From: Morens, David (NIH/NIAID) [E]
Sent: Tue, 12 May 2020 16:28:52 +0000
To: Taubenberger, Jeffery (NIH/NIAID) [E]; Howard Markel; Peter Daszak
Subject: Fwd: Final Decision made for mBio00812-20R1

Sent from my iPhone
David M Morens
OD, NIAID, NIH

Begin forwarded message:

From: "mbio@asmusa.org" <mbio@asmusa.org>
Date: May 12, 2020 at 12:25:11 EDT
To: "Morens, David (NIH/NIAID) [E]" (b)(6)
Subject: Final Decision made for mBio00812-20R1
Reply-To: <mbio@asmusa.org>, <mbiojournal@gmail.com>

Dear Dr. Morens:

Here is a copy of the decision letter for manuscript mBio00812-20R1 ("PANDEMIC COVID-19 JOINS HISTORY'S PANDEMIC LEGION") by David Morens, Peter Daszak, Howard Markel, and Jeffery Taubenberger, for which you were a Contributing Author.

Sincerely,

Arturo Casadevall
Editor in Chief, mBio

Subject: mBio00812-20R1 Decision Letter

May 12, 2020

Dr. Jeffery K Taubenberger
National Institute of Allergy and Infectious Diseases, NIH
33 North Drive
Room 3E19A.2, MSC 3203
Bethesda, MD 20892-3203

Re: mBio00812-20R1 (PANDEMIC COVID-19 JOINS HISTORY'S PANDEMIC LEGION)

Dear Dr. Taubenberger,

I am pleased to inform you that your Perspective has been accepted for publication in mBio.

Thank you for contributing such outstanding work. If you have any questions, feel free to contact our editorial office.

Sincerely,

Arturo Casadevall
Editor in Chief, mBio
mBioEditorInChief@asmusa.org
(Signing for the editors)

Editor comments:

The authors have addressed the reviewers'/editors' comments satisfactorily.

Invited Editor:

The authors have addressed all raised comments.

Staff comments:

Before publication, your manuscript will be checked by the mBio staff to make sure that all elements meet the technical requirements. The mBio staff will contact you if anything needs to be addressed before copyediting and production can begin. mBio articles are published online as soon as they are processed, so delays should be minimal.

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Please contact us if you have any questions.

Maisha Miles
Managing Editor, mBio

Rob Arthur
Assistant Managing Editor, mBio

mBio@asmusa.org

American Society for Microbiology
1752 N St. NW
Washington, DC 20036
(202) 737-3600

From: Morens, David (NIH/NIAID) [E]
Sent: Mon, 23 Mar 2020 19:27:32 +0000
To: Howard Markel
Cc: Markel, Howard; Taubenberger, Jeffery (NIH/NIAID) [E]; Peter Daszak
Subject: Re:

It's an honor to be a co-author with you! The second time, I think

On a different subject, somewhat different at least, the time is right and ripe, now before someone else does it, to write on the parallels between the beginning of 1918 pandemic and the beginning of this one, from the point of view of epi, PH responses, public and fear responses, and so on

It might be that one person should do that or more than one. Your name is the first that comes to mind. If you can do it with or without others, I think you should. If someone does it first it is bound to be not as good. I think John Barry and Laura Spinney did good stuff, but John got some of the science wrong and neither can see things from the broad biomedical perspective.

Just tryin' to put some pressure on you.

My best to you, and I am grateful you made the effort at a difficult time to get this recent papers done. David

Sent from my iPhone
David M Morens
OD, NIAID, NIH

> On Mar 20, 2020, at 16:33, Howard Markel (b)(6) wrote:
>
> David,
> This is terrific and a real delight to read. Thanks so much for including me—Howard
>> On Mar 20, 2020, at 4:28 PM, Markel, Howard (b)(6) wrote:
>>
>> <PANDEMIC COVID 03 20 20 DMM final draft.docx>
>

From: Morens, David (NIH/NIAID) [E]
Sent: Thu, 19 Mar 2020 17:09:00 +0000
To: Taubenberger, Jeffery (NIH/NIAID) [E]
Cc: Howard Markel; Peter Daszak
Subject: Re: Pandemic history manuscript, tracked

Guys, I am totally jammed at the moment but should have time to over by tomorrow. Any one who has time please charge on! D

Sent from my iPhone
David M Morens
OD, NIAID, NIH

On Mar 19, 2020, at 13:06, Taubenberger, Jeffery (NIH/NIAID) [E]
(b)(6) wrote:

Hi guys,

I did a read through with some additional tracked changes and saved a new version here. With tracked comments from Peter, Howard, and me, it is looking a bit messy. David, do you want to have the next go at it? It might be easiest to make an accepted version for the next round of edits.

We have all suggested references which are great. It will be easy to add those with endnote when we get to a closer to final draft. I am working from home today and do not have access to my endnote library.

Thanks all,

Jeff

<HMPANDEMIC COVID draft 03 19 20 PD comments JKT.docx>

From: Morens, David (NIH/NIAID) [E] [b6 ([b6])]
Sent: 8/18/2021 9:20:37 PM
To: Kevin Olival [b6]
BCC: Morens, David (NIH/NIAID) [E] [b6 ([b6])]
Subject: Re: PRO/AH/EDR> Undiagnosed die off, deer - USA: (ID) RFI

Yes, i did see your work and think that this is an important under appreciated issue. If you have contacts in Idaho, you might want to ping them. ! d

Sent from my iPhone
David M Morens
OD, NIAID, NIH

On Aug 18, 2021, at 16:16, Kevin Olival b6 wrote:

Hope this finds you well, and totally agree David.

We've been working with USGS, USFWS, and National Wildlife Health Center, on this issue of spillback. I can reach out to USGS colleagues and see what new testing is happening. I think you saw our paper about "spillback" risk to North American bats out a while ago? https://journals.plos.org/plospathogens/article?id=10.1371/journal.ppat.1008758

And this one: https://pubs.er.usgs.gov/publication/ofr20201060 Same applies to all N. American wildlife, to different degrees, but evidence definitely points to deer being susceptible too! https://www.nature.com/articles/d41586-021-02110-8

Cheers,
Kevin

Kevin J. Olival, PhD
Vice President for Research

EcoHealth Alliance
520 Eighth Avenue, Suite 1200
New York, NY 10018

b6 (direct)
(mobile)
1.212.380.4465 (fax)
www.ecohealthalliance.org

EcoHealth Alliance develops science-based solutions to prevent pandemics and promote conservation

On Aug 18, 2021, at 3:10 PM, Morens, David (NIH/NIAID) [E]
b6 wrote:

Guys, these deer need to be tested for SARS-CoV-2, which has apparently been spreading from humans to deer in the US.

David M. Morens, M.D.
CAPT, United States Public Health Service
Senior Advisor to the Director
Office of the Director
National Institute of Allergy and Infectious Diseases
National Institutes of Health
Building 31, Room 7A-03
31 Center Drive, MSC 2520
Bethesda, MD 20892-2520
☎ b6 (assistant: Whitney Robinson)
301 496 4409
b6

From: ProMED <promed@isid.org>
Sent: Wednesday, August 18, 2021 1:12 PM
To: Morens, David (NIH/NIAID) [E] b6
Subject: PRO/AH/EDR> Undiagnosed die off, deer - USA: (ID) RFI

UNDIAGNOSED DIE OFF, DEER - USA: (IDAHO) REQUEST FOR INFORMATION
****
A ProMED-mail post
http://www.promedmail.org
ProMED-mail is a program of the
International Society for Infectious Diseases
http://www.isid.org

Date: Mon 16 Aug 2021
Source: KLIX News radio [edited]
https://newsradio1310.com/unknown-disease-kills-150-deer-in-north-central-idaho/

Around 150 white-tailed deer have died of some sort of disease in north central Idaho and it isn't clear what is causing it according to game officials.

Idaho Department of Fish and Game officials in the Clearwater region said reports continue to come in of dead deer in the Kamiah area, as of [13 Aug 2021]. So far, tests for bluetongue and epizootic hemorrhagic disease, and adenovirus hemorrhagic disease have come back negative in the corpses tested.

People in the area have been asked to report any dead or sick deer to Idaho Fish and Game. Officials have asked people to remove food and water sources that may cause deer to congregate out of a concern that whatever is making the animals sick is spreading from animal to animal. Idaho Fish and Game first reported deer had been dying of some sort of illness on [5 Aug 2021] and began running tests. Idaho Fish and Game said it appeared to be a localized situation.

--
Communicated by:
ProMED from HealthMap Alerts
promed@promedmail.org

[Hemorrhagic disease (HD) in cervids, caused by viruses in either the epizootic hemorrhagic disease virus (EHDV) group or the bluetongue virus (BTV) group, is the most important disease of white-tailed deer and is more common in the eastern USA. In western states, an adenovirus (CdAdV-1 or OdAdV-1) causes fatal hemorrhagic disease in black-tailed deer and moose. Tests to detect those diseases were negative and there are no data on signs or pathological findings to speculate a possible cause. We await the results of any studies being conducted by the Idaho Department of Fish and Game. - Mod.PMB

HealthMap/ProMED map of Idaho, United States:
http://healthmap.org/promed/p/68515]

[See Also:
Epizootic hemorrhagic disease - USA: (NY) deer
http://promedmail.org/post/20210811.8585742
Adenovirus hemorrhagic disease - USA (03): (WA) deer
http://promedmail.org/post/20210806.8573558
2015

Bluetongue - USA (03): (ID) cervid
http://promedmail.org/post/20151009.3703577
2003

Epizootic hemorrhagic disease, cervids - USA (ID)
http://promedmail.org/post/20030809.1974]
.....sb/pmb/mj/jh
##
****

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Unsubscribe Preferences

##########
##########

From: Morens, David (NIH/NIAID) [E] [b6]
[b6]
Sent: 12/11/2019 10:29:57 PM
To: Ellen Carlin [b6]
Subject: Re: Journal contact?
Attachments: Carlin et al Building resilience Draft 10.31.19.docx; ATT00001.htm

Ellen, i have contacts at nejm, jid, and several other journals but not lancet. b6 left and although i knew b6 slightly, i don't think i can do any good there.

I agree: go big. Sometimes you hit a bulls eye, other times not

But your work is good, and it will be published, read, and considered. I mean, after all, this is important stuff

david
Sent from my iPhone
David M Morens
OD, NIAID, NIH

On Dec 11, 2019, at 15:03, Ellen Carlin b6 wrote:

Hi David! I hope all is well.

I wanted to ask if you know any editors at The Lancet who might be receptive to an email from you about our paper (attached)? Billy tried an editor he knows there but has received no response. We thought a pre-submission inquiry would be better than a cold submission.

I also thought if The Lancet is a no-go, perhaps you might have a contact at NEJM or another high-impact journal? NEJM has a Commentary article type. I figure we should go big if we can!

Thanks!!
Ellen

Ellen P. Carlin, DVM
Senior Health and Policy Specialist

EcoHealth Alliance
b6 (direct)
(mobile)
b6
www.ecohealthalliance.org

Research Associate, Smithsonian Conservation Biology Institute
Adjunct Research Scientist, Columbia University National Center for Disaster Preparedness
Courtesy Lecturer, Cornell University College of Veterinary Medicine

EcoHealth Alliance leads cutting-edge scientific research into the critical connections between human and wildlife health and delicate ecosystems. With this science, we develop solutions that prevent pandemics and promote conservation.

Title
Global health security: targeting investments toward unmet needs

Authors
Ellen P. Carlin, DVM
EcoHealth Alliance, 460 West 34th Street, New York, NY 10001
b6

Catherine Machalaba, MPH
EcoHealth Alliance, 460 West 34th Street, New York, NY 10001

Kanya C. Long, PhD
University of California San Diego, 6304 Atkinson Hall, La Jolla, CA 92093
Dr. Long was a fellow at the World Bank at the time of the study.

Franck C. J. Berthe, DVM
World Bank, 1818 H Street, NW, Washington, DC 20433

David Morens, MD
National Institutes of Allergy and Infectious Diseases, 5601 Fishers Lane, Bethesda, MD 20892

William B. Karesh, DVM
EcoHealth Alliance, 460 West 34th Street, New York, NY 10001

As the second largest Ebola outbreak in history finally appears to be waning in the Democratic Republic of the Congo, a global reckoning is due. Understanding why especially dangerous pathogens are emerging with increasing frequency continues to take a back seat to response and response preparedness. This crisis-centered approach is bound to keep us trapped in a perpetual cycle of panic and neglect.[1]

To document this dynamic and reveal its extent, we collated the functions needed for effective defenses against major biological incidents and assessed which areas are receiving insufficient attention.[2] Our organizing construct included four "pillars"—prevent, detect, respond, and recover. Through extensive review of the scientific and gray literature, and with expert input via roundtable discussions, interviews, and peer review, we identified 60 functions that undergird these four pillars and to which countries must have sufficient access to optimize their health security. We also identified 22 major initiatives global in architecture or oversight and designed to support the development of local, country, or regional capacities. We then mapped the initiatives to the pillars to reveal areas of global neglect (Figure 1).

[Insert Figure 1 here]

As the figure shows, activities directed at prevention are minimal in number. We defined prevention as a multi-dimensional concept that captures prevention of 1) epidemics at pre-initiation (*before* pathogens emerge into people); 2) bioweapons development and deployment; and 3) accidental releases of pathogens, such as from laboratories. The majority of funded efforts do not address prevention at all, and even fewer deal with the underlying risk factors that lead to epidemic emergence. Most programs view epidemic prevention narrowly (i.e., preventing small outbreaks from growing) rather than addressing what drives outbreaks to occur in the first place. The latter entails politically challenging decisions about societal priorities ranging from land use and agricultural practices to urbanization and climate change.

Few efforts address recovery, and the very inclusion of recovery as a core pillar in our construct is novel among frameworks. (A recent World Bank publication on which some of the authors worked, which is designed to strengthen human, animal, and environmental public health systems at their interface, is one of the only examples and has not yet been adopted into global efforts.[3]) Since strong recovery from one epidemic event can pre-empt future outbreaks, systematic and sustained attention to this pillar is badly needed.

We also found two strategic points of concern. One is that, by current design, global health security implementation efforts and their attached financing tackle particular objectives—vaccine development, regional surveillance, training—while no governance effort or strategic inter-institutional guiding framework aligns them toward a commonly defined set of goals. The other is that there seems to be a tendency to view biothreats in terms of the single end consequence that worries people the most: our own health. The problem with this approach is that it drives reverse engineering of structures and decisions to deal with only human health consequences, and forward engineering of response activity tailored to human health needs. Defense, environment, and animal health are often treated as needs outside of human health security frameworks, even though their full inclusion would restore the breadth of the health *security* concept. Ebola in DRC exists at this nexus: viral circulation in an ecological

environment that supports spillover and a fragile, violent, and conflict-ridden setting that hampers both prevention and response.

