common. Increasingly, donors are partnering with the biomedical industry to shepherd important scientific research into usable products efficiently. Product-development and public-private partnerships (PDPs and PPPs) are mechanisms frequently used to incentivize these collaborations.

Public and private philanthropic funding is subject to politics, local particularities, and changing priorities. Fear and mounting panic often drive a surge of funding for emerging infectious diseases. With the 2014-2015 outbreak of Ebola in West Africa, governments and charities pledged nearly US$8 billion for control programs and R&D. But once an outbreak recedes, funding invariably does as well. Meanwhile, endemic infectious diseases like malaria and tuberculosis do not generate a similar response. They infect large numbers of people, but they have little money to pay for life-saving products, and because they are not perceived as an imminent threat to wealthier nations, they attract less funding. Finally, although governments may have significant resources, priority-setting and decision-making processes can be spread across several different agencies, with independent mandates and funding processes.

10 Reasons to Invest in Global Health R&D

Global Health R&D:
1. Saves lives
2. Creates jobs and opportunity for [donor country citizens]
3. Helps countries maintain competitive edge in the global economy
4. Benefits citizens and soldiers when they are abroad
5. Supports research universities and fulfills students' interest
6. Intersects with domestic R&D to drive cutting-edge medical discovery
7. Contributes to economic development and export markets
8. Investments save money in the long term
9. Is supported by a majority of Americans – and likely the citizens in other G7 countries
10. And finally, global diseases do not recognize national borders

Adapted from: *Research!America's Top 10*

Proposed Solution

More funding is needed for all stages of innovative global health R&D in order to secure critically needed vaccines, diagnostics, medicines and other tools. We propose that the G7 should double their investments in global health innovation over the next five years to ensure a robust pipeline of new products that will radically improve the health of the people who need them. This applies to ongoing

initiatives as well as the need for explore the establishment of a funding mechanism to support the development of vaccines for emerging infections and epidemics for which there is no market incentive such as Ebola, Marburg and Lassa infections.

We propose, in particular, that Japan initiate this doubling with a pledge to double its investment in innovative global health R&D, beginning with a replenishment of the Global Health Innovative Technology (GHIT) Fund. This Japanese model is demonstrating that pairing front-loaded investments with incentives for partnerships among research institutions and the pharmaceutical industry is highly effective in accelerating global health innovation. Within three years since its conception, GHIT has invested in more than 40 potential products, facilitating the use of Japanese technology in the process. Further, the government funding invested through GHIT is leveraged one-to-one with contributions from philanthropic and corporate partners.[15] With this strong foundation, GHIT's partners are poised to generate major contributions to global health innovation, particularly as industry partners are engaged early in the process. Doubling Japan's financial commitment would also push Japan into the top ten public funders of global health research and product development (for more detail see Figure 2 in Appendix A).

II. Streamline Regulatory Review Processes Globally

The Problem

Regulatory policies are critically important – they exist to ensure the safety of consumer products. However, in most instances, each country requires the data for each new vaccine, diagnostic or medicine to be reviewed and approved by its national regulatory agency (NRA). In some instances, the NRA may require additional clinical trials to be conducted locally. The many requirements, some of which are redundant, and the pervasive lack of adequate resources at the NRAs in developing countries, contribute to notoriously slow review and approval process timelines.

Should individual countries actually have to act independently in these processes, especially if they lack the capacity to do so efficiently? This brief argues that supranational policies or practices could be used to expedite approvals for new vaccines, diagnostics and medicines for priority endemic diseases.[16] Already, international law allows regulatory review processes to be expedited in cases of "public health emergency of international concern". For Ebola, WHO served as a convening body which negotiated expedited regulatory processes for new tools. A vaccine and other products were moved into clinical trials in a matter of months rather than years.[17] When, inevitably, there is another outbreak in the future, critical tools will be available which did not exist this time around.

Yet as these approvals jumped ahead in the queue, other products for endemic diseases continue to languish for years.[18] WHO's "pre-qualification program" for essential medicines aims to obviate some of the obstacles. The program, which generates "unified standards of quality, safety and efficacy/performance" for use in product assessment, offers one proven model for avoiding redundancies in regulation.[19] Other models include the *Pan American Network for Drug Regulatory Harmonization* and the unified registration procedures of the European Union. These examples indicate that it is possible to engage nations in harmonizing and streamlining regulatory mechanisms in order to expedite reviews and approvals of new vaccines, diagnostics and medicines for priority diseases. Policy options to consider would include the use of surrogate endpoints (e.g., biomarkers) for licensure, priority and/or expedited licensing mechanisms for diseases with low market potential and the facilitation of mutual recognition of licensure among countries, based on common technical guidelines.

Regulatory processes can be difficult to change. Achieving reform through legislation necessitates

the engagement, and ultimately the agreement, of high-level decision makers. And if the intent is to create supranational policies and structures, lawmakers may have concerns about national autonomy, maintaining standards and protecting citizens.

Proposed Solution

In the short-term, G7 countries should empower WHO or other convening bodies to establish an expedited path of review for new products for infectious diseases or to combat antimicrobial resistance. Over the longer term, the G7 should convene stakeholders to design a process to streamline national regulatory processes, as well as to invest in building capacity within the NRAs.

III. Create Efficient Mechanisms for Collaboration and Knowledge-Sharing

The Problem

When a highly infectious disease outbreak like Ebola occurs, leaders and policy makers frequently commit resources to creating new tools. Time and again, however, as the various actors rush to implement a flurry of activities, some efforts are needlessly duplicated while large gaps exist. Developing mechanisms for working collectively emerge more gradually.[20] Intense global collaboration is required to minimize the damage and control further spread.[21] As was evident during the Ebola outbreak, however, sharing information and knowledge can be an endeavor fraught with difficulties.

Further, the urgency and the resulting political commitment is often lacking when addressing endemic diseases and AMR. And in many instances, the collaborations that do emerge are bilateral, not global. The lack of an efficient global "ecosystem" for sharing and coordinating activities significantly hampers the ability of funders to pursue innovations in global health product development. Prior initiatives aimed at coordinating work across multiple funders and organizations have been perceived as adding work without bringing the desired benefits of efficiency and effectiveness. Even the creation of coordination mechanisms faces duplication, as new funding mechanisms, frameworks and collaboration platforms are developed. While the major global health innovation funders also agree that better collaboration and knowledge sharing could speed support for innovations, many stakeholders are skeptical of ceding authority, proprietary information or priority-setting to a third party.