The international community's approaches diverge from what may be fundamentally needed to grapple with the new epidemic threat reality and ultimately stave off its worst consequences. Some of the functions we identified require less investment than others to achieve great benefit—addressing drivers of epidemics is a case in point. The World Bank estimates that an annual expenditure of ~$3.4 billion to prevent one in every eight severe pandemics will save $30 billion.[4] Assessing cost-benefits and returns on investment of particular activities is precisely what a unifying strategic framework could do. The release of the 2019 Global Health Security Index, which finds among 195 countries assessed an average preparedness score of 40·2 out of a possible 100, may provide new impetus to act.[5] A substantial but feasible rethinking of the orientation of global and national investment is achievable within the major guiding frameworks and efforts that are already underway. As the Global Health Security Agenda embarks on its second five years, this is a timely opportunity to strengthen neglected lines of effort and support a holistic approach to dealing with the global health challenge of epidemic disease.

Acknowledgements
This work was funded by the Smith Richardson Foundation, which had no other role in the development of the study.

References

1. World Bank. *From panic and neglect to investing in health security: Financing pandemic preparedness at a national level.* Washington, DC: World Bank;2017.
2. Carlin EP, Machalaba C, Berthe FCJ, Long KC, Karesh WB. *Building resilience to biothreats: An assessment of unmet core global health security needs.* New York, NY: EcoHealth Alliance;2019.
3. World Bank. *Operational framework for strengthening human, animal and environmental public health systems at their interface.* Washington, DC: World Bank Group;2018.
4. World Bank. *People, pathogens, and our planet: The economics of one health, volume 2.* Washington, DC: World Bank;June 2012.
5. Nuclear Threat Initiative. *Global health security index: Building collective action and accountability.* Washington, DC: Nuclear Threat Initiative;2019.

Figure 1: Mapping of global health security initiatives to core needs

Initiative	[redacted]
Australia Group	
CEPI*	
CP3	
Gavi†	
GLASS	
GLEWS‡	
Global Financing Facility	
Global Fund	
GHSA§	
GHSI	
Global Partnership	
International Reagent Resource	
OIE WAHIS	
Proliferation Security Initiative	
World Bank PEF‖	
World Bank Pandemic Preparedness Plan	
WEF Epidemics Readiness Accelerator	
WHO CFE	
WHO Global Influenza Programme	
WHO GOARN	
WHO Health Emergencies Program	
WHO R&D Blueprint	

Major global health security initiatives were mapped to four pillars of global health security activity: prevent, detect, respond, and recover, revealing a predominance of focus on detection and response. Figure reprinted from Carlin EP, Machalaba C, Berthe FCJ, et al. *Building Resilience to Biothreats: An assessment of unmet core global health security needs*. EcoHealth Alliance. 2019.

*Committed to funding through Phase 2 investigational stockpiles; not funded for Phase 3 or linked to a system for procurement, distribution, or dispensing. †To the extent that Gavi covers Prevent it is for the specific prevention of yellow fever spillover through vaccination in high-risk areas; does not address drivers. ‡Predominantly focused on risk monitoring and information alerts for Rift Valley fever in livestock. §Addresses prevention in the sense of containing outbreaks; attention to and capacity for spillover risk management is extremely limited. ‖Disbursement of funds only applies to select viruses.

From: Ellen Carlin [b6]
Sent: 4/18/2019 6:10:52 PM
To: Morens, David (NIH/NIAID) [E] [b6]
b6
Subject: Re: Global health security gaps analysis

Awesome! I will let her know to plan for post-April 26. Working around b6 crazy schedule is usually the best bet ☺

I will also be in touch on the paper… Meantime enjoy the weekend,
Ellen

From: "Morens, David (NIH/NIAID) [E]" b6
Date: Friday, April 12, 2019 at 4:30 PM
To: Ellen Carlin b6
Subject: RE: Global health security gaps analysis

All good ideas! Happy hours included. With b6, I think working around her schedule is the starting point. Saturday nights should work for me beginning after the weekend of April 26.

David

David M. Morens, M.D.
CAPT, United States Public Health Service
Senior Advisor to the Director
Office of the Director
National Institute of Allergy and Infectious Diseases
National Institutes of Health
Building 31, Room 7A-03
31 Center Drive, MSC 2520
Bethesda, MD 20892-2520

☎ b6 (assistants: Meaghan Vance; Whitney Robinson)
301 496 4409
b6

From: Ellen Carlin b6
Sent: Friday, April 12, 2019 3:42 PM
To: Morens, David (NIH/NIAID) [E] b6
Subject: Re: Global health security gaps analysis

I'm impressed—I never did receive that reply, and I don't know how you keep tabs on the vagaries of cyberspace!

I'm pretty (100%) certain that the policy stuff is not over your head. More to the point, credible scientists are needed to make worthwhile policy, which is why we included you on the project! I will get to work on an outline and a plan.

I saw b6 last week and we hatched a plan for her to have a Saturday night dinner party! Does that idea work for you? We can find an evening that works for all. That does not preclude getting together downtown as well. I can try to make the next OH meeting although I think I might be in NYC that week. Maybe we just find a good happy hour.

From: "Morens, David (NIH/NIAID) [E]" b6
Date: Friday, April 12, 2019 at 12:21 PM
To: Ellen Carlin b6
Subject: RE: Global health security gaps analysis

Hi Ellen, just doing my weekly check of correspondence and I found that my reply to you a few days ago isn't in my sent mail, so will re-reply just in case it went astray (yes, I can be a bit obsessive compulsive on occasion).

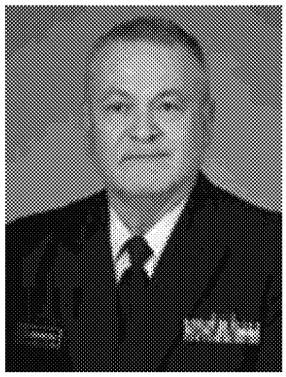
What I said was something like, of course, I'd be glad to work with you on this, with the caveat that I'm just a scientist and a lot of this policy stuff is over my head. But of course, important, which is why scientists and policy folks need to talk together and work together.

Let me know if you and b6 can get free some time, maybe at a One Health meeting downtown?

David

David M. Morens, M.D.
CAPT, United States Public Health Service
Senior Advisor to the Director
Office of the Director
National Institute of Allergy and Infectious Diseases
National Institutes of Health
Building 31, Room 7A-03
31 Center Drive, MSC 2520
Bethesda, MD 20892-2520

☎ b6 (assistants: Meaghan Vance; Whitney Robinson)
301 496 4409
b6



From: Ellen Carlin b6
Sent: Tuesday, April 9, 2019 12:45 PM
To: Morens, David (NIH/NIAID) [E] b6
Subject: Re: Global health security gaps analysis

Thank you, David! That means a lot. It's amazing how much work goes on behind the scenes for two years to culminate in a 15-minute presentation!

I am definitely interested in drafting something for a journal. Would you be interested in co-authoring a piece with us? You are after all a contributor to the report and it would be great to have you join us.
Ellen

From: "Morens, David (NIH/NIAID) [E]" b6
Date: Friday, April 5, 2019 at 1:07 PM
To: Ellen Carlin b6
Subject: RE: Global health security gaps analysis

Ellen, great talk last night. You should think about writing it up for some biomedical science journal, maybe centered around the 5 key points you had on a later slide. Maybe have someone like Dr. Kadlec as a coauthor, plus Billy or Peter.

David

David M. Morens, M.D.
CAPT, United States Public Health Service
Senior Advisor to the Director
Office of the Director
National Institute of Allergy and Infectious Diseases
National Institutes of Health
Building 31, Room 7A-03
31 Center Drive, MSC 2520
Bethesda, MD 20892-2520

☎ b6 (assistants: Meaghan Vance; Whitney Robinson)
301 496 4409
b6

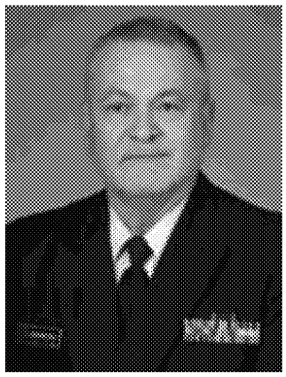
From: Morens, David (NIH/NIAID) [E]
Sent: Tuesday, April 2, 2019 3:24 PM
To: 'Ellen Carlin' b6
Subject: RE: Global health security gaps analysis

Thanks, and I presume I can thank u also for the Eventbrite conformation that just came!

David

David M. Morens, M.D.
CAPT, United States Public Health Service
Senior Advisor to the Director
Office of the Director
National Institute of Allergy and Infectious Diseases
National Institutes of Health
Building 31, Room 7A-03
31 Center Drive, MSC 2520
Bethesda, MD 20892-2520

☎ b6 (assistants: Meaghan Vance; Whitney Robinson)
301 496 4409
b6



From: Ellen Carlin b6
Sent: Tuesday, April 2, 2019 1:54 PM
To: Morens, David (NIH/NIAID) [E] b6
Subject: Re: Global health security gaps analysis

I'll let them know you're coming! You can just show up. 6pm cocktails, 7pmm reception per usual!

Ellen P. Carlin, DVM
Senior Health and Policy Specialist

EcoHealth Alliance
b6 (direct)
(mobile)
b6
www.ecohealthalliance.org

Research Associate, Smithsonian Conservation Biology Institute
Adjunct Research Scientist, Columbia University National Center for Disaster Preparedness
Courtesy Lecturer, Cornell University College of Veterinary Medicine

EcoHealth Alliance leads cutting-edge scientific research into the critical connections between human and wildlife health and delicate ecosystems. With this science, we develop solutions that prevent pandemics and promote conservation.

From: "Morens, David (NIH/NIAID) [E]" b6
Date: Tuesday, April 2, 2019 at 10:45 AM
To: Ellen Carlin b6
Subject: RE: Global health security gaps analysis

Ellen, I'm glad you ping'd me on this because although I am planning to go to the EcoHealth meeting I think I forgot to RSVP and now I can't find the invite letter. I have the hardcopy which I printed out, but misfiled or accidentally erased the original invite. If you still have it could you send? Otherwise I'll just email them "cold" to say I'm coming.

See ya then,

David

David M. Morens, M.D.
CAPT, United States Public Health Service
Senior Advisor to the Director
Office of the Director
National Institute of Allergy and Infectious Diseases
National Institutes of Health
Building 31, Room 7A-03
31 Center Drive, MSC 2520
Bethesda, MD 20892-2520

☎ b6 (assistants: Meaghan Vance; Whitney Robinson)
301 496 4409
b6

From: Ellen Carlin b6
Sent: Monday, April 1, 2019 7:26 PM
To: Morens, David (NIH/NIAID) [E] b6
Subject: Re: Global health security gaps analysis

Thanks, David! I'm just back from Panama, having attending a SOUTHCOM health security conference. I didn't get to see the canal… but I did see some tree sloths!

Looking forward to seeing you on Thursday. b6 told me that you helped her out at b6 and that she'd love us to all get together. She's going to try to come late on Thursday, walking over b6 b6 So hopefully we can look at our calendars then!

Enjoy LA,
Ellen

Ellen P. Carlin, DVM
Senior Health and Policy Specialist

EcoHealth Alliance
b6 (direct)
(mobile)
b6
www.ecohealthalliance.org

Research Associate, Smithsonian Conservation Biology Institute
Adjunct Research Scientist, Columbia University National Center for Disaster Preparedness
Courtesy Lecturer, Cornell University College of Veterinary Medicine

EcoHealth Alliance leads cutting-edge scientific research into the critical connections between human and wildlife health and delicate ecosystems. With this science, we develop solutions that prevent pandemics and promote conservation.

From: "Morens, David (NIH/NIAID) [E]" b6
Date: Friday, March 22, 2019 at 11:48 AM
To: Ellen Carlin b6
Subject: RE: Global health security gaps analysis

Ellen, this looks so cool, thanks! I just scanned through it for a few minutes and I can see it was well thought out and researched. Kudos to you and the team.

Yes, I plan to be there on the 4th, thanks!

Also, I spent the morning with b6 a few days ago! The context was she asked me to b6 b6, which I did. Was fun! See you soon, I have to go to LA for a meeting but will be back before the 4th.

David

David M. Morens, M.D.
CAPT, United States Public Health Service
Senior Advisor to the Director
Office of the Director
National Institute of Allergy and Infectious Diseases
National Institutes of Health
Building 31, Room 7A-03
31 Center Drive, MSC 2520
Bethesda, MD 20892-2520

☎ b6 (assistants: Meaghan Vance; Whitney Robinson)
301 496 4409
b6

From: Ellen Carlin b6
Sent: Wednesday, March 20, 2019 7:25 AM
To: Morens, David (NIH/NIAID) [E] b6
Subject: Global health security gaps analysis

Dear David,

I am writing to let you know that my colleagues and I at EcoHealth Alliance have completed the high-level gaps analysis of global health security efforts that you helped us with last year. Your comments at the roundtable at the World Bank very much helped informed our assessment and the way we think about the problem. Please find the report attached!

We invite you to join us at the Cosmos Club on April 4 where we will discuss our findings. Our invited guest that evening will be Assistant Secretary for Preparedness and Response Bob Kadlec. You probably already received an invitation, but just in case, you can RSVP here.

Looking forward to seeing you at Cosmos hopefully… I am going to try to get b6 to come. If she can't, I will bug her for a proper happy hour for the three of us!

Ellen

Ellen P. Carlin, DVM
Senior Health and Policy Specialist

EcoHealth Alliance
b6 (direct)
(mobile)
b6
www.ecohealthalliance.org

Research Associate, Smithsonian Conservation Biology Institute
Adjunct Research Scientist, Columbia University National Center for Disaster Preparedness
Courtesy Lecturer, Cornell University College of Veterinary Medicine

From: Ellen Carlin [b6]
Sent: 3/20/2019 11:25:04 AM
To: Morens, David (NIH/NIAID) [E] [b6]
[b6]
Subject: Global health security gaps analysis
Attachments: EHA Building Resilience to Biothreats 2019.pdf

Dear David,

I am writing to let you know that my colleagues and I at EcoHealth Alliance have completed the high-level gaps analysis of global health security efforts that you helped us with last year. Your comments at the roundtable at the World Bank very much helped informed our assessment and the way we think about the problem. Please find the report attached!

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EcoHealth Alliance leads cutting-edge scientific research into the critical connections between human and wildlife health and delicate ecosystems. With this science, we develop solutions that prevent pandemics and promote conservation.

BUILDING RESILIENCE TO BIOTHREATS

An assessment of unmet core global health security needs

EcoHealth Alliance

Suggested citation: Carlin EP, Machalaba C, Berthe FCJ, Long KC, Karesh WB. *Building resilience to biothreats: an assessment of unmet core global health security needs*. EcoHealth Alliance. 2019.

BUILDING RESILIENCE TO BIOTHREATS

An assessment of unmet core global health security needs

AUTHORS AND CONTRIBUTORS

Ellen P. Carlin
Senior Health and Policy Specialist, EcoHealth Alliance
Catherine Machalaba
Policy Advisor and Research Scientist, EcoHealth Alliance
Franck C.J. Berthe
Senior Livestock Specialist, World Bank
Kanya C. Long
AAAS Roger Revelle Fellow in Global Stewardship/Health Specialist, World Bank
William B. Karesh
Executive Vice President, EcoHealth Alliance

ACKNOWLEDGEMENTS

Numerous individuals contributed to this endeavor. We wish to thank the participants who attended our Washington, D.C. roundtable, many of whom came from great distances to do so, including across the Atlantic Ocean. We thank the World Bank Group for hosting the roundtable and for generously providing additional expertise and collaboration throughout the study process, including through a Knowledge Exchange event. The written report benefitted considerably from the input of many interview participants and peer reviewers. Officials from the government of Liberia were especially gracious with their time to provide valuable country perspective. Jim Desmond and Amanda Andre, both from EcoHealth Alliance, provided significant guidance, coordination, and assistance. The kind help of Barbara Machado and Timothy Bouley from the World Bank was also sincerely appreciated. Finally, we gratefully acknowledge the generous support and enthusiasm of the project's funder, the Smith Richardson Foundation.

In addition to literature research, the following events and experts formed the backbone of this project's information gathering phases, and allowed for substantial deliberation of results and conclusions:

Roundtable
Washington, DC

James Allen, Chevron
Casey Barton Behravesh, U.S. Centers for Disease Control and Prevention
Franck Berthe, World Organisation for Animal Health and World Bank
Lance Brooks, U.S. Department of Defense
Elizabeth Cameron, Nuclear Threat Initiative
Justin Cormier, U.S. Centers for Disease Control and Prevention
Ricardo Echalar, U.S. Agency for International Development
Hamid Jafari, U.S. Centers for Disease Control and Prevention
Franca Jones, U.S. Department of Defense
William B. Karesh, EcoHealth Alliance
Mario Libel, Ending Pandemics
Kanya Long, World Bank
David Morens, National Institute of Allergy and Infectious Diseases
Gerald Parker, Texas A&M University
Dademanao Pissang Tchangai, Food and Agriculture Organization of the United Nations
Ronald Waldman, Georgetown University

Liberia mission
Monrovia, Liberia

The research team traveled to Liberia to ground truth its findings from a cross-ministerial, country-level perspective. In a roundtable setting, partners from the National Public Health Institute of Liberia (NPHIL), Central Veterinary Laboratory, and Forestry Development Authority provided their expert perspective on how well the identified functions and initiatives align with the assessments, experience, and needs in their sector and at a national level. While in Liberia, we also benefitted considerably from attending additional meetings convened through Liberia's One Health Coordination Platform to learn more about the country's cross-cutting efforts across public health, forestry, environmental protection, agriculture, and other agencies. We especially thank Tolbert Nyenswah and Sonpon Sieh for their generosity in welcoming us and allowing us to learn from Liberia's efforts.

World Bank Knowledge Exchange
Washington, DC

Project investigators held an exchange of ideas with World Bank colleagues on the study's findings to share views, with a focus on operational and practical experiences and lessons learned from World Bank operations. The event was chaired by Olusoji Adeyi. The insight from all participants, including Discussant John Paul Clark, was greatly appreciated.

Interviews and consultations
Stéphane de la Rocque, World Health Organization
Rebecca Katz, Georgetown University
Nicole Lurie, CEPI – Coalition for Epidemic Preparedness Innovations
Dawn O'Connell, CEPI – Coalition for Epidemic Preparedness Innovations

Peer reviewers
James Allen, Chevron
Ryan Morhard, World Economic Forum
Simo Nikkari
Erin M. Sorrell, Georgetown University
Claire J. Standley, Georgetown University
Gary A. Vroegindewey, Lincoln Memorial University
Paul van der Merwe, South Africa Defence Force
Chadia Wannous, Towards a Safer World Network for Pandemic Preparedness

PREFACE

The Ebola crisis of 2014-2016 in Guinea, Liberia, and Sierra Leone spurred a substantial rethinking of how the global community must orient itself toward preventing, mitigating, and responding to the impacts of major infectious disease events. Nations, companies, and philanthropies poured billions of dollars into direct Ebola response and into activities and initiatives designed to ensure against another Ebola-like event.

Four years later, we sought to understand where this self-reflection and new-found commitment to global health security has brought us. We looked not to the country level, where abundant programs and assessments are ongoing, but instead to the global stage of actors. Our intent was to capture the systematic initiatives operating worldwide to address the core functions outlined in prominent global health security frameworks. We suspected that behind the many and productive policy and programmatic efforts there remain core capabilities that are insufficiently addressed or not addressed at all at this level. We began with the assumption that progress was abundant yet uneven. We also assumed that the major frameworks themselves might be drawn too narrowly to account for the full scope of outbreak sources—intentional and unintentional spillover or release—and the distinct but complementary capacities needed to address them.

We know of no group that has undertaken an end-to-end review of the primary functions needed for effective prevention through recovery from pandemics, regardless of their origin, and an assessment of which functions are receiving insufficient attention. Any weak link in the global health security system can jeopardize the ability to prevent and manage high-consequence outbreaks. A high-level evaluation, therefore, is necessary and timely. Much of the work needed to build a world resilient to catastrophic health threats is really just beginning; we hope that this assessment will play a role in building the scaffolding to create that world.

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GLOSSARY

Recognizing that many of the following terms have multiple meanings or usages, this glossary provides definitions for the purpose of this report; these have been sourced or adapted from a variety of existing and published definitions.

Biodefense. Activities directed to thwart biothreats of intentional or unintentional origin.

Biosecurity. 1) Prevention of theft, diversion, or deliberate misuse of knowledge, skills, materials, and/or technologies from the biological sciences. 2) Prevention of the inadvertent release or transport of pathogens from hospitals, laboratories, farms, and other settings.

Biothreat. Short for "biological threat;" a biological pathogen or toxin with high-consequence potential for human or animal health or national security.

Build back better. The phases implemented after a disaster to increase resilience of nations and communities through integrating disaster risk reduction measures into restoration of physical infrastructure and societal systems, and into the revitalization of livelihoods, economies, and the environment.

Collective health security. The reduction of vulnerability of societies to disease threats (generally those that are caused by pathogens or acute toxic exposures) that spread across national borders.

Detect. A global health security pillar characterized by systems, policies, and procedures to gather and analyze information, provide early warning, and inform strategies.

Emerging infectious disease. An infectious disease caused by a pathogen previously unknown to science, previously unknown to infect humans, or markedly increasing in incidence or geographic range.

Epidemic. An occurrence of an infectious disease in a defined population at a level exceeding normally expected incidence.

Global health security. A state characterized by sufficient epidemic and pandemic preparedness and capabilities in order to minimize vulnerability to acute public health events that can endanger the health of populations across geographical regions and international boundaries.

Pandemic. An infectious disease epidemic that occurs on more than one continent.

Preparedness. The knowledge and capacities developed by governments, response and recovery organizations, communities, and individuals to effectively anticipate, respond to, and recover from the impacts of likely, imminent, or current disasters.

Prevent. A global health security pillar characterized by systems, policies, and procedures to determine, assess, avoid, mitigate, and reduce threats and risks by reducing vulnerability and exposure.

Recover. A global health security pillar characterized by systems, policies, and procedures to restore and strengthen normal operations.

Re-emerging infectious disease. An infectious disease that had declined in prevalence or impact but which is again becoming a health problem for a given population.

Respond. A global health security pillar characterized by systems, policies, and procedures aimed at controlling or mitigating the impact of disease and saving lives.

Zoonosis. An infectious disease transmissible between animals and humans.

ACRONYMS

AMR	antimicrobial resistance
AU-IBAR	African Union - Interafrican Bureau for Animal Resources
BWC	Convention on the Prohibition of the Development, Production and Stockpiling of Bacteriological (Biological) and Toxin Weapons and on their Destruction
CBD	Convention on Biological Diversity
CCHF	Crimean-Congo hemorrhagic fever
CDC	U.S. Centers for Disease Control and Prevention
CEPI	Coalition for Epidemic Preparedness Innovations
CFE	Contingency Fund for Emergencies
CORDS	Connecting Organizations for Regional Disease Surveillance
CITES	Convention on International Trade in Endangered Species of Wild Fauna and Flora
CP3	Community Pandemic Preparedness Program
DAH	Development Assistance for Health
DALY	disability-adjusted life year
DRC	Democratic Republic of Congo
EID	emerging infectious disease
FAO	Food and Agriculture Organization of the United Nations
GHSA	Global Health Security Agenda
GHSI	Global Health Security Initiative
GLASS	Global Antimicrobial Resistance Surveillance System
GLEWS	Global Early Warning System
GOARN	Global Outbreak Alert and Response Network
IDA	International Development Association
IHR	International Health Regulations
IRR	International Reagent Resource
JEE	Joint External Evaluation
NGO	non-governmental organization
NPHIL	National Public Health Institute of Liberia
OIE	World Organisation for Animal Health
PEF	Pandemic Emergency Financing Facility
PSI	Proliferation Security Initiative
PVS	Performance of Veterinary Services
R&D	research and development
REDISSE	Regional Disease Surveillance Systems Enhancement
RVF	Rift Valley fever
SARS	Severe Acute Respiratory Syndrome
UN	United Nations
U.S.	United States
USAID	United States Agency for International Development
WAHIS	World Animal Health Information System
WEF	World Economic Forum
WHO	World Health Organization

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Global health security is the bulwark against catastrophic public health events. Building this security is a timely and urgent challenge for the world as it faces an increasing rate of emergent and re-emergent infectious disease events tied to changing pressures on animals and ecosystems, resistance to antimicrobials, and avenues for intentional dissemination—all with prospects of rapid spread through our highly mobile population. To date, no end-to-end review of the components needed for effective prevention, detection, response, and recovery from major biological events of any cause, nor an assessment to determine those components that are receiving insufficient attention, has been published.

An optimized global health security system is one that effectively implements and integrates core functions and is enabled by collaborations between governments, non-governmental organizations (NGOs), industry, academia, and communities. Many efforts in various stages at subnational, national, and global levels are directed toward contributing to global health security. Some are advanced by international governing bodies and incorporated into formal frameworks through which activities are funded and coordinated. Others are put forth by networks, coalitions, and consortia of stakeholder groups to identify and implement ways of organizing, advocating for, and contributing to new approaches to health security.

Here we present a framework for rethinking global health security in a way that captures, under a single umbrella, functional areas requiring inputs from the healthcare and public health, animal health, agriculture, environmental, law enforcement and counterterrorism, defense, and disaster risk reduction sectors. It also explicitly considers functions needed to defend against events regardless of their source, whether intentional or unintentional.

OBJECTIVES

We sought to provide perspective on the question of how well the global community has situated itself with respect to building defenses against biological threats. Our specific objectives were to:

1. Comprehensively identify the functions needed to optimize global health security against biothreats regardless of cause (intentional or unintentional), including those that may be missing from current constructs; and
2. Determine which of these functions are insufficiently supported by global-level initiatives.

This was a qualitative evaluation designed to identify the broad pillars and core functions needed to prevent and manage major threats to human health security, and to determine which pillars and functions are unsupported or under-supported by global initiatives. We framed our scope by a published definition of "global governance for health" that encompasses health in the context of global organizations across various sectors, as well as the many mechanisms, institutions, and health professionals that contribute to global health strategy and implementation.[1] It includes "those institutions and processes of global governance that do not necessarily have explicit health mandates, but that have a direct and indirect health impact" (e.g., related to environment, food production, trade, etc.).

We identified major existing frameworks (international and U.S. domestic) and reviewed them to identify the pillars and functions that each put forth as imperative for achieving a state of collective health security:

Prevent: Systems, policies, and procedures to determine, assess, avoid, mitigate, and reduce threats and risks by reducing vulnerability and exposure.

Detect: Systems, policies, and procedures to gather and analyze information, provide early warning, and inform strategies.

Respond: Systems, policies, and procedures aimed at controlling or mitigating the impact of disease and saving lives.

Recover: Systems, policies, and procedures to restore and strengthen normal operations.

We then identified a list of global initiatives to manage biothreats—operationally-oriented efforts and major financing mechanisms aimed at building capacity or otherwise closing health security gaps in particular functional areas—and mapped them against pillars and functions. Our focus on global efforts does not ignore the utility of regional, bilateral, and country-level efforts, but acknowledges the substantial good that global bodies and mechanisms could offer to all pillars of global health security if they chose to. Using expert input via interviews and three roundtable workshops, we assessed the validity of the pillars and functions we captured; our choice of initiatives; the mapping of the initiatives to the pillars; and our findings and recommendations.

FINDINGS

Under the four pillars, we identified 60 functions to which countries must have sufficient access at the country, regional, or global level. We also identified 22 major global health security initiatives. Mapping these 22 initiatives against the 60 functions revealed that response activities clearly emerge as the dominant focus of global health security initiatives, with 16 of 22 notionally or actually addressing this pillar. While effective response mechanisms are requisite, they should not be pursued to the exclusion of functions in other pillars. We found that the following major challenges characterize the landscape:

- **Global initiatives to manage biological threats largely operate independently of one another.** No strategic inter-institutional guiding framework attempts to align all of these global initiatives toward a commonly defined objective or set of goals.

- **Biothreat planning and implementation is dominated by the human health sector.** A tendency to think about biothreats in terms of human health drives planning and implementation processes, even though dozens of sectors are relevant for prevention, detection, response, and recovery.

- **Prevention is scarcely addressed.** The Prevent pillar is at once the most important and most underappreciated, with only seven of 22 initiatives supporting prevention as we define it. Only four of these address the prevention of unintentional sources of outbreaks or incidents.