The challenges of incentivizing and facilitating information-sharing among global health innovators was acknowledged by the G7 during its 2015 meeting in Schloss Elmau, Germany. However, concrete steps to improve the situation have not been forthcoming.

Proposed solution

Japan can lead the G7 to build on the foundation laid in Germany. The Ise-Shima Summit offers an opportunity to follow up by clarifying a process and concrete milestones for the rapid development and deployment of functional global platforms to allow information-sharing, knowledge dissemination and creation of collaborative efforts across national and regional lines and among public, philanthropic and for-profit sectors. A G7 commitment to develop and announce a plan to realize this solution by the 2017 G7 Summit is achievable.

The Way Forward: Implementation Considerations

The world's arsenal of tools – vaccines, diagnostics and medicines, among others – against infectious

diseases remains insufficient, particularly when considering endemic diseases in poor countries. Effective vaccines and medicines are not yet available for prevalent killers. Powerful existing diagnostic technologies are often unsuitable for widespread use in the developing world. And for many existing medicines, the formulations and costs present insurmountable problems in patient access and adherence. Further, the development of AMR threatens the many gains that have already been made.

Global health innovation is therefore necessary to sustaining and expanding efforts to control and eradicate infectious diseases with heavy global burdens. Yet while developing countries experience a disproportionate burden of infectious disease, the majority of funding remains in high-income countries, and among for-profit companies. This results in a lack of urgency, poorly aligned incentives, and ineffective market structures.

The 2016 Ise-Shima G7 Summit offers nations a critical opportunity to develop and promote new mechanisms to incentivize global health innovation and to increase global public accountability. The Summit is a chance to create blueprints for increasing innovation in the discovery, development, and regulatory approval of essential new vaccines, diagnostics, and medicines.

The following steps are therefore recommended for consideration by Japan and its colleagues at the G7 Summit:

1. **Double the current global funding for global health innovation.** We recommend setting a global goal of reaching US$6.4 billion per year for global health R&D within ten years. This level of funding would enable a sea change in GHPD, in particular by making later stage clinical trials possible. Japan, for instance, could lead by doubling its support to initiatives such as the GHIT Fund.

2. **Convene a process to harmonize and streamline regulatory pathways. Allowing** endemic and emerging infectious diseases, as well as instances of emerging anti-microbial resistance, to be eligible for accelerated and/or coordinated review will reduce duplication and time to market for new products. Further, additional resource capacity for regulatory review must be developed in endemic country governments. Japan can support high-level meetings to champion harmonization of policies.

3. **Initiate a process to follow through on establishment of knowledge-sharing platforms for global health innovation.** The G7 countries have already made commitments in this area; now, with Japan as the organizer, next steps need to be elaborated to support platforms to share information on global health R&D strategies in order to identify duplication, encourage collaboration and limit gaps. A commitment to announce a plan to realize this solution by the 2017 G7 Summit is achievable.

A significant increase in funding, a more streamlined process for product approval, and a global platform for collaboration would, together, lead to more innovation. Establishing and advancing a robust pipeline for, and portfolio of, new products we need to control, eliminate, and eradicate infectious diseases. These diseases continue to pose significant risks to human security and health; they also menace the global economy.

At this Summit, the G7 countries have an unprecedented opportunity to radically transform the environment for global health innovation; Japan, which is known for its support of health innovations and global health policy, can offer critical leadership by championing these recommendations.

Acknowledgements: The authors would like to thank Professor M.R. Reich and Dr. Tachi Yamada for their invaluable comments and suggestions in the writing of this White Paper.

Appendix A: Backgrounder on the Global Landscape for Developing New Vaccines, Diagnostics and Medicines for Infectious Diseases

Introduction

Today, diseases like malaria, HIV and tuberculosis are the leading cause of death in children worldwide[1]. Infectious diseases are a persistent threat to global economic growth, health, security, and human development in many of the world's poorest countries. Each year the major diseases kill almost nine million people, many of them children under five. They also cause enormous burdens of life-long disability that disproportionately impact those who are poor[2]. Stepping up research and investments into Global Health Product Development (GHPD) that can effectively treat infectious diseases and prevent them from spreading could have an enormous impact on fulfilling global commitments to lift people out of poverty and build a better world for future generations.

Considerable progress has been made in controlling and even eradicating some infectious diseases in some nations. However, progress has stalled in many areas. Getting the right treatments to those who need them most remains a challenge. Further, new tools are needed to sustain and expand control efforts. Many infectious diseases are still under-researched and poorly understood, and the innovations to address them are of limited commercial interest. This paper focuses on the state of research and development of new vaccines, diagnostics, and medicines to combat infectious disease.

An Innovation Gap

Despite the widespread need for many new vaccines, diagnostics and medicines for infectious diseases, innovator companies and manufacturers see few incentives to invest in developing and producing the products. Among the twenty endemic infectious diseases shown in Table 1, only one has an effective vaccine available. Most diagnostics that do exist cannot be properly used in developing countries. Available medicines for infectious disease have safety and efficacy limitations. Other than HIV/AIDS medicines and dengue vaccines, most of the needed tools for these diseases could not yield enough of a market return to make them an appealing investment[3].