- **Recovery is all but missing.** Recovery functions remain the most significantly overlooked. Initiatives to meaningfully and systematically advance recovery planning and implementation are almost non-existent. Recovery is supported by only five of 22 initiatives.

- **Cross-cutting functions provide under-utilized entry points for participation.** Several cross-cutting functions needed to support every pillar of the entire global health security enterprise are critically under-emphasized, including community engagement; risk communication and education; research and development in areas beyond surveillance or medical countermeasures; and data and information management.

RECOMMENDATIONS

To mitigate these challenges, we offer the following:

1. **Global biothreat initiatives should be more strategically aligned.** Coordination and harmonization will help ensure coverage and synergy. The now-forming Global Pandemic Monitoring Board may be well suited to this activity. The proposed Global Health Security Agenda (GHSA) 2024 Framework is anticipated to reaffirm the need and set the stage for preparedness, and could be upscaled to include additional nations or become a global compact.

2. **Multi-sectoral participation must be recognized as a requisite tenet of the entire global health security enterprise.** Three weaknesses in multi-sectoral participation, if rectified, could provide substantial benefit to the health security of global citizens. These might be effected through a renewed push per the GHSA 2024 Framework development process:

   Defense and security. A shifted paradigm toward complete engagement of this sector from the country to the global level is necessary. Efforts from this sector can play a central role in preventing outbreaks in the first

instance, and also in detection, response, and recovery. Law enforcement, military, customs and border control, and other entities can assist with core functions, including protection of critical infrastructure, bioforensics and attribution, logistics of essential services surge, and medical countermeasure distribution and dispensing. The GHSA could leverage existing regional security agreements toward this end.

Environment. The environment sector can be leveraged to contribute key information for threat detection and sentinel surveillance, lynchpin capabilities for prevention. It can also help provide intervention options to mitigate disease risks from wildlife and other environmental sources. Donors can coordinate more systematically with relevant sectors to ensure approaches that incorporate the environmental sector are built into programs prospectively in One Health fashion.

Private sector. The enthusiasm of the private sector through efforts like the Global Health Security Private Sector Roundtable offers opportunity for its inclusion in biothreat planning and implementation. We recommend the development of aggressive, early, and transparent public-private partnerships. These efforts should begin by defining the many and unique health security functions the private sector is best positioned to provide, and mapping the many potential contributions of it to global health security.

Valuable cooperation across sectors and disciplines is not limited to these three areas. There is a need for better engagement across many others, including trade, travel, and finance as well as with civil protection and disaster management authorities.

3. **Strategic gaps at the margins must be aggressively addressed.** Of the four pillars that define global health security in our construct, two are dramatically overlooked:

Prevent. Funders and implementers should embrace Prevent as an area of need and target investments accordingly beyond vaccination efforts designed to contain new outbreaks. Improved prediction and prevention science can be utilized to assess and manage risks upstream of outbreaks, but will require new approaches to address proximal and distal drivers of disease emergence. Building capacity for the functions in this pillar will require sustained investments from donors, including those who traditionally secure and allocate resources for response. The GHSA's next iteration should include metrics that measure prevention of spillover not only in terms of surveillance efforts, but of other behaviors, policies, and practices that minimize that spillover.

Recover. Granting biothreat recovery functions attention similar to that provided for other types of disasters will promote a more systematic understanding of needs and should strengthen functions to prevent, detect, and respond to future risks and impacts. Nascent programs in this area that contribute to global health security should be strongly supported. Proactive collaboration with disaster response and humanitarian aid entities may help anticipate needs, establish coordination channels, and provide opportunities to build back better to strengthen overall systems and support future disease prevention.

The architects of global health security programs, be they countries, major donors, NGOs, or other such entities, are the primary audience for this report. By defining a comprehensive set of core functions for effective global health security, mapped against ongoing initiatives to reveal weaknesses, global commitments can be more strategically informed and directed. The results of this study can allow improved strategic planning and can assist the integration of prospective initiatives into the global health security enterprise in a way that optimizes their utility. Of course, the ultimate goal of all global health security activities is to optimize country-level capabilities, so we hope that the comprehensive identification of pillars and functions will provide national governments the opportunity to refine and message their particular needs via their national planning processes. Many sectors and disciplines beyond the public health and medical communities are relevant and can offer solutions in the form of regulatory policies, industry standards, investments, surveillance networks, and technical innovation. This study provides a foundation for follow-on work that might take the form of designing and ultimately implementing a system of partnerships to meet the identified needs.

The 2009 H1N1 influenza virus, which emerged in Mexico and spread to much of the rest of the world in less than a year, caused the first declared influenza pandemic in more than 40 years. In little more than a year, it caused more than 18,000 laboratory confirmed deaths, although the actual number of deaths is likely closer to 300,000.[2] Yet predictions of its impacts had been even more dire. H1N1's failure to meet its own catastrophic potential, combined with the relative numbness of developed nations to influenza as a pathogen, may have lessened what might have been dramatic policy shifts.

The 2014–2016 West Africa Ebola crisis was different. Even though any one global citizen was much less likely to know an Ebola victim than an H1N1 victim, the tremendous media coverage, visceral fear of hemorrhagic fever, higher case fatality rate, and shock that the pathogen—previously unknown in West Africa and limited to relatively small outbreaks in deep forests and villages—had emerged at all set up a new era of pandemic awareness.

The emergence and spread of Ebola and Zika viruses reminded us that pathogens know no borders and that all countries and regions will continue to face the threat of high-consequence outbreaks for the foreseeable future. Prior to the appearance of Ebola virus in Guinea, Liberia, and Sierra Leone, national-level infectious disease events that garnered an international response typically emerged following humanitarian disasters or were part of acute but isolated events in an under-resourced setting that required short-term intervention.[3] The response to SARS improved awareness of needed capacity strengthening, but Ebola in West Africa changed the global landscape, provoking a prolonged humanitarian response and transitioning actors from a containment-driven mindset to one of longer-term planning. This drastic shift challenged existing mechanisms for coordination, deliberation, and funding, and forced a recognition of the need to balance response and sustained capacity building.[3]

Developed nations and other entities invested billions in this region to reduce spread of the disease and help prepare for future Ebola outbreaks. The United States alone appropriated an unprecedented $5.4 billion in emergency response funding, about $2 billion of which was directed internationally to the affected areas as well as other nations.[4] As important as these investments were, their impact has had limits. These dollars were primarily allocated to response for the particular Ebola Zaire epidemic in the region, not prevention or recovery efforts for Ebola Zaire or other emerging pathogens.

In the four years since the West Africa Ebola outbreak was acknowledged as a global crisis, the world has mobilized to prepare for what is now the infectious disease normal. The infusion of billions of dollars from the public and private sectors has enabled global partners to better identify risks, research causes, and create policy and programmatic initiatives to manage pathogen emergence. These efforts are targeted largely at epidemic-prone and emerging pathogens. (Endemic diseases and diseases in the elimination pipeline have long been targeted by other initiatives and funding streams.) The work is bearing fruit in establishing collective health security in both low- and high-income countries. All nations, however, remain at considerable risk of disease introduction or emergence. This is true whether emergence occurs through a biological process, intentional deployment of a biological weapon, or unintentional release of biological agents or material. Each country is vulnerable, even those with more advanced health security systems, and country-level vulnerabilities place all in the global community at risk.

Major strategic and operational gaps remain, perpetuating global vulnerabilities in parallel with the growing threat of infectious diseases. The rate of disease emergence and international spread is increasing;[9,10] the bioterror threat level is rising;[11] and laboratories that handle high-containment pathogens are proliferating in the United States[12] and abroad,[13] which may signal improved detection and containment capacity but may potentially also add to other risks. Emerging disease threats include both novel pathogens—those previously unseen, re-emerging, or found in new geographic regions or demographic sectors—as well as more common pathogens that acquire antimicrobial resistance (AMR). Zoonotic agents alone cause more than a billion human cases of disease each year[14] and constitute the majority of human pathogens (over 60%)[14,15] and emergent disease events[9]. The relentless encroachment of humans on pathogen reservoirs such as wildlife and their habitats creates enormous technical and political challenges with which governing bodies are only beginning to come to terms. The impacts of outbreaks and costs of response are borne by individuals, governments, local societies, development funders, and industry and others in the private sector.[16] Of course, in addition to pathogens that

jump between animal and human populations, the continued prevalence of non-zoonotic livestock disease threats also destabilizes economic and food security. The approach we took to developing pillars and functions captures these biothreats as well.

Several recent reports have highlighted the high and rising cost of pandemics and the need for coordinated action at country and global levels.[17] Rapid trade and travel facilitates disease spread and escalates economic impacts.[18] These impacts can be substantial: the World Bank estimates a severe influenza pandemic could cost tens of millions of lives and up to 4.8% of global gross domestic product. The expected return on investment for prevention and swift resolution of disease events is high; investing in One Health systems for mitigation could yield savings of an estimated $30 billion in any given year, and potentially more than double that if paired with investments in R&D and preparedness. These savings occur through avoided impacts of a severe pandemic (impacts of a once-in-a-hundred-year pandemic have been estimated at upwards of $3 trillion).[17,19]

The Blue Ribbon Study Panel on Biodefense views biodefense as those activities directed to thwart biothreats, regardless of their origin. Its members wrote in 2015, "Biodefense touches many aspects of society, falling within the purview of national security, homeland security, public health security, and economic security. As such, it requires an enterprise approach—eliminating stovepipes; transcending agency-centric activity; drawing upon stakeholders throughout government, academia, and the private sector across health as well as other disciplines; and recognizing the extraordinary breadth of the challenge—to provide flexible solutions that address the full spectrum of the threat."[11] We concur that effective biodefense demands this multisectoral approach. We assert that the existence and maturity of activities needed to prevent and respond to high-consequence outbreaks is highly uneven across countries and sectors, and that these weaknesses leave us vulnerable to intentional and unintentional releases of biological agents alike.

BOX 1. 2009 H1N1: THE LAST MAJOR PANDEMIC

In April 2009, a novel H1N1 strain of influenza virus emerged in the Western Hemisphere, spreading from Mexico into the southern United States. While seasonal influenza is endemic around the globe, antigenic shifts that allow a strain to emerge in humans against which we have neither immunity nor vaccine are relatively rare. This strain had never been seen in people or animals, although it contained genes most closely related to H1N1 strains found in pigs. The disease quickly spread worldwide, moving it out of the epidemic category into pandemic.

This was the first influenza pandemic in more than 40 years. H1N1 resulted in more than 60 million cases and 12,000 deaths in the United States.[5] Although its global impact is not fully known, the virus may have caused nearly 300,000 fatalities in its first twelve months[2] and infected as much as one-quarter of the world's population[6]. Mexico lost nearly $3 billion due to a decline in tourism in the months following H1N1's emergence.[7] The pork industry lost revenue because the inaccurate naming of the disease as "swine flu" caused consumers to avoid pork products, even though these products posed no health risk,[7] costing the U.S. pork market $200 million.[8]

This outbreak tested numerous elements of global health systems. It tested technological capabilities to rapidly diagnose an unknown disease and then, after the virus was identified, the ability to develop and distribute laboratory assays to detect it. It tested capacity for rapid vaccine manufacturing: one year after the first detection, sufficient vaccine to protect only 17% of the world's population had been produced. It tested community willingness to accept those vaccines and the effectiveness of risk communication needed to engender public and consumer trust in government recommendations and actions. It tested hospital surge capacity to meet the large influx of patients. It tested political willingness to make decisions about quarantines and border closures. Like all notable outbreaks in the last 15 years, H1N1 revealed both strengths and substantial weaknesses in the global capacity to prevent and respond to infectious diseases.

Every type of outbreak, whether intentional or unintentional, has a cause behind it, usually related to a human action. Intentional outbreaks may result from human decisions to engage in biowarfare, bioterrorism, or biocrimes. Unintentional outbreaks may result from human behaviors that lead to accidental pathogen releases from laboratory, hospital, or other settings. Unintentional can also be used to describe the kinds of outbreaks often referred to as "natural" or which come at us from nature—the spillover of Ebola from bats to people, the spread of highly pathogenic avian influenza from migratory waterfowl to poultry to people, the dramatic increase in the prevalence of antimicrobial resistance. These events are in fact largely driven by anthropogenic activities that facilitate pathogen exposure and which create dispersal and selection pressures that change the natural histories of infectious diseases. Thus, accidents and spillover events (and related issues like antimicrobial resistance) are all captured under the term "unintentional" in this report. The result of this dynamic is that we cannot expect to mitigate the effects of outbreaks by managing their health consequences alone; we must address the risk factors inherent in human behaviors, and this can only be done through equal inclusion of institutions designed to deal with those behaviors.

Absent major intervention, the continued appearance and impact of new infectious diseases of epidemic and pandemic potential in human populations is certain. Bill Gates has repeatedly stated his concern that disease epidemics, be they spillover events or the result of biowarfare or bioterrorism, are the most likely phenomena to kill 10 million or more people globally, with potentially much higher mortality.[22] The World Economic Forum's 2018 Global Risks report ranked the spread of infectious disease as among the top 10 high-impact concerns for the world.[23]

Our vulnerability to these threats is a function of how ready we are as a society to meet them. From initial pre-event awareness through dynamic post-event recovery, have we fostered capabilities in communities and countries that enable a baseline competence that reduces or at least manages these inherent vulnerabilities? Have we done so regardless of the source of outbreak, and yet with special consideration for the unique activities that those different scenarios may demand?

Information gathering and analysis

This high-level evaluation was designed to identify the pillars and core functions needed to prevent and manage major biological events, and to determine which pillars and functions are unsupported or under-supported by global initiatives. The evaluation addressed needed functional capacity regardless of origin (i.e., human, animal, or environmental origin; warfare or terrorism; or accidental/unintentional release). It drew from preparedness approaches in both international and U.S. domestic health security spheres. We examined expert and institutional sources from the peer-reviewed and gray literature, and from health security frameworks and related government documents; solicited expert opinion via roundtable discussions; attended and participated in meetings and conferences of relevance domestically and abroad; and directly consulted with experts across a range of settings from public health, animal health, security, environment, development, and industry (see Acknowledgements). Information capture and evaluation were enriched by a series of country case studies and ministerial perspectives, including through consultation with experts in Liberia. Findings were incorporated into a comprehensive table of global health security pillars and functions. Based on our research and judgement, and with the feedback of the experts described, we determined which functions are, in general, insufficiently addressed by the listed initiatives based on considerations including scope, mandate, funding, and geographic coverage that point to their relative emphasis and attention in the health security community.