Table 1: Current Repertoire of Vaccine, Diagnostics, and Drugs for Endemic Diseases

	Vaccine	Diagnostic	
HIV/AIDS	No	Yes	Yes –treatment but not cure
Tuberculosis	No	No – low tech, rapid dx needed	Yes – treatment and long timeline to cure
Malaria	Yes – limited protection	Yes	Yes – one dose cure needed
Buruli Ulcer	No	No – clinical symptoms	Yes – 80% cure rate but oral treatment sought
Chagas Disease	No	No	Yes – better drugs needed
Dengue and Chikungunya	Yes (Dengue)	Yes	No
Dracunculiasis	No	Yes – with limitations	No – cure is through worm extraction
Echinococcosis	No	No	Yes – in addition to surgery
Endemic treponematoses	No	No – clinical symptoms	Yes
Foodborne trematodiases	No	No	Yes
Human African trypanosomiasis	No	Yes – with limitations	Yes – better drugs needed
Leishmaniasis	No	Yes	Yes – oral drugs with few side effects needed
Leprosy	No	No – clinical symptoms	Yes -
Lymphatic filariasis	No	Yes – with limitations	Yes – better drugs needed
Oncocerciasis	No	Yes – with limitations	Yes – treatment but not cure
Rabies	Yes – post bite	No	No
Schistosomiasis	No	Yes – with limitations	Yes
Soil-transmitted helminthiases	No	Yes – with limitations	Yes – treatment not cure
Taeniasis/Cysticercosis	No	No	Yes – drugs needed for neuro stage
Trachoma	No	No	Yes

The need for innovation in GHPD efforts goes beyond just expediting the development of new drugs. We need to be improving upon the products already on the market. Many of the available treatments for infectious diseases were developed decades ago and their effectiveness is diminishing due to anti-microbial resistance (AMR)[5]. This is not a hypothetical threat. From the 1970s through the 1990s, malaria deaths in Africa, and globally in children under 5, rose sharply due to resistance to the affordable drug chloroquine[6]. The compounding effect of increasing AMR and a slowdown of new antibiotics discovery have created new challenges for treating infectious diseases.

To counter the lack of a commercial incentive, governments and foundations are increasingly partnering with industry to convert important scientific research into needed products. This investment has grown dramatically to US $3.2 billion in 2013[7], and the pipeline of products has increased substantially over the past two decades. But that level has plateaued and this pipeline needs to grow if we are to address the demand. New innovation is vital to control, eliminate and eradicate infectious diseases that primarily affect those who are poor.

Case Study Box:

MenAfriVac Success

Sub-Saharan Africa is known for its consistent outbreaks of meningitis within thirteen countries composing "the Meningitis belt." MenAfriVac was developed through a public private partnership and introduced in the affected countries in 2010. A dramatic decrease in cases was seen immediately[4].

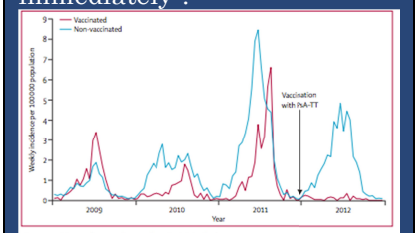


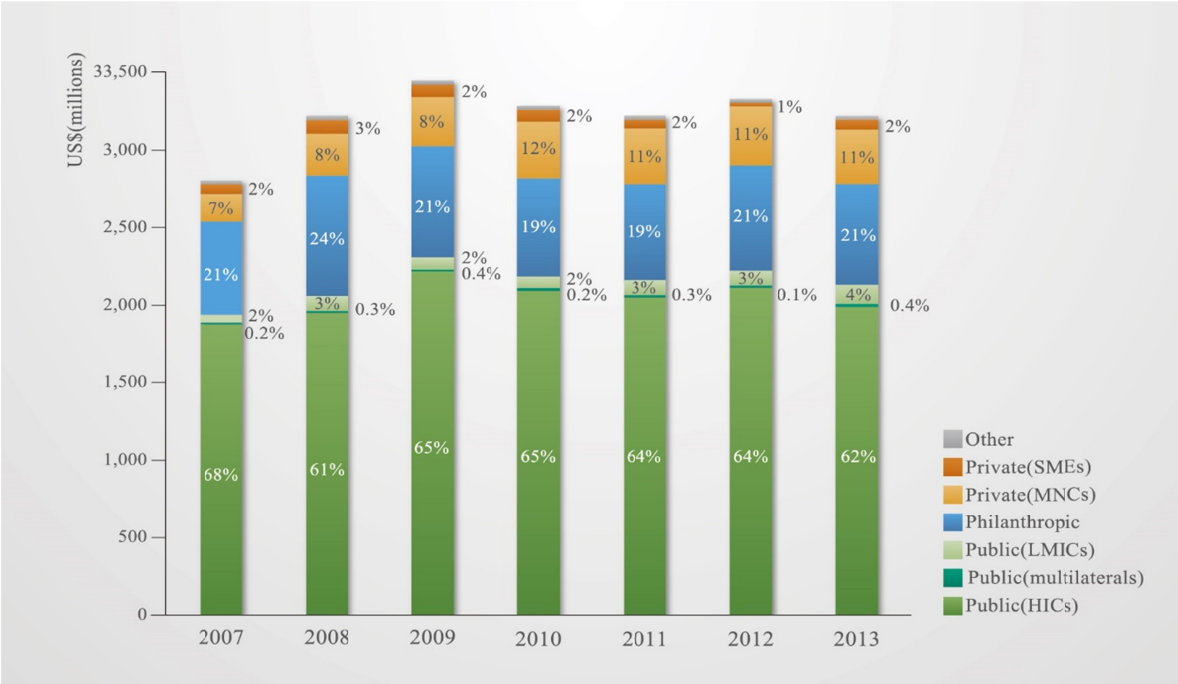
Figure 3: Incidence of reported cases of meningitis in Chad, 2009–12
Vaccination with PsA–TT was undertaken in patients aged 1–29 years at the end of 2011 (arrow).
PsA–TT=serogroup A meningococcal polysaccharide–tetanus toxoid conjugate vaccine.

GHPD: An Overview of the Product Development Landscape

There is no one entity in the public or philanthropic sectors that manages the innovation pipeline for infectious diseases. The coordination of activities and the sharing of knowledge are largely bilateral rather than global, and agreements are non-binding. Early stage innovation can be driven by an individual funder or a partnership of organizations, investors, and countries. Below is an outline of the various sectors and entities that are investing in and developing new GHPD.

Today, Over 80% of the GHPD efforts are funded by governments and foundations[8] (Figure 1), with the vast majority of funding from the world's high-income countries (HICs). In 2013, the United States government was the largest funder of global health R&D – investing more than ten times The European Commission, the second top funder (Figure 2).