BOX 2. 2001 AMERITHRAX: THE LAST MAJOR BIOTERRORISM EVENT

As the United States reeled from the September 11th attacks, it was hit with another asymmetrical insult. In late September and early October, 2001, letters laced with spores of Bacillus anthracis, or anthrax, were sent to U.S. news outlets and congressional offices. Delivery of the letters led to massive contamination in facilities up and down the East Coast, not only to the offices of the targeted individuals but also postal offices and the home of a non-targeted citizen.

At least 22 people developed active anthrax infections from exposure to these letters.[20] Half suffered cutaneous anthrax, a skin infection. The other half contracted the extremely serious inhalational form of the disease, and, in five of these individuals, infection proved fatal. Anthrax can be treated with antibiotics, and 10,000 potentially exposed people received antibiotic prophylaxis; however, a number of the victims' infections were too advanced by the time of diagnosis to be treated effectively.

What the U.S. Federal Bureau of Investigation termed the "Amerithrax" case became an unprecedented driver of biodefense investment, policy, statute, and regulation in the United States. Security structures were put in place to prevent and mitigate another such occurrence. These ranged from enhanced regulation of laboratory pathogens and scientists to establishment of major medical countermeasure development initiatives. Annual investments in biodefense surpassed $6 billion dollars.[21] Many of these investments extended beyond U.S. borders to fund intelligence collection, biosurveillance, and threat reduction activities globally. The United States advanced its leadership role in preventing, detecting, and responding to intentional acts to exploit microbes as weapons. The biosafety and biosecurity elements of these and other programs also directly or indirectly addressed the inadvertent release of pathogens from facilities such as laboratories and hospitals.

Key definitions

Acknowledging that there are different definitions of "health security," we generally approached our assessment through the lens of "collective health security," or the reduction of vulnerability of societies to infectious disease threats that spread across national borders.[24] Indeed, the reduction of *risk*—a function not only of vulnerability but also of threat and consequences—poses even further opportunity for intervention, and it was the reduction of risk in which we were most interested. A closely related definition of "global health security" also framed our view: activities supporting epidemic and pandemic preparedness and capabilities at the country and global levels in order to minimize vulnerability to acute public health events that can endanger the human and animal population health across geographical regions and international boundaries.[25] Our assessment was organized around the pillars Prevent, Detect, Respond, and Recover,[a] defined as:

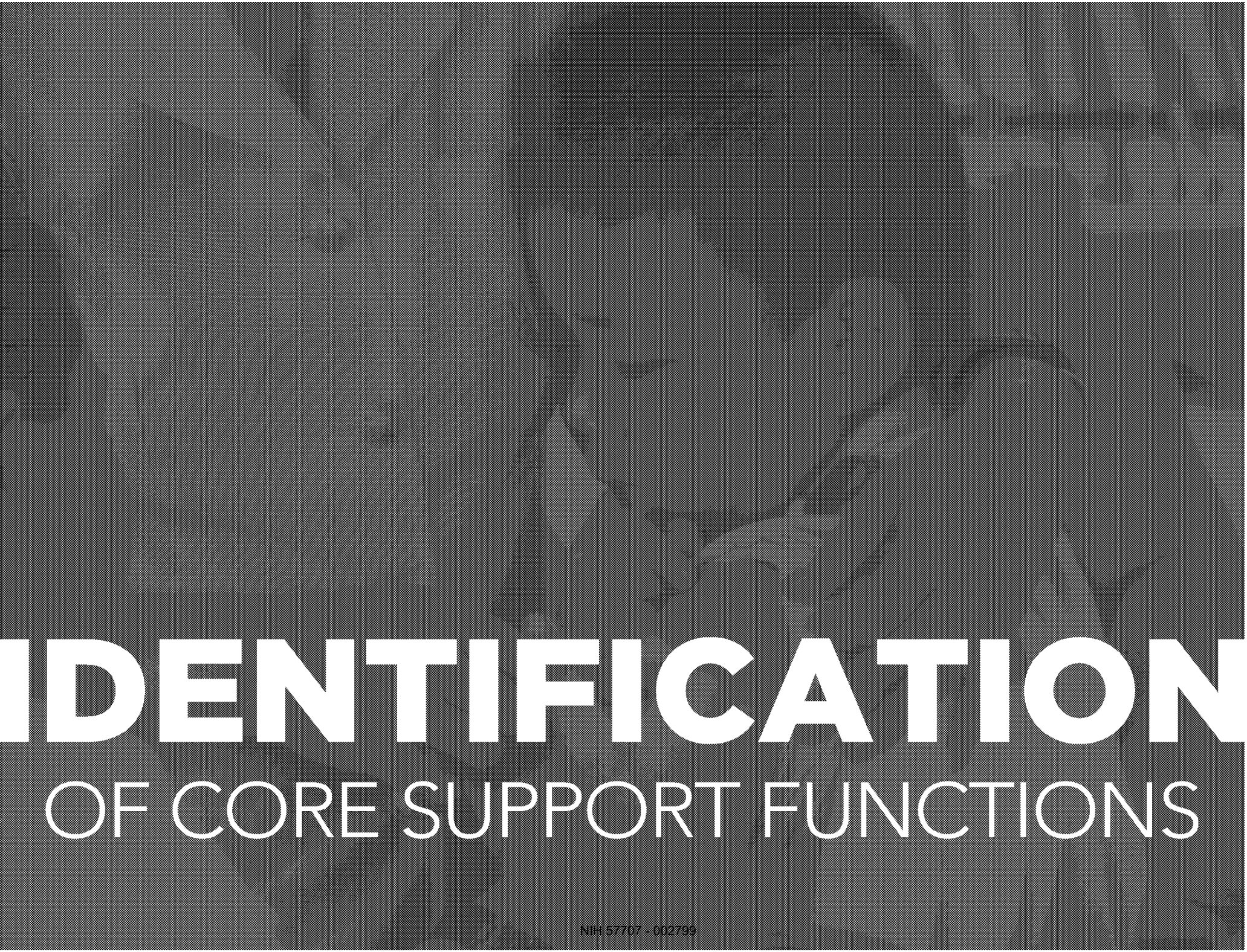
PREVENT
Systems, policies, and procedures to determine, assess, avoid, mitigate, and reduce threats and risks by reducing vulnerability and exposure.

DETECT
Systems, policies, and procedures to gather and analyze information, provide early warning, and inform strategies.

RESPOND
Systems, policies, and procedures aimed at controlling or mitigating the impact of disease and saving lives.

RECOVER
Systems, policies, and procedures to restore and strengthen normal operations.

[a] This approach models closely that found in: World Bank. *Operational Framework for Strengthening Human, Animal and Environmental Public Health Systems at their Interface.* Washington, D.C.: World Bank Group; 2018.



"... nations across the world, including the United States, have failed to invest in the necessary infrastructure and capacities. By sacrificing prevention and preparedness, nations have inevitably compromised the ability of public health systems to respond rapidly to health threats."

– National Academies of Sciences, Engineering, and Medicine 2017 [26]

Central to an optimal state of global health security is the assurance that each nation is capable of carrying out a set of critical functions. To build a comprehensive set of such functions, we reviewed a suite of legal instruments, frameworks, tools, guidance documents, and other sources in and outside of the health sector, and interviewed subject matter experts. We gathered each function into a table (Table 1) organized by pre-determined pillars.

One characteristic that makes the framework presented here unique is that it is not sector-specific. Our framework captures, under a single umbrella, functional areas requiring inputs from the healthcare and public health, animal health, agriculture, environmental, law enforcement and counterterrorism, defense, and disaster risk reduction sectors. It also considers functions needed to defend against events regardless of their source, whether intentional or unintentional.

Capturing pillars and core functions relevant to all sources of disease introduction necessitated combining some major functions that might otherwise be viewed as distinct. For instance, under "Prevent," we collated activities that might, under different rubrics, fall under "Awareness" or "Protection" pillars. As with many frameworks, some functions could reasonably be placed under multiple pillars; in general, we have captured these as cross-cutting functions instead.

Governments and public health researchers have expended considerable capital to identify the spectrum of capacities needed to function well within and across countries to ensure optimal health security capability. This optimal capacity is now generally viewed by the global health security community through the lens of the Prevent-Detect-Respond triad seen in major human health security frameworks, including the Global Health Security Agenda (GHSA). Launched in 2014, the GHSA has defined goals for disease prevention, detection, and response and has gained high visibility and traction in assessing and strengthening country capacity for health security. To ensure alignment with ongoing efforts, we build on this existing structure, expanding it to include upstream prevention aspects and a dedicated recovery pillar consistent with building blocks for One Health operations presented in the World Bank's 2018 *Operational Framework for Strengthening Human, Animal and Environmental Public Health Systems at their Interface.*[27]

The pillars and functions in Table 1 are designed to be undergirded by a backbone of existing functional health systems. That is to say, these functions are necessary but not sufficient to achieve global health security. They can also reinforce overall health systems strengthening.

TABLE 1: PILLARS AND SUPPORTING FUNCTIONS FOR GLOBAL HEALTH SECURITY

PILLAR	PREVENT	DETECT	RESPOND	RECOVER
MAJOR ELEMENTS	Awareness, Prevention, and Protection	Surveillance and Detection	Response	Recovery
DEFINITION	Systems, policies, and procedures to determine, assess, avoid, mitigate, and reduce threats and risks by reducing vulnerability and exposure	Systems, policies, and procedures to gather and analyze information, provide early warning, and inform strategies	Systems, policies, and procedures aimed at disease control and saving lives	Systems, policies, and procedures to restore and strengthen normal operations
FUNCTIONS	• Identification of EID drivers • Threat assessment • Hazard profiling and risk assessment • Critical infrastructure protection • Biosafety • Pathogen security • Research governance • Counterproliferation • Deterrence and dissuasion • Interdiction and disruption • Screening and detection • Disarmament • Risk reduction of EID drivers • Prophylactic medical countermeasures • Hygiene and sanitation	• Security intelligence • Environmental and sentinel detection • Early warning • Case identification • Point-of-care diagnostics • Laboratory diagnostics • Indicator-based (including clinical/syndromic) surveillance • Event-based surveillance • Epidemiologic investigation • Event determination • Multi-level and multi-sectoral reporting • Sample movement logistics and tracking • Forensics and attribution	• Planning and response simulation • Command and control/emergency response operations management • Healthcare surge • Essential services surge • Laboratory services surge • Mental health services surge • Transportation and equipment • Diplomatic and military intervention • Case management • Cascading effects/crisis management • Medical countermeasures • Non-pharmaceutical interventions • Evidence-based control measures • Epidemiological investigation • Multi-level and multi-sectoral reporting • Disposition of remains	• Needs assessment • Health consequence management • Economic and societal consequence management • Socio-cultural sequela management • Health system (re)establishment • Decontamination • Remediation • Mental health • Bioweapons disposal and decommissioning
CROSS-CUTTING FUNCTIONS	• Governance: leadership, policy, statute, regulation, enforcement • Resource allocation and coordination • Community engagement and resilience • Risk communication and education • Workforce development and sustainment • Research and development • Data and information management			

In general, "prevent" refers to components that thwart the introduction of the disease; "detect" includes those components that contribute to finding and identifying disease; "respond" comprises components that aim to contain and control disease; and "recover" addresses re-establishment of a disease-free status and normalized operations once a disease has been controlled. All functions may occur simultaneously and some functions may carry over from one pillar to the next during an outbreak. Functions should be addressed jointly by public health, healthcare, animal health, agriculture, environmental health, law enforcement/counterterrorism, and defense sectors. EID = emerging infectious disease.

Table 1 presents several unique elements:

Prevention as a multi-dimensional concept. Pathogens are opportunistic in term of their ability to survive and spread. The distinctions between unintentional and intentional sources of pathogen release therefore become somewhat superficial once they begin to spread. The main distinction among outbreaks are the human-mediated factors that shape disease risk and the appropriate interventions needed to mitigate this risk. "Prevent" in this construct captures prevention of epidemics at their source before pathogens spill over, bioweapon development and deployment, and laboratory-based and other pathogen release incidents. This column delineates the numerous functions needed to prevent each of these originations, emphasizing certain functions, particularly in the defense sector, that are either not explicitly seen in global health security frameworks or whose representatives are not routinely represented at the decision-making table.

- ***Unintentional.*** Prevention of unintentional sources encompasses pathogen emergence from its origin into people (i.e., transmission via contact with the natural reservoir or host species for a pathogen, contaminated food or water, etc.), as well as sources such as accidental release from laboratories. While prevention is an element of several frameworks in name, it typically refers to *prevention of disease spread or impact in human populations*, rather than *prevention of initial pathogen emergence in a novel host, including humans*. The GHSA and the Joint External Evaluation (JEE), designed to assess country implementation of the International Health Regulations (IHR), do state their intention to foster behaviors, policies, and practices that minimize spillover, but also indicate that the impact of these efforts would be measured by strengthened *surveillance* systems. Unless surveillance information is acted on with risk reduction practices, this is not prevention—this is detection. Many of the leading factors that appear to drive risk of emergence and spread, such as problematic land use change and environmental conditions, food acquisition and production practices, and global trade and travel, fall far outside the purview of the health sector. In addition to those factors that enable transmission and geographic movement of pathogens, pathogens may be inadvertently released as a result of a breach in laboratory/hospital biosecurity protocol or biohazardous waste management practices, or from the unintentional release from a bioweapon. The GHSA and JEE incorporation of biosafety into their Prevent categories (and as part of the larger IHR core capacities) is relevant to preventing such unintentional transmission.

- ***Intentional.*** The prevention of intentional acts, whether carried out or sponsored by states or non-state actors, is a core consideration in the Prevent pillar. The Prevent column in our construct explicitly includes defense-oriented functions. The GHSA and JEE do address biosecurity, one critical element of prevention, but do not cover the many diplomatic and defense functions necessary to achieve comprehensive security from intentional biothreats. Some of these exist outside of the health sector domain, such as counter-proliferation. While this may be justified in the context of those documents' purposes, we include them in our own framework for the reasons described earlier, and in the hope that they will engender honest discussion about where further engagement of the defense sector could be most beneficial.

Recovery as a pillar. After the cavalry has come and gone, communities and nations must somehow resume their former health improvement and economic growth trajectories. How can this recovery be achieved when communities, workforces, economies, and governance structures have been diminished or even decimated, particularly in already-fragile states? Recovery is a complete outlier captured neither in the JEE nor the GHSA. This is significant given the chains of disruption that in the recent past have been triggered by epidemics and pandemics. In the animal health community, steps are outlined by the World Organisation for Animal Health (OIE) for countries or sub-national zones to restore trading freedom after a country's return to a disease-free status. The World Bank *Operational Framework*, as well as U.S.-based policies and guidance such as the National Biodefense Strategy and the Department of Homeland Security Threat and Hazard Identification and Risk Assessment process, stress recovery in their constructs. Any global health security framework should do the same.