Figure 1. Total R&D funding by sector 2013



National Governments

National governments primarily finance global health R&D in three different ways: 1) through investigator initiated research led by the government (24% of total funding), 2) through investigator initiated grants to research institutions and companies (59% of total funding), and 3) by granting money to Product Development Partnerships (PDPs) and other intermediaries (17% of total funding). The bulk of government funding is often directed to the early development phases of pharmaceuticals, with less money being devoted to later-stage clinical trials

Figure 2. Top Public R&D Funders 2013

Country	US$(millions)							2013 % of total	2007-2013 trend
	2007	2008	2009	2010	2011	2012	2013		
United states of America	1,381	1,402	1,617	1,540	1,507	1,605	1,432	67	
Europian Commission	132	143	130	101	117	104	123	5.8	
United Kingdom	99	101	141	155	125	88	120	5.6	
France	17	32	53	44	67	59	92	4.3	
India		38	25	39	43	43	50	2.4	
Germany	13	4.1	38	41	35	61	49	2.3	
Australia	25	34	31	34	43	54	28	1.3	
Netherlands	37	30	32	20	27	17	26	1.2	
Canada	22	26	19	11	11	20	22	1.0	
Brazil	27	29	38	13	14	25	20	0.9	
Switzerland	8.0	5.1	9.1	16	16	18	18	0.9	
South Africa	4.1	5.3	7.5	8.1	7.3	5.9	13	0.8	
Subtotal of top 12^	1,826	1,909	2,182	2,041	2,048	2,113	1,994	94	
Total public funding	1,946	2,061	2,323	2,194	2,163	2,232	2,128	100	

In the U.S. and other HICs, global health R&D spending are spread across multiple agencies, which can lead to cumbersome and inefficient processes. Advocacy groups have called for a "whole-of-government approach for global health R&D" to reduce silos, and increase transparency and information-sharing across agencies. When this issue is expanded to multinational global health efforts, it quickly becomes apparent how exceedingly difficult it is to align toward a single objective.

In addition to providing financial support, governments can also create policy initiatives, such as the Orphan Drug Legislation (ODL) and the Priority Review Voucher (PRV), which both have enabled the development of products for rare diseases and could foster greater GHPD.

Philanthropy

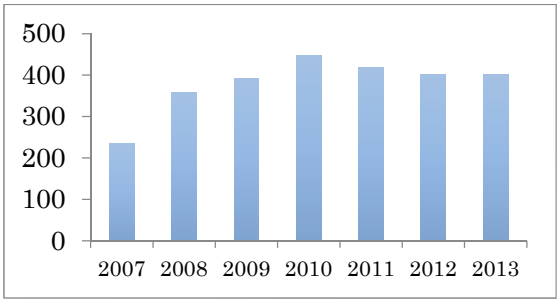
Philanthropic investments in global health R&D comprise a little more than one-fifth of total funding. And just two foundations – the Wellcome Trust and the Bill & Melinda Gates Foundation— account for nearly all of this contribution[9]. Both organizations have broad global views of the product development pipeline for diseases they fund, conduct considerable due diligence prior to funding, and continue to influence product decisions for funded projects.

At the Gates Foundation, grantmaking decisions are usually made internally by Foundation staff, although some funding decisions may be outsourced to Product Development Partnerships (PDPs) or organizations such as the Foundation for NIH, which manages the Grand Challenges program. The Wellcome Trust has an internal staff structure that's similar to the Gates Foundation and many of their funding decisions are made by external committees.

Industry

Biotechnology and pharmaceutical companies are integral to product development and innovation. Prior to the 1980s, these companies played an enormous role in developing life-saving treatments for infectious diseases, but the epidemiological transition to non-communicable diseases and the push for profits changed their positioning. Citing high research costs, poor returns, and onerous regulations, drugmakers have lagged in finding needed treatments for the infectious diseases plaguing dozens of poor countries.

Figure 3. Industry Funding for GHPD



In the late 1990s, the public sector emerged as a strong partner to industry, a move that dramatically sparked engagement and activity. In FY 2013, pharmaceutical companies spent $400 million on global health R&D and that number continues to increase through expanding research initiatives[10] (Figure 3).

Product Development Partnerships

Product Development Partnerships (PDPs) are independent, nongovernmental organizations that manage large product portfolios in a number of diseases and interventions. Over 16 PDPs[11] cover the focus areas of HIV, malaria, tuberculosis and neglected tropical diseases (NTDs). PDPs have been termed "intermediaries" as they collect and consolidate funding, primarily from national governments and philanthropies, and then partner with academic researchers and private companies. The primary advantages of the PDPs are 1) understanding and working across the pharmaceutical discovery, development, delivery continuum, and 2) the speed and flexibility to fill gaps and partner with minimal bureaucracy. About 20% of total funding ($482 million) from charities and governments was programmed through PDPs in 2013[12].

Purchase Funds

Purchase funds play an important role in shaping the product market for needed drugs, vaccines and diagnostics as they provide a vital procurement link that has been missing from other efforts. The creation of entities such as the Global Alliance for Vaccines and Immunization (GAVI) and the Global Fund for AIDS, Tuberculosis and Malaria in the early 2000s brought billions of dollars of financing to the improvement of health delivery systems and purchasing power to poor countries for lifesaving drugs, vaccines, and diagnostics.

Over 500 million children have received DPT-HIB, Hepatitis B, measles, rotavirus, and pneumococcal vaccines thanks to GAVI, saving 7 million lives. GAVI follows the Advanced Market Commitment (AMC) process that provides an assured market to pharmaceutical companies that will create and mass produce pneumococcal vaccines that meet developing country needs.

New Models of Global Health R&D

The Global Health Innovative Technology (GHIT) Fund is a unique collaboration between the

Government of Japan, five of Japan's largest pharmaceutical companies, the Bill & Melinda Gates Foundation and the United Nations Development Program. Founded in 2013, the GHIT Fund has increased Japan's R&D contributions to infectious diseases more than five-fold in one year, from US$2.4 million in 2012 to more than US $12 million in 2013.

While the GHIT Fund views global health as an investment with tangible returns, it treats its R&D grants as an investment without a financial return. The pharmaceutical companies that contribute to GHIT are encouraged to work across sectors and leverage international partnerships to develop new products.