Animal and environmental considerations as integral to a complete framework. The importance of a One Health approach that recognizes human-animal-environment health connections is often stated, but to the extent that it is actually seen, it tends to be concentrated at the human-livestock interface, largely omitting wildlife and the environment. Because human health is a function of the health of animals with which we share our environment, addressing health security holistically requires inclusion of all of these components.

Cross-cutting functions as foundational. We identified seven functional areas that transect the pillars. These represent critical functions throughout the continuum of prevention through recovery. These are not specific to any one sector, and often require multisectoral and multidisciplinary involvement to be optimized. They must operate not only during emergencies but also between emergencies.

- ***Governance.*** The success of collective health security at a country level is predicated on the strength of the governance that underlies it. Leadership to ensure strategic focus and prioritization, policy to provide structure, statute and regulation for the legal backbone, and enforcement to ensure effective implementation must all be in place.

- ***Resource allocation and coordination.*** Resources (whether funds, training, in-kind personnel, supplies, or others) may be useful for any given function. However, many resources can be optimized to ensure they contribute to overall system strengthening, avoid unnecessary duplication and, importantly, ensure necessary allocation of resources for priority and gap areas. This is especially important for coordination across sectors, as resource support sources and priorities may vary, and there may be opportunities to refine existing investments (e.g., in environment or livestock) to generate shared benefits both for their specific sector and more broadly for health security.

- ***Community engagement.*** Engagement at the community level is a crucial underpinning of local and global health security. The local community must be involved from the start and throughout implementation activities. Workforce development, emerging threat detection and reporting, trust establishment, and risk reduction opportunities are all a function of community-level capability and implementation. Health security approaches must be designed with these end users in mind, including building in assessment and understanding of knowledge, attitudes, and practices in communities.

- ***Risk communication and education.*** An analysis of recent Ebola, Zika, and yellow fever outbreaks demonstrated that emergency risk communication is a vitally important element of public health.[28] Effective risk communication can enable success in each pillar. Although some avenues of risk communication will take shape based on the characteristics of a given pathogen, general principles, when applied correctly and in a sustained fashion, are needed and useful across pillars. Pathways for message delivery can transect public and private sectors; for example, employers offer central communication channels that reach large segments of the general population and are often a trusted source of information and a direct provider of services for employees and communities, which can help avert unnecessary costs resulting from fear-based aversion actions.

- ***Workforce development and sustainment.*** Because outbreaks may rapidly escalate to the point at which they overwhelm already-limited systems, strong public health systems supported by a trained workforce are critical to timely detection, trace-back, containment, and treatment. Addressing critical workforce deficiencies can mitigate vulnerabilities. Developing and sustaining a workforce for health security will require multi-year and likely multi-decade commitments, and can drive huge value if conceived as part of strengthening overall health systems to tackle all challenges. Local communities can also contribute to the workforce as the eyes and ears on the ground as a critical source of information for threat detection. Support for national and regional training programs and other paths to career opportunity will help generate a flow of skilled workers who, with additional supports, might be incentivized to remain in country.

- ***Data and information management.*** The effective generation, collection, sharing, analysis, and storage of data and information related to global health security must underpin evidence-based planning and response. This function applies not only to activities around surveillance data, perhaps most often considered in a data management context, but to every function across the pillars.

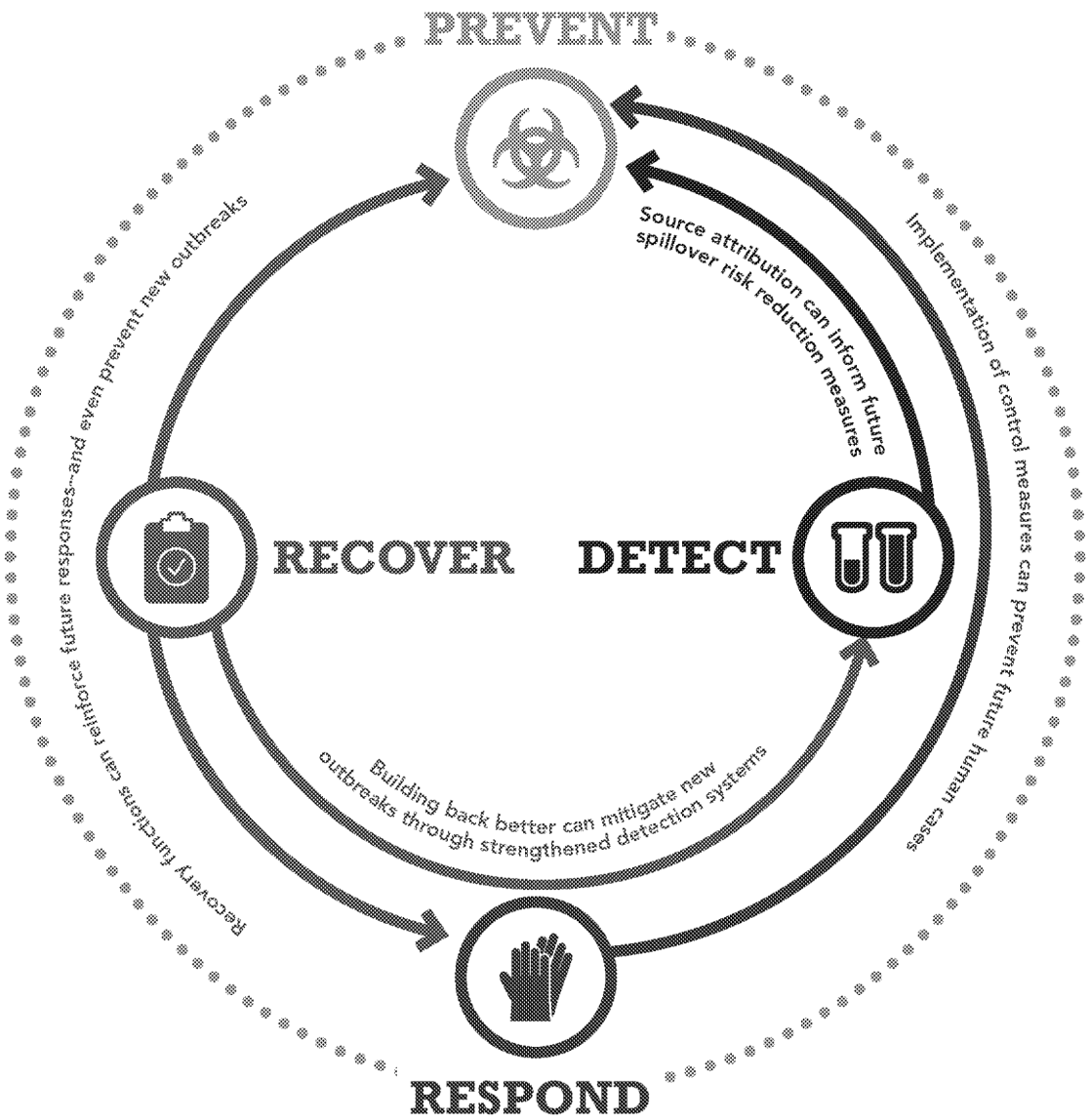
- ***Research and development.*** Collaborative research and development (R&D) is a force for enhancing health security. Health security is enriched by long-term partnerships between institutions with different capacities, including those that form while addressing a specific research objective. A 2011 report by the Center for Strategic & International Studies on the value of U.S. military research laboratories around the world notes the ability of these laboratories to attract productive international and local research partners, in part because of their longevity in a region and trust established with the host country.[29] This trust built on research partnerships can be invaluable in a health crisis, and its value is evident across all pillars. Identification of drivers of disease, expansion of surveillance sites, and contributions to community resilience can all grow from R&D collaborations.

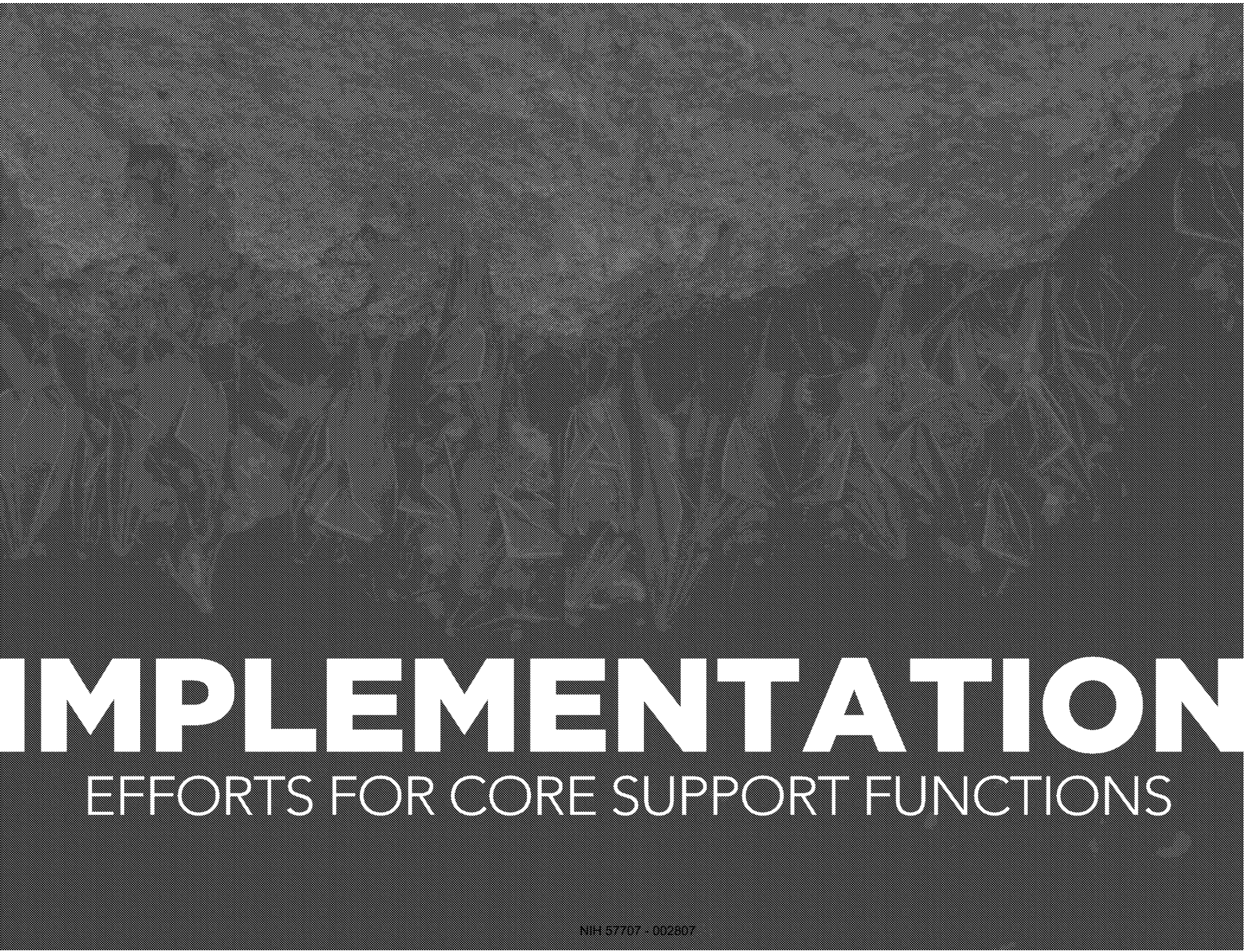
Some might view such a comprehensive framework as operationally unwieldly; we issue it here, however, for a few reasons. The impacts on human and animal life, the environment, and the economy are felt regardless of the pathogen source, and across many sectors. The U.S. National Biodefense Strategy approaches the problem just as comprehensively,[30] and the global community should similarly acknowledge the need for a more universal, less health discipline-specific and sector-specific, framework. Further, outside of highly targeted activities like personnel surety and intelligence collection (designed to prevent deliberate use of an infectious agent) or efforts to establish biosurveillance early warning systems that stem spillover events at their source, most investments will produce benefits regardless of outbreak source.

Policy-wise, there is value in viewing the necessary functions collectively to determine how best to allocate resources among them. Politically, there is value in demonstrating to decision-makers the benefits of investments whether viewed through security or more traditional public health lenses. Table 1 helps to place security concerns and skillsets into health terms, and in this way may help make synergies between sectors more apparent. While in practice it may at times be necessary to make distinctions—and, indeed, sometimes there will be no overlap—we saw value in joining these capacities to demonstrate the overwhelming mutual benefit of these sectors working together.

Figure 1 reimagines Table 1 not as a sequence from left to right but as a circular flow of capability. The pillars that comprise the scaffold can also be viewed as phases of management for outbreaks. But the phases are not really discrete: the dynamic situations that outbreaks present require the Prevent through Recover pillars to be viewed as continuous, concurrent, and overlapping for any high consequence outbreak, not as a chronological process specific to preventing, detecting, responding to, or recovering from a particular outbreak. Sufficient established capacity is required to perform needed activities between emergencies, as well as to address more than one crisis at a time.

FIGURE 1. GLOBAL HEALTH SECURITY PILLARS AS A CIRCULAR FLOW OF CAPABILITY.
The four pillars of global health security as a continuum, with arrows demonstrating examples of reinforcing areas.





IMPLEMENTATION

EFFORTS FOR CORE SUPPORT FUNCTIONS

"Global health governance requires the constant 'vertical' exchange between engaged actors from the national, regional and global levels, and 'horizontal' exchange between institutions and organizations with very different goals and stakeholders – indeed an extraordinary challenge for network governance."

– Kickbush and Szabo 2014 [1]

Governance and Legal Frameworks

Fortunately, much of the global mechanics needed to support core functions for health security is already in place. Various governance frameworks and international legal instruments specifically or indirectly address global health security and/or weapons of mass destruction. These represent significant global commitments, whether legally binding or voluntary, that countries and in some cases other stakeholders have committed to and that often come with substantial financial investment. The list is constructed based upon our defined scope of functions needed to address prevention, detection, response, and recovery.