In just two-and-a-half years since it was formed, GHIT has invested in the development of more than 40 new products, with allocations totaling more than US $50 million. As of 2015, GHIT is advancing six clinical trials in Burkina Faso, the Republic of Côte d'Ivoire, Tanzania, Uganda, Thailand, Peru, and Bolivia, and two more clinical trials will begin in 2016. The first product is scheduled to complete development in 2018. As a novel model for funding product development, GHIT is transforming the portfolio for infectious disease products for Japan and the global community.

Similar to GHIT, the Global Health Investment Fund (GHIF), headed by the Bill & Melinda Gates Foundation, aims to increase collaboration between investors and provide long-term funding for GHPD[13]. Launched in late 2013, GHIF will finance late-stage clinical trials of high-impact drugs, vaccines, and diagnostic tools, specifically focused on reducing childhood death rates. Sponsors and partners include pharmaceutical companies, charities, investment banks, and governments. GHIF has yet to publicly announce its first investment.

Global Health R&D Ecosystem

Global investments in technology and R&D are pivotal to supporting innovation, and must be well-managed to effectively create and produce life-saving treatments. We need to find innovative methods to translate and customize health interventions and products to local settings, and engage communities so that these treatments are administered in the long-term.

The World Health Organization plays a substantial role in this effort. In some cases, it occasionally serves as de facto regulators for countries lacking a recognized national regulatory agency, and frequently creates policies for the use of new drugs, vaccines and diagnostics. Both of these processes are essential for moving an infectious disease drug, vaccine or diagnostic into the marketplace. But few would call these processes innovative or even efficient.

On a more global scale, there is no mechanism for creating and maintaining a "rational" portfolio of pharmaceutical products. While that work is in the domain of the funders and it is unrealistic to expect the champion of a specific new drug or vaccine to step back from their proprietary interests, more can be done to better coordinate a global portfolio to reduce duplication and focus resources on the highest value projects.

Conclusion

The leading developed nations and philanthropies have identified innovation as a key strategy for controlling, eliminating, and eradicating infectious diseases. The global ecosystem that would align those strategies and bring efficiency to that effort does not currently exist.

The emergence of new institutions, partnerships, and funding streams focusing on infectious diseases is proof that there is political will and hope for the eradication of these maladies.

However, it is still not sufficient. A significant increase in funding for the discovery, development and delivery of new drugs, vaccines and diagnostics and enhanced global collaboration would create a much-needed sea change in GHPD.

The scientific community, especially in countries heavily burdened by infectious diseases, needs a more enabling environment to access resources and share knowledge that can contribute to new treatments and disease control efforts. Partnerships need to be forged and sustained to capitalize on resources and to build capacity for R&D on emerging infectious diseases like Ebola, MERS, and SARS. We need to view all global infectious diseases as a public health emergency that warrants a coordinated international response.

Appendix B: Interviews with Top Global Health Product Development Funders

I. Objective

Interview top funders in global health product development (GHPD) to better understand how GHPD fits into their overall infectious disease strategies, how they convert strategy into grants to product developers, and the barriers—"bottlenecks"—they and their grantees experience.

II. Methodology

This study was conducted with an inductive approach using qualitative research. Seven interviews were conducted using a semi-structured interview method. The data were collected, coded and analyzed for key themes. The results are presented in this appendix.

A. Interview Selection

The target groups consisted of 1) top public GHPD funders who are G7 members, and 2) top philanthropic funders.

Public Funders

The top ten public funders were identified using the 2014 G-FINDER study "Neglected Disease Research and Development: Emerging Trends"[14]. Six of the top ten funders are members of the G7. Invitations were issued to the six G7 members, and five were interviewed. The interview with Canada was unable to be interviewed due to scheduling. The only G7 members not among the ten largest public funders in 2013 were Japan and Italy.

Ten Largest Public R&D Funders

1. United States
2. European Commission
3. United Kingdom
4. France
5. India
6. Germany
7. Australia
8. Netherlands
9. Canada
10. Brazil

Ten Largest Funders who are G7 Members

1. United States
2. European Commission
3. United Kingdom
4. France
5. Germany
6. *Canada

The five G7 members interviewed comprise 86% of public GHPD funding, and 57% of

total funding.

Philanthropic Funders

The top ten philanthropic funders were identified using the 2014 G-FINDER study[15]. Funders who contribute more than 10% of the total philanthropic funding were chosen for the study. The Bill & Melinda Gates Foundation (75%) and the Wellcome Trust (19%) were invited to participate.

Ten Largest Philanthropic R&D Funders

1. Gates Foundation
2. Wellcome Trust
3. Gavi
4. MSF
5. Fundacio La Caixa
6. UBS Optimus Foundation
7. MMRF
8. amfAR
9. Medicor Foundation

Philanthropic R&D Funders (>10% of total sector)

1. Gates Foundation
2. Wellcome Trust

The combined funding of the respondents is US$2.48 billion or 77% of the total 2013 funding.

B. Interview Methodology

Interview Guide

High-level experts in government agencies and the two philanthropies were identified through GHIT. An interview guide was developed based on direction from the Global Health Working Group and used for all interviews. Three questions guided the research:

1. What is the role of product innovation in the control, elimination, and eradication of infectious diseases for different funders?
2. What approaches do different funders use for the discovery, development and delivery of product innovation?
3. What are the bottlenecks to achieving these product innovation strategies?

Data Collection

Seven interviews were held. Qualitative data were collected in one to one, semi-structured interviews via telephone in August – September 2015. An independent researcher with over 20 years of experience in GHPD was hired to conduct the interviews and the analysis. Each interviewee gave verbal informed consent to participate in the study prior to being interviewed.

> *This semi-structured interview is aimed at learning more about your organization's strategy and decision-making process for funding of the discovery, development, and delivery of global health innovation. The information from the interview will be used solely to inform the work of the GHWG. No presentation or discussion of an individual organization's strategy and decision-making processes would be shared outside the use of the GHWG. A public report summarizing aggregate observations may be developed. Do you consent to be interviewed?*

The notes were typed into the interview guide by the consultant during the interview, and were reviewed for completeness and clarity immediately afterward. A daily interpretive analysis was conducted on the interview days to ensure integrity of the data with the passage of time.

Data Analysis

A thematic analysis approach[16] was used to analyze and interpret the data. Provisional insights referencing the three guiding questions were recorded, and a list of initial codes was developed. Following completion of the interviews, the raw interview notes were coded. The primary codes included:

- The role of product development in the control of infectious diseases
- Methods for determining product development strategy
- Sources of information used for product development strategy formation
- Methods for providing funding to product developers
- Decision-making processes for product development project grants
- Sources of information used for grant-level decision making
- Lessons learned from Ebola
- Barriers or "bottlenecks" to converting their strategy into results
    - Funding
    - Regulatory
    - Collaboration
    - Knowledge sharing
    - Links to Delivery/Target Product Profiles (TPPs)
    - Focus and momentum

For coding of the barriers, each phrase was first coded as "barrier." These phrases were then sub-coded as to the type of barrier as noted above. The barriers were analyzed for frequency of occurrence across interviews.

III. Results

A. Global Health Product Development Strategy Formation

Focus on infectious diseases

Each government and foundation interviewed devotes considerable resources to global health, and infectious disease control, elimination, and eradication figure prominently in their programs. The stated rationales for significant investments in infectious disease differ, but fall into two categories: 1) ensuring global stability and security, and 2) addressing global inequities. This rationale is driven by political imperatives, as in the case of Ebola, and by evidence of disease burden, as in the cases of HIV, tuberculosis and malaria.

> *"Why does the government fund anything? To remain stable and productive."*

> *"Our approach is based on solid epidemiology. We examine the data, and decide where to intervene to make the most impact."*

Focus on innovation

Each government and foundation interviewed features innovation prominently in its strategies to control, eliminate and eradicate infectious diseases. All stated that the available tools to fight these diseases are inadequate; effective vaccines are not yet available for the biggest killers, the

available drugs do not fit modern technology product profiles, and very few of the powerful diagnostic technologies available are suitable for the developing world. In addition, the respondents represent countries and foundations with extremely strong research bases. The desires to expand the impact of those scientific resources beyond national borders and to help the poor were cited frequently as reasons to focus on innovation.

> *"[W]e try to use R&D as a basis to propel innovation and commit ourselves to internationalizing our innovation system."*

> *"Our strategy is based on scientific approaches. Let's develop the best science and see where that leads us to impact on a disease."*

Respondents stressed that progress against infectious diseases has been made, but innovation is necessary to maintain control efforts and to expand toward elimination and eradication. The theme of "market failure" was cited frequently by respondents as the reason that government and philanthropic involvement and funding are critical.

> *"We have made progress but we have major gaps in the tools needed to fight infectious diseases."*

> *"[N]o vaccine for TB, no malaria vaccine with high efficacy, no single dose radical cure for malaria. We have not yet cracked the science that will get to the solutions."*

> *"For poverty-related diseases, there is a market failure. The proper incentives for the pharma industry do not exist."*

How innovation strategies are developed

Government respondents report that in addition to scientific evidence, political interests are major drivers of their innovation strategies. Politicians decide strategy at the highest levels, and provide direction to the agencies charged with controlling infectious diseases. Advocates lobby politicians and government agencies for their ideal solutions. The political agenda is melded with the scientific expertise of agency leaders to form specific innovation strategies. Examples cited include:

- United States - The primary themes of government are security and stability so emerging threats such as Ebola are a political priority.
- France - The politicians in France pushed for innovative financing, leading then-president Jacques Chirac to propose an airline tax to fund global health R&D. This money (over US $1 billion) is provided to UNITAID, which grants money to specific projects.
- United Kingdom – In the product development space, the U.K. government highly values collaboration with other donors.
- European Commission – The EC focuses on funding science that is conducted by partnerships between European countries.

The two largest philanthropic funders of GHPD are the Bill & Melinda Gates Foundation (U.S.) and the Wellcome Trust (U.K.). Their strategies are formed internally by Trustees and staff, with varying degrees of external input. Both foundations described their strategies as evidence based, relying on rigorous analysis to drive their decision-making.

All the responses on this high-level strategy formation cited drivers that are primarily internal to the government or foundation. It was not until specific product development strategies were

discussed that respondents cited the importance of external sources of information and collaboration.

B. Approaches to the Discovery, Development and Delivery of new Drugs, Vaccines and Diagnostics

Each funder reported using different mechanisms to convert its innovation strategies into product development activities. Some work across the spectrum of product development from discovery through delivery, while others focus primarily on the discovery and development phases.

The largest funders reported using a mix of intramural funding, investigator-initiated grants, contracts with companies and suppliers, and grants to product development partnerships (PDPs) to achieve their innovation strategies. Smaller funders, or those with few technical staff, report primarily programming their funding through PDPs because they have their own technical staff and many independent experts advising them. Funds like UNITAID and GHIT also serve this role.

The majority of government respondents stated that they have more than one agency in the country funding product development. Research agencies usually fund more basic research and discovery activities across the spectrum of infectious diseases, and are less often funders of late stage clinical trials. The overseas development assistance agencies often fund product development aimed specifically at new vaccines, drugs and diagnostics. Biosecurity agencies focus resources on emerging diseases and emerging threats. It is common for several agencies in one country to be funding similar R&D work with little internal communication.

The funders were asked how they obtain information about the global portfolio of infectious disease products. Responses were similar among funders. They reported that technical staff attend scientific meetings and stay abreast of the scientific literature. These activities provide numerous opportunities for bilateral talks each year when funders exchange information and, in some cases, set up collaborations. WHO frequently convenes meetings on product development topics; for example, they convened meetings around the Phase 3 trial design and regulatory review of the GSK malaria vaccine, and they convened a meeting of donors and product developers working on Ebola R&D in 2015. Several respondents pointed out that funders use a very similar group of scientific experts for guidance and review and that this helps to carry information between different funders. When asked if they felt there was duplication in the global portfolio, respondents said they feel there may be a small amount, but stressed that some amount is important to increase scientific validity.