These are globally-endorsed agreements with scopes encompassing health security. Of course, there are other important constructs not included here. Policies for industry groups, such as the International Air Transport Association, may also be relevant and expressly address infectious disease risks. Others, such as the UN Convention on International Trade of Endangered Species of Wild Fauna and Flora (CITES), the FAO/WHO Codex Alimentarius for food safety, the UN Framework Convention on Climate Change, and the New Urban Agenda may be relevant for the spread of disease, but have not formally emphasized biothreats in the context of global health security. Some governing bodies address health security indirectly, e.g., recent resolutions under the Convention on Biological Diversity (CBD) noting the drivers of disease emergence and the need for integrated biodiversity and disease risk monitoring.

Governance Frameworks and Legal Instruments

- 2005 International Health Regulations (IHR) and WHO Monitoring and Evaluation Framework (including the Joint External Evaluation [JEE])
- Convention on the Prohibition of the Development, Production and Stockpiling of Bacteriological (Biological) and Toxin Weapons and on their Destruction (BWC)
- Protocol for the Prohibition of the Use in War of Asphyxiating, Poisonous or Other Gases, and of Bacteriological Methods of Warfare (CWC)
- Bangkok Principles for the Implementation of the Health Aspects of the Sendai Framework for Disaster Risk Reduction 2015–2030
- World Organisation for Animal Health (OIE) Terrestrial and Aquatic Animal Health Code (and the OIE Performance of Veterinary Services [PVS])
- United Nations Convention on Biological Diversity Decision CBD/COP/DEC/XIII/6 – Biodiversity and Human Health (2016)
- United Nations Security Council Resolution 1540 (2004)
- United Nations Security Council Resolution 1810 (2008)
- Sustainable Development Goals

In addition to international agreements, other forms of governance may be highly relevant, such as review boards that approve large-scale funding for development projects, research programs, or investments. Industry groups may also introduce binding or voluntary best practice guidelines or industry standards to manage risks. In addition, convening groups such as the JEE Alliance have helped join stakeholders to promote a shared vision of the GHSA. The JEE Alliance's stewardship of the JEE tool ultimately led to adoption of the tool by WHO to assess gaps in country capacity to meet the IHR, in addition to the regular self-reporting by countries.

The major frameworks cited above each address, in some fashion, the global need to achieve a state secure from the threat of high-consequence pathogens. Overseen by voting countries that constitute their governance bodies, they drive much of the overall focus for implementation initiatives and often financing. Such governance and legal frameworks are fundamental to the strength of any of the pillars. These relevant governance and legal frameworks cover many sectors, including health, security, agriculture, environment, and disaster risk reduction. Some are designed for specific purposes, such as the treaty mechanism for verification and compliance on use of weapons of mass destruction under United Nations (UN) Resolution 1540. A major challenge of operating within UN structures is that their strict sector-specific mandates leave some needs unaddressed. While recent agreements aim to coordinate between particular institutions on specific topics (e.g., FAO/OIE/WHO Tripartite Collaboration), these are primarily high level, lack the provision of guidelines, policies, or investments for countries to work together on coordinated efforts, and ultimately have not translated to routine global coordination and country-level operations. Individual sectors are still responsible for achieving their individual commitments; incentives to work across institutions are lacking, contributing to limited application of a One Health approach in global and country operations despite broad support for such an approach. The decision-making, obligations, and reporting for each institution operate through separate channels, without regard for completeness of coverage and gaps in practice. The UN General Assembly has taken up health only four times in its history, otherwise relying on the mandates and activities of individual UN agencies. An inter-UN agency coordination approach was taken during the global avian influenza crisis (2003–2009) and again during the West Africa Ebola epidemic, but this approach has not been sustained in terms of facilitating a comprehensive, multisectoral approach within the UN system to assist countries in preparing for future threats.

Other international governance bodies also have a role in accountability for global health security. For example, an Independent Oversight and Advisory Committee for WHO's Health Emergencies Program, established in 2016 as part of WHO reforms, has eight members sourced from country ministries of health, funders, and other UN agencies. In addition, in April 2018 the WHO and World Bank launched a Global Preparedness Monitoring Board with a goal to advance "system-wide preparedness" for health emergencies. It is a successor to the UN Secretary-General's Global Health Crises Task Force, which was created in 2016 in response to the West Africa Ebola outbreak. While its specific monitoring systems and scope have not yet been defined, its leaders have expressed intent to engage beyond the two founding institutions.

Overall, the specificity of international agency mandates leads to diverging agendas and potential gaps in implementation and associated financing for global health security. In general, the public health community has driven the major metrics, assessments, and investments going into global health security. Because of this, we suspected that certain functions and, in some cases, entire pillars, were not being captured by the deliberative planning, assessment, and implementation processes for global health security. In addition, some of those that *are* captured may not be sufficiently emphasized or systematically addressed and therefore may not translate into effective action. These areas of coverage and gaps are the subject of the sections that follow.

"In a global health climate characterised by the need to demonstrate outcomes, it is difficult to 'sell' prevention and preparedness. Governments should acknowledge that health security has a cost with no immediate apparent outcome, but that such investment is irreplaceable in the face of an imminent health emergency."

— *Kluge et al. 2018* [31]

Financing

Country and external donor financing constitutes an important resource for developing health security infrastructure. An estimated $37.4 billion in development assistance for health (DAH), a broad metric for all health spending and not specific to health security, was allocated in 2017.[32] In low-income countries, this assistance constituted a large portion of health spending (approximately one-third) but, at an average of $122 per capita,[32] the shortfall in adequate resources leaves countries vulnerable to disease outbreak and spread. At the same time, this is not just an issue of absolute dollars, but of what functions are (and are not) funded and through what mechanisms.

The majority of global health resources for infectious diseases are dedicated to combatting specific endemic infections, namely HIV/AIDS, malaria, and tuberculosis. In 2017, $9.1 billion (24.2% of total DAH) was allocated for HIV/AIDS.[32] This financing is essential to address a critical public health issue, and speaks to the high cost of ongoing infection when a disease emerges and becomes established in human populations. Yet funds committed to infectious diseases other than HIV/AIDS, malaria, and tuberculosis collectively received only 3.9% of DAH in 2016, despite contributing to a third of total disease burden[b] in low- and middle-income nations.[33]

Pandemic preparedness funding has been short-term, ad hoc, and dispersed to single countries or regions or through specific response mechanisms. While annual reported spending for global pandemic preparedness has doubled over the past decade, the level of funding for pandemic preparedness still contrasts starkly with financing for pandemic response and is vastly outweighed by that of disease-specific programs. There is also poor coordination and clarity to track and optimize dedicated resources for health security; for example, officially reported DAH for pandemic preparedness as part of health systems strengthening in 2017 was estimated at only $204.2 million, with over 80% of funds channeled through WHO,[32] but this estimate does not capture wider health security investments being made at country and regional levels. Short-term funding spikes during recent avian influenza, Ebola, and Zika epidemics further signal that health investments and systems remain largely reactive and sporadic, and that associated recovery efforts are limited. Determining the long-term return on investment of current and future funding is notoriously challenging, given the lack of established baseline measures of pandemic probability and impact and the potential for spillover and spread; however, risk mitigation may have extremely high potential return on investment.

[b] Here, measured by Disability-Adjusted Life Years (DALYs), a common metric of health status that encompasses the impact of poor health, disability, and early death.

BOX 3: INVESTING IN PUBLIC AND ANIMAL HEALTH SYSTEMS, WITH LESSONS FROM VIETNAM

Health systems are still largely oriented to human health (and often human medicine), with limited capacity in funding for or collaboration with animal and environmental health programs, particularly wildlife programs. Globally, an estimated US$1.8–3.4 billion per year is needed to bring public and animal health systems up to minimum standards in middle- to low-income countries to attain the capacity to prevent pandemic threats.[19] This is roughly on par with the losses suffered by the tourism industry in Mexico from the H1N1 pandemic influenza ($2.8 billion over five months).[7] In 2016, the Commission on a Global Health Risk Framework for the Future followed up on this recommendation, calling for $4.5 billion per year to strengthen animal and human health systems, R&D, and preparedness.[17] The associated return on investment is projected to be high: more than $30–60 billion toward the global public good of pandemic prevention and broader public health benefits, as well as animal production gains that are likely to result.[17,19] As public health and animal health services are improved, capacity should also be extended to address wildlife and environmental health services—a largely non-existent capacity. Government resource allocation to wildlife services overall is extremely limited: a World Bank study indicated a per-country annual average allocation of ~$100,000 in the six nations surveyed, with the portion dedicated to wildlife health services a paltry 5% of this limited funding.[19]

Investment in coordination to optimize human, animal, and environmental health systems should also be considered. Under the World Bank Global Program on Avian Influenza, the Vietnam Avian Influenza and Human Pandemic Preparedness project built in provisions from the onset for integration and coordination to support communication and collaboration between human and animal health sectors, helping to maintain continuity even when funding levels to each shifted during project implementation. More recently, Vietnam has piloted a Health Security Financing Assessment developed by the World Bank, which seeks to track the source and flow of funds along the JEE technical areas to support coordination and assess financing needs.

Significant resources have been allocated to certain global programs directed toward health security (Table 2). While some of these support capacity building and system strengthening that will enable core operational functions, most are highly specific in scope and objectives. Examples of major investments branded as epidemic and pandemic preparedness financing include initial funding to CEPI for the development of vaccines against three prioritized pathogens and resource mobilization mechanisms established through the WHO and World Bank for emergency response (the Contingency Fund for Emergencies and the Pandemic Emergency Financing Facility, respectively). The GHSA is notable in its support for consistent and coordinated epidemic prevention, detection, and response, mobilizing resources from an extensive network of donor countries for capacity assessment and country operations.

Some of the investments in Table 2 do fill gaps highlighted in past recommendations (e.g., for R&D). However, these, too, are focused on certain countries, specific diseases, or single-outbreak approaches, and are heavy on response.

Funding of global initiatives for health security occurs largely through public health sector channels. Yet investments from or in other sectors could be highly relevant: e.g. biodiversity monitoring initiatives that can detect and report wildlife disease events, or livestock investments that build in biosecurity in food production operations. But such investments are relatively lacking, and to the extent that they exist, have not been optimized for health security.

TABLE 2. MAJOR GLOBAL-LEVEL FINANCIAL RESOURCES MOBILIZED FOR GLOBAL HEALTH SECURITY (FUNDING RECEIVED OR REQUESTED)

Program	Funding source(s)	Year(s)	Funding level	Prevent	Detect	Respond	Recover	Details
CEPI	Wellcome Trust, Gates Foundation, Japan, Germany, and Norway	2017–22	$560 million (as of 2017)			✊		Vaccine development; $1 billion target for first 5 years
Contingency Fund for Emergencies	WHO member contributions (17 countries have contributed to date)	2015–	$69 million received (as of June 2018); $100 million target for 2018-19			✊		Separately funded component of the WHO Health Emergencies Program; rapid response to health emergencies: up to $500,000 mobilized within 24 hours; $21 million utilized in 2017 in 23 countries
Gavi	Governments, Gates Foundation, private sector	2016–20	$9.2 billion in donor contributions and pledges	☣*		✊	📋	Immunization delivery (includes health system strengthening aspects)
GHSA	G7 nations	2014–22	>$1.44 billion	☣	🚨	✊		GHSA itself does not allocate/ appropriate funds; support is allocated by countries under the principles of GHSA to advance prevent, detect, and respond capacities
Pandemic Emergency Financing Facility (PEF)	World Bank	2017–22	$320 million (Class A pathogens: $225 million, Class B: $95 million); separate cash window			✊	📋	Surge financing (insurance window + cash window) in response to activation criteria (outbreak size, spread, and growth); premiums and bonds financed by donor governments
Pandemic Preparedness Plans	World Bank IDA18 Replenishment	2017–20	Dependent on client country requests			✊	📋	Support to 25 IDA countries to develop frameworks for governance and institutional arrangements for multi-sectoral health emergency preparedness, response, and recovery
WHO Health Emergencies Program	WHO member states	2016–	$485 million requested for 2016-17 (73% funded)		🚨	✊		Core budget for essential functions, plus an appeals budget that covers additional work in response to acute and protracted health emergencies

* To the extent that Gavi covers Prevent it is for the specific prevention of yellow fever spillover through vaccination in high-risk areas; does not address drivers

Examples of global-level health security programs with significant funding or intention to mobilize significant resources. Because funding mechanisms and use vary, and to avoid double-counting from donors and recipients, listings reflect reported funds issued, received, or requested at a global level. Funds may contribute to regional or country-level programs (for example, GHSA funding directed to the U.S. Centers for Disease Control and Prevention (CDC) global health programs or the U.S. Agency for International Development (USAID) Emerging Pandemic Threats program). Under the PEF, Class A and B denote different groupings of pathogens for insurance payout levels; the cash window can be mobilized rapidly separately from the insurance mechanism, including as a funding stream to respond to non-Class A or B pathogens. While the allocation of regional and domestic financing is important for sustaining country-level operations for health security and preparing for disease introduction, these allocations occur at a single country or regional level and on short-term budgetary or project bases, and are thus not captured here. IDA=International Development Association, the World Bank's lending arm to the poorest countries.

A response-heavy approach to biothreats is characterized by resource allocation to curb disease spread once outbreaks have already occurred, costing both lives and money. Despite this, Table 2 reflects a clear bias toward response. Additional analyses demonstrate the same. Of the nearly $6 billion mobilized from donors over the 14 months of the Ebola epidemic, 79% was allocated for response, 18% for recovery, and 3% for R&D.[34] Even R&D financing during and immediately after epidemics is largely subject to a narrow focus on biomedical innovation primarily for medical treatment and control measures in the context of major epidemics, rather than for wider threats and broader solutions. This surge financing includes upscaling of efforts for known pathogens when outbreaks manifest in new ways, such as via spread in urban populations; for example, investment in treatment and control of Ebola, which had caused outbreaks previously two dozen times, rose 942.7-fold after the West Africa outbreak.[35] Previous R&D efforts to create an Ebola vaccine had been cut short due to lack of funding and interest, an issue that has also affected other "priority diseases" for public health.

Funding streams are typically highly specialized and, if not coordinated, may result in duplication of efforts or may not result in functional capacity. For example, screening capacity under Detect may require laboratory equipment procurement, supply chains, staff training, and infrastructure improvement—all of which may be funded by separate initiatives. Similarly, capacity to screen for particular pathogens may not provide the agility necessary to respond to a wider range of known and novel diseases, and having sophisticated laboratories to detect disease will do little to stem outbreaks if capacity is not in place for field epidemiological investigation and implementation of control measures. At the same time, too, suitability of investments, while well meaning, may in some cases be misunderstood. For example, high biosafety-level laboratories (e.g., BSL-3 and BSL-4) are often high-profile investments, but the BSL designation simply indicates extent of precautions to protect against staff exposure or release of dangerous pathogens, not the extent of diagnostic capacity.