C. Barriers to Global Health Product Development

Respondents were asked to identify the major barriers to achieving their GHPD strategies. This was first asked as an open-ended question. Following this question, a specific follow-up question was asked on the effectiveness of current knowledge sharing and collaboration efforts around the management of the global portfolio of drugs, vaccines and diagnostics. The barriers are presented in order of priority as determined by the frequency with which they were cited by respondents.

Funding

Lack of sufficient funding for R&D was cited as the most significant barrier by each

interviewee. Raising new funds was seen as difficult as there are many competing needs and priorities for governments. The view expressed by many was that more money in the system would provide greater returns than any other potential intervention.

> *"It is a long and expensive process to develop drugs, vaccines, and diagnostics. The costs are a problem over time."*

> *"Industry is not set up to automatically engage based on their business model. We have to be creative to incent their involvement."*

> *"The bottlenecks identified are usually things money can solve."*

Regulation

One specific policy arena cited by several funders as a barrier is the regulatory ambiguity in the licensure of products that will be used in developing countries that lack a strong national regulatory agency. One respondent noted that the regulatory process for malaria vaccines was being created as the lead vaccine was in clinical trials. Several respondents noted that regulatory processes are accelerated when faced with outbreaks like Ebola, but for endemic diseases and AMR they are still a source of significant delays.

> *"The most pain is in countries that don't have NRAs [National Regulatory Authorities] and experience with clinical trials."*

> *"It [international regulatory system] has never worked well. We should take the lessons learned from Ebola. Maybe the G7 could be a key player in this."*

Review Processes

Government respondents explained that they are directly accountable to politicians and citizens for their investments. Part of that accountability is addressed through peer review processes. Respondents said that peer review creates a conservative approach where it is challenging to introduce new ideas, especially when the science behind the product is very complex. Two respondents expressed that the research community makes it challenging to fund a smaller number of large projects (needed to solve complex problems) because of the fear of losing funding. Other respondents stressed that each "disease community" operates very differently and it is hard to generalize from one to the next. Nearly all funders interviewed used the peer review process to determine funding decisions, but many expressed concerns that this may not be the best way to make product development decisions.

> *"Many reviewers are siloed in fields they know very well, but they do not have the multi-disciplinary view required for product development."*

Linkages to Delivery

Many of the funders of innovation stated that they have a more natural fit with the discovery and development phases and not as much with the delivery space. They rely on others to develop Target Product Profiles aimed at bringing the field's needs into product development

considerations. There is a feeling expressed by some respondents that the TPPs do not really represent the realities of the situations in clinics and hospitals but rather represent a researcher's interpretation of what is needed. Some funders worry that the TPP process may not fully take into account the psychosocial factors that can make or break the introduction and scale-up of a new intervention. This lack of confidence limits their ability to use the TPPs in product development decision making.

Momentum

Respondents noted that maintaining focus and momentum on initiatives in a political environment could be very challenging. Several respondents from government agencies stated that the political environment tends to react to issues that have the greatest public concern. It was noted that significant funds were allocated to Ebola during the height of the outbreak, but that those funds are diminishing as the current risk recedes. As most of the burden of infectious diseases is in developing countries and most of the funding is in high-income countries, the public accountability for that spending will never be as strong. Respondents stressed the importance of the focus that the G7 could bring as it would raise the accountability level above that of any one nation.

> *"All are enthusiastic at the beginning. The problem is maintaining momentum over time."*

> *"Pandemics are disruptive. This is also true for malaria and more standard diseases. There is a huge imbalance of lives lost – we don't want to over focus on pandemics."*

Collaboration and Knowledge Sharing

Specific questions on barriers in collaboration and knowledge sharing were asked following the open question on barriers, as these two areas have been a focus for the G7.

All respondents stressed that any proposed collaboration solutions be framed in terms of the problem that needs to be solved. Are efforts being duplicated? Can resources be invested more efficiently? Are there critical gaps that need investment?

Several respondents stated that their own governments or organizations are working to ensure a coordinated approach within their country or organization, but few cited known problems of significance when examined globally. Two respondents felt there is some duplication of effort in product development but could not name specifics. Others stated that they did not think there was a problem with duplication of activities and one simply stated that there is no evidence this is a problem. Several respondents stressed that some amount of duplication is healthy competition, and raises the validity of the results.

On the subject of duplication, respondents were more concerned with what they viewed as duplication in the "global architecture." Examples of duplication of collaboration and information sharing efforts were cited, such as duplication of effort for the Global Health Primer and the Global Health Observatory. Funders are expected to participate in these efforts, and several of those interviewed were frustrated by the time and attention needed to make those agreements and try to make their reporting systems interoperable.

Three cautions were expressed in the interviews about creating new collaboration and

knowledge sharing platforms. The first is the view that most initiatives aimed at “coordinating” the players and activities almost always add work and time without bringing the desired benefits of efficiency and effectiveness. The second was that any additional coordinating mechanisms should build on existing initiatives rather than creating something new and should have WHO at the center. The third was that most funders would not pool funds, or turn over their decision making to third parties. In addition, several respondents questioned whether the behaviors and decisions of the dominant funders would actually change in response to additional information or collaboration initiatives.

Respondents cited an “enormous amount of noise” in the system around new funding mechanisms, new frameworks, new collaboration platforms, etc. The conflicting briefings provided by advocacy groups to policy makers contributes to the churn, and dilutes the focus and energy of funding agencies.

Reference

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http://apps.who.int/ebola/current-situation/ebola-situation-report-18-november-2015

[2] WHO, 2015a.

[3] MSF, 2015, p.6-7.

[4] Under IHR regulations, a PHEIC is defined as an extraordinary event which is determined (i) to constitute a public health risk to other States through the international spread of disease and (ii) to potentially require a coordinated international response.

[5] SG Statement, 2015.

[6] However, it has also been indicated that a segmented governance structure is not necessarily an obstacle, and it also has the advantage of robustness in terms of flexibility and adaptability (Keohane and Victor (2011), Shiroyama et al (2011)).

[7] Briand et al (2014), Gostin (2014), Gostin and Friedman (2014), Kruk et al (2015), Friedman,and Hougendobler (2015) Burkle (2015), Heyman et al. (2015), Garrett (2015), etc.

[8] Formerly, the Institute of Medicine (IOM).

[9] The WHO Ebola Interim Assessment Panel (2015, p.15, Box) pointed out the following as the reasons for the WHO's PHEIC delay: (1) country factors (weak health systems, insufficient community mobilization, unsafe practices in burials, etc.), (2) country politics (concern about political and economic impact), (3) WHO politics/dilemmas (concerns about challenging governments, understandable worries about economic and trade implications, hesitation since the H1N1 response, lack of data, etc.), (4) WHO's organizational culture (it has a technical, normative culture, not accustomed to dealing with such large-scale, long-term and multi-country emergency responses occurring in member states), and (5) international community (it failed to heed warnings because previous Ebola outbreaks were small and contained; there was no intermediate level of warning between outbreak and the declaration of a PHEIC).

[10] WHO stated that it does not fully agree with the WHO Ebola Interim Assessment Panel's assessment that a PHEIC determination was delayed. While it acknowledged "the understanding of the international community is that a PHEIC determination should act as an international alert signal for disease outbreaks of this nature," it stated that this understanding is not "entirely accommodated by the current IHR criteria." but it supported the recommendation to consider intermediate alert to mobilize international response (WHO Secretariat, 2015, para.10)

[11] Density of physicians (total number per 1000 population, latest available year)
http://www.who.int/gho/health_workforce/physicians_density/en/

[12] Coordination among international organizations is carried out by the Inter-Agency Standing Committee (IASC), which is chaired by OCHA's Under-Secretary-General and Emergency Relief Coordinator (OCHA serves as the Secretariat).

[13] As for the nationalities of staff affiliated with the regional office in the African, United States and European regions, 80% have been hired from within the same region (by contrast, WPRO is more diversified, having employed approximately 40% of its staff from within the same region, somewhat less than 30% from Europe and 16% from the United States). This point relies on research conducted by Kayo Yasuda.

[14] The Director General prior to Gro Harlem Brundtland attempted to strengthen coordination between Headquarters and the regional offices during her term, but there is still a low level of movement of personnel among the regional offices and between the Headquarters and regional offices. For instance, in 2013, approximately 80% of personnel transfers were within the same regional office, 15% between Headquarters, and movement among the regional offices was a mere 7%. This point relies on research conducted by Kayo Yasuda.

[15] The WHO's medium-term strategic plan for 2008-2013 was revised in the backwash of the 2008 financial crisis, resulting in the initially allocated budget for IHR implementation in 2010-2011 being slashed by roughly half (the original USD98 million was reduced to USD54.84 million). WHO, 'Proposed Programme Budget 2010-2011', 2009, pp.3-5. This point relies on research conducted by Kayo Yasuda.

[16] The MSF General Director stated, "WHO should have been fighting the virus not MSF."

[17] In fact, after the PHEIC declaration, carriers suspended flights. So, from the second meeting of the IHR emergency committee and thereafter recommendations were repeatedly issued that restrictions on overseas travel and trade, particularly bands on travel abroad and flights, lead to economic loss

and isolation of the country where the outbreak occurred (2nd meeting), and hinder personnel responding to Ebola (4th meeting), so such measures should not be taken. Statement on the 4th meeting of the IHR Emergency Committee regarding the 2014 Ebola outbreak in West Africa 21 January 2015.

[18] At the time of H1N1, criticism was leveled that the agency issued a PHEIC even though the fatality rate was a mere 0.2% (Gostin, 2014).

[19] Polio is also an infectious disease but as experience has been accumulated in responding to it, the response has also been implemented in cooperation with the humanitarian sector. This was not the case for Ebola.

[20] WHO Ebola Interim Assessment Panel (2015) also stated it was clear that leadership at the UN Secretary General level was needed in September 2014. However, it goes on to state that when large-scale health crises arise in the future, the UNMEER model is not appropriate and strongly opposes the establishment of a UN Mission. It points out that an emergency coordinator may be set up at the regional level for operations and that the Sub-regional Ebola Operation Coordination Centre (SEOCC) could have coordinated the Ebola response. (WHO Ebola Interim Assessment Panel (2015), para77-81).

[21] The need for emergency grading levels is also recommended in the WHO Panel's report. A PHEIC determination is a single binary decision, and the Panel recommends that the IHR Review Committee for Ebola consider the possibility of alerts at an intermediate level to mobilize the international community (WHO Ebola Interim Assessment Panel, 2015, para.23).

[22] Although established within the WHO, it is an independent organization. It provides centralized management of units and functions at all levels, national, regional and the WHO Headquarters. Discussions have been held about the necessity for having this program cite PHEIC cases and IHR contact points (WHO Advisory Group, 2015, para. 6)

[23] In September, the WHO and World Bank held a meeting on global pandemic financing. Also, the WHO's Contingency Fund is scheduled to be discussed at a financing dialogue in November 2015. Other modes of structuring financing with humanitarian cases is being coordinated with IASC (WHO Secretariat, 2015, para. 30).

[24] This point relies on research conducted by Sayako Kanamori , Jonas Kemp and Charlotte Sauter.

[25] (1) national legislation, policy and financing, (2) coordination and NFP communication, (3) surveillance, (4) response, (5) preparedness, (6) risk communication, (7) human resources, (8) laboratory services.

[26] Although it is to be established soon, issues have also been raised as to what extent it will be able to carry out its activities with a staff of 11 personnel and funding of 6.9 million.

[27] This point relies on research conducted by Sayako Kanamori , Jonas Kemp and Charlotte Sauter.

[28] There have been discussions that this sort of approach may be useful in preventing surrounding countries from adopting overly restrictive measures on the movement of people and goods during IHR implementation.

[29] Although the response will also be limited using conventional means for procuring funding, the defense sector is also a potential source of public funding. The US government's budget for health security in 2016 is $13.7 billion, of which $2.5 billion has been allocated for bio-defense, pandemics and other all-purpose preparedness. It has been pointed out that such a budget allocation may also be useful in developing vaccines. This point relies on research conducted by Sayako Kanamori , Jonas Kemp and Charlotte Sauter.

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