The true costs of disease emergencies are often incompletely or inconsistently captured, with line items varyingly included in impact calculations. Yet estimates point to extremely high direct response costs to donors and societies and cascading economic disruption to other services and sectors (e.g., transport, tourism, education).[27] From 2014 to 2017, more than $8 billion in emergency funding was spent by international health, development, and other donors for response and recovery to the Ebola and Zika crises, in addition to widespread societal disruption and billions of dollars of economic losses to local governments and industry operating in countries with heightened transmission.[36-39] Despite long-term health and economic consequences from epidemics, commitment to long-term funding wanes all too easily: as of January 2018, less than a third of total pledges announced by donors at the International Ebola Recovery Conference in 2015 had materialized, and the U.S. Congress diverted over $500 million in Ebola recovery funds to the Zika response[40,41]

The role of financing in creating incentives, or disincentives, for long-term capacity strengthening and risk reduction for health security is relevant to the support of functions across pillars. Insurance for epidemic and pandemic risks is relatively new and currently emphasizes assistance to countries for response and recovery (with payout once outbreak events reach certain triggers) or to industry for business continuity. If countries and donors are protected against the economic damages from outbreaks, such as through global insurance mechanisms, they may have little incentive to invest in upstream prevention. However, future iterations of insurance mechanisms could encourage safer practices, with precedent from other sectors in insurance encouraging risk reduction. Examples include lower insurance premiums for safe driving records or the use of smoke detectors, and the effect of workers' compensation plans driving safer employer practices. Shifting incentives to prevention and detection may have a remarkable effect on how we handle pandemic risk. Some investments recognize from the onset the importance of being implemented alongside investments in other pillars to optimize coverage, though to date this has not translated to continuity or coordination in investments.

Financing coordination channels have recently been established through the WHO's Strategic Partnership Portal[42] and at Georgetown University within the Center for Global Health Science and Security's Global Health Security Funding Tracking Dashboard[43]. Incentives to align investments, however, are still not formalized and any such alignments are dependent on the will of individual donors. Relevant investments and funding needs from other sectors to contribute to global health security functions also go largely unaccounted for. Funds committed to pandemic preparedness were recently added to the annual DAH tracking report, which may help increase visibility of preparedness resources (or the lack thereof) in global health.[32]

Funders are increasingly using upward changes in JEE and PVS scores as indicators of improved capacity.[27] However, investments for selected capabilities under each sector's assessments should be considered in the context of overall health security functions to ensure continuity between programs and to optimize the effectiveness of funding and efficiency of its use. As antimicrobial resistance increasingly challenges our ability to control known diseases, leading to the need for higher-cost second- and third-line treatment regimens, new infectious diseases are also looming on the horizon. Investments should be structured for long-term efficiency and effectiveness and multi-hazard preparedness.

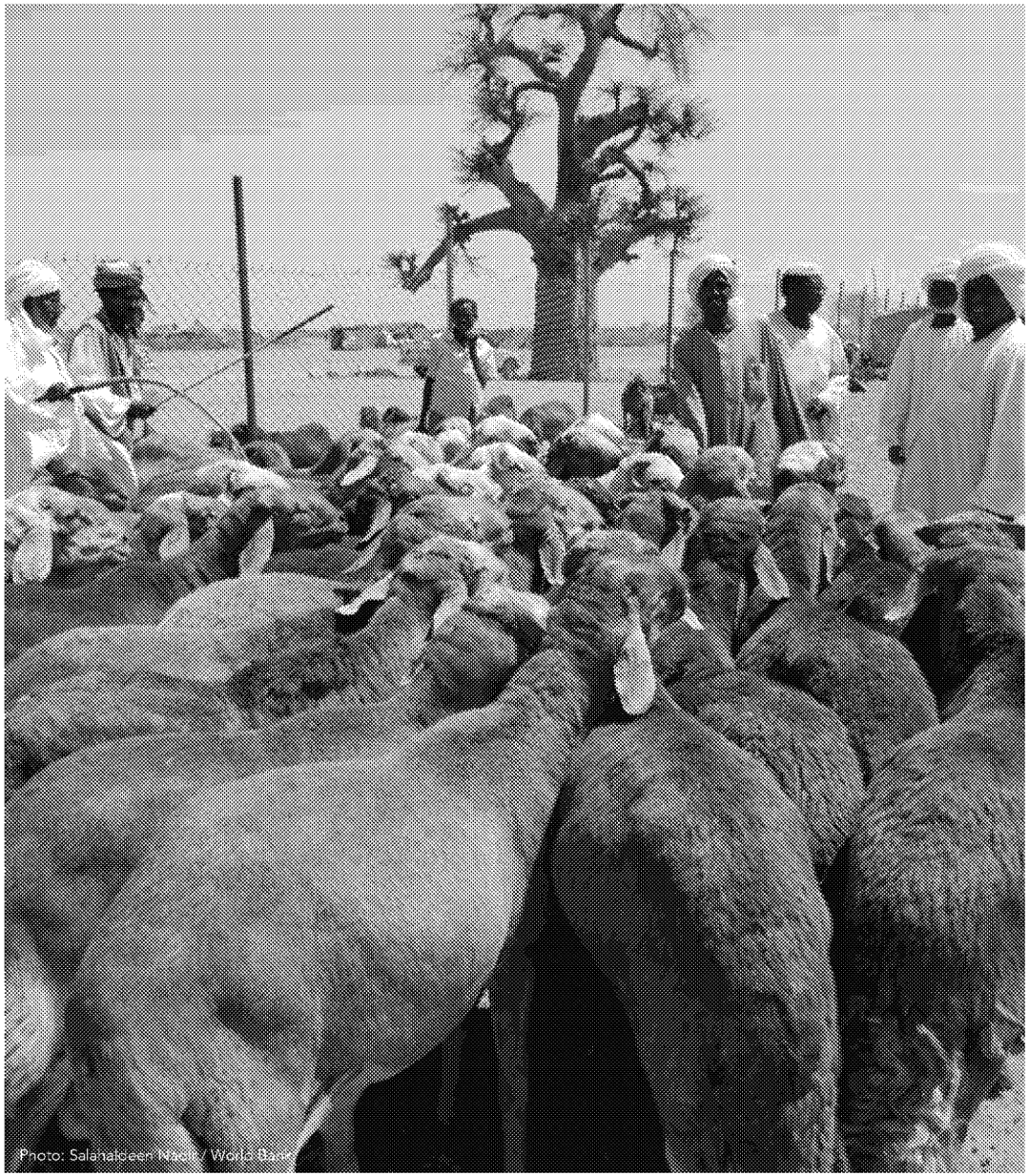


Photo: Salahaldeen Nadir / World Bank

"Despite efforts by the United States and a few other countries, there are still big holes in the world's ability to respond to an epidemic. Other countries may be more likely to step up if they see an overall plan and understand their role in it."

— *Bill Gates 2015* [22]

Initiatives

The governance structures described in the previous section create a structural and leadership platform from which to build and sustain global health security functions. Indeed, many structures have been developed and many initiatives are now underway to implement these functions.

The following are global-scale initiatives operating in the health security mission space, what we term "global initiatives to manage biothreats":

- Australia Group for chemical and biological weapon proliferation
- Coalition for Epidemic Preparedness Innovations (CEPI)
- Community Pandemic Preparedness Program (CP3)
- Gavi, The Vaccine Alliance
- Global Antimicrobial Resistance Surveillance System (GLASS)
- Global Early Warning System (GLEWS) for major transboundary animal diseases, including zoonoses and Global Animal Disease Information System (EMPRES-i)
- Global Financing Facility
- The Global Fund to Fight AIDS, Tuberculosis and Malaria (Global Fund)
- Global Health Security Agenda (GHSA)
- Global Health Security Initiative (GHSI)
- Global Partnership Against the Spread of Weapons and Materials of Mass Destruction (Global Partnership)
- International Reagent Resource (IRR)
- Proliferation Security Initiative (PSI)
- World Bank Pandemic Emergency Financing Facility (PEF)
- World Economic Forum (WEF) Epidemics Readiness Accelerator
  World Health Organization Contingency Fund for Emergencies (CFE)
- World Health Organization Global Influenza Programme
- World Health Organization Global Outbreak Alert and Response Network (GOARN)
- World Health Organization Health Emergencies Program
- World Health Organization R&D Blueprint for Action to Prevent Epidemics
- World Organisation for Animal Health World Animal Health Information System (OIE WAHIS)

We recognize the value of initiatives at other levels, from local to regional to national, but have not included these in our assessment. The sheer number of initiatives would be too great and the information capture too challenging for the scope of this study. Regional and sub-regional initiatives for response and capacity building are critical efforts and include programs like those managed by African Union Interafrican Bureau for Animal Resources (AU-IBAR), Connecting Organizations for Regional Disease Surveillance (CORDS), the Gulf Co-op Council, and Mekong Delta Surveillance. The World Bank's Regional Disease Surveillance Systems Enhancement Project (REDISSE) in West Africa is notable in that it represents a large-scale regional initiative with both development donor and country commitment and investment. The FAO Emergency Centre for Transboundary Animal Diseases provides crucial support against the threat of cross-border animal health emergencies, and the USAID Emerging Pandemic Threats program is strengthening capacity to examine pathogen spillover risks from wild and domestic animals to humans, but cover only ~30 countries and are based on project funding. The U.S. CDC Field Epidemiology Training Program and its veterinary counterpart are also implemented in many countries, but are predominantly funded bilaterally. Bilateral programs—that is, programs funded by a single country to a single country—were similarly excluded from analysis because of the limitations in our scope. While such programs are often critical to advancing health security goals and can lay the groundwork for sustained and even larger investment from donor countries, such programs can also bring challenges of coordination and resource provision, hindering progress in addressing the very problems they seek to mitigate.[3]

Given these limitations, and because the purpose of the current study was to help advance globally sourced solutions to health security, our list of initiatives was limited to those that could be defined as global. We viewed "initiative" as something global in architecture and/or oversight but designed to support the consistent development of local-, country-, or regional-level capacities or provision of something that could be disseminated based on global need rather than a specific geographic scope. Some of these initiatives were developed specifically to implement legal frameworks, whereas others were expressly developed to fill gaps in governance. While differing in their technical and geographic scopes, funding sources, timescales, and implementing institutions, the listed initiatives are recognized widely and routinely included in multi-donor planning meetings, have mobilized funding at significant scales (i.e., tens of millions to billions of dollars), or are firmly established in international institutions and the international biothreat and public health research, academic, or service delivery communities.

Within these parameters, we assessed the extent to which current global initiatives address the identified functions shown in Table 1. Table 3 reveals the relationships between the initiatives and pillars defined in this report. In addition to reviewing published information about each initiative, we have used our own experience and judgement as well as that of outside experts to determine placement into categories. Designations indicate that an initiative addresses a pillar per its stated mission or the judgement of the authors; it was beyond the scope of this study to assess whether it is successfully doing so.

Some of these are dedicated programs implemented primarily through one institution, while others are based on partnerships. Notably, GHSA is in this latter category. "Agenda" is perhaps a poor descriptor of what the GHSA actually is: a partnership of 64 nations, international organizations, and non-governmental stakeholders that facilitate collaborative capacity-building efforts around biological threats.[44] Each of the listed initiatives may also have many sub-initiatives that operate at different scales (e.g., country or regional) and may cut across pillars and sectors to some extent. Other conceptual and operational initiatives not included in this list may benefit global health security in important ways, but to date are not systematically recognized in global health security planning. More such efforts will hopefully take hold through public-private cooperation and be included in future updates of Table 3.

TABLE 3: MAPPING OF GLOBAL HEALTH SECURITY INITIATIVES TO PILLARS[c]

Initiative	Prevent		Detect	Respond	Recover
	Unintentional	*Intentional*			
Australia Group		✓			
CEPI*				✓	
CP3				✓	
Gavi†	✓			✓	✓
GLASS			✓		
GLEWS‡	✓		✓		
Global Financing Facility				✓	
Global Fund			✓	✓	✓
GHSA§	✓	✓	✓	✓	
GHSI	✓	✓	✓	✓	
Global Partnership		✓			
International Reagent Resource			✓		
OIE WAHIS			✓	✓	
Proliferation Security Initiative		✓			
World Bank PEF‖				✓	✓
World Bank Pandemic Preparedness Plan				✓	✓
WEF Epidemics Readiness Accelerator				✓	✓
WHO CFE				✓	
WHO Global Influenza Programme			✓	✓	
WHO GOARN			✓	✓	
WHO Health Emergencies Program			✓	✓	
WHO R&D Blueprint				✓	

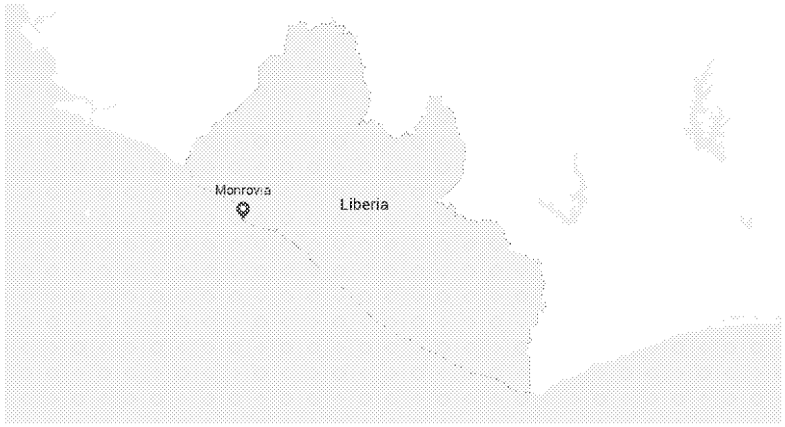
[c] It was beyond the scope of this study to assess whether the initiatives are successfully supporting the pillars. Thus, a checked column does not necessarily mean the effort is actually occurring or occurring in a way that impacts health security.
* Committed to funding through Phase 2 investigational stockpiles; not funded for Phase 3 or linked to a system for procurement, distribution, or dispensing.
† To the extent that Gavi covers Prevent it is for the specific prevention of yellow fever spillover through vaccination in high-risk areas; does not address drivers.
‡ Predominantly focused on risk monitoring and information alerts for Rift Valley fever in livestock.
§ Addresses prevention in the sense of containing outbreaks; attention to and capacity for spillover risk management is extremely limited.
‖ Disbursement of funds only applies to select viruses.

BOX 4: ONE HEALTH COORDINATION FOR HEALTH SECURITY IN LIBERIA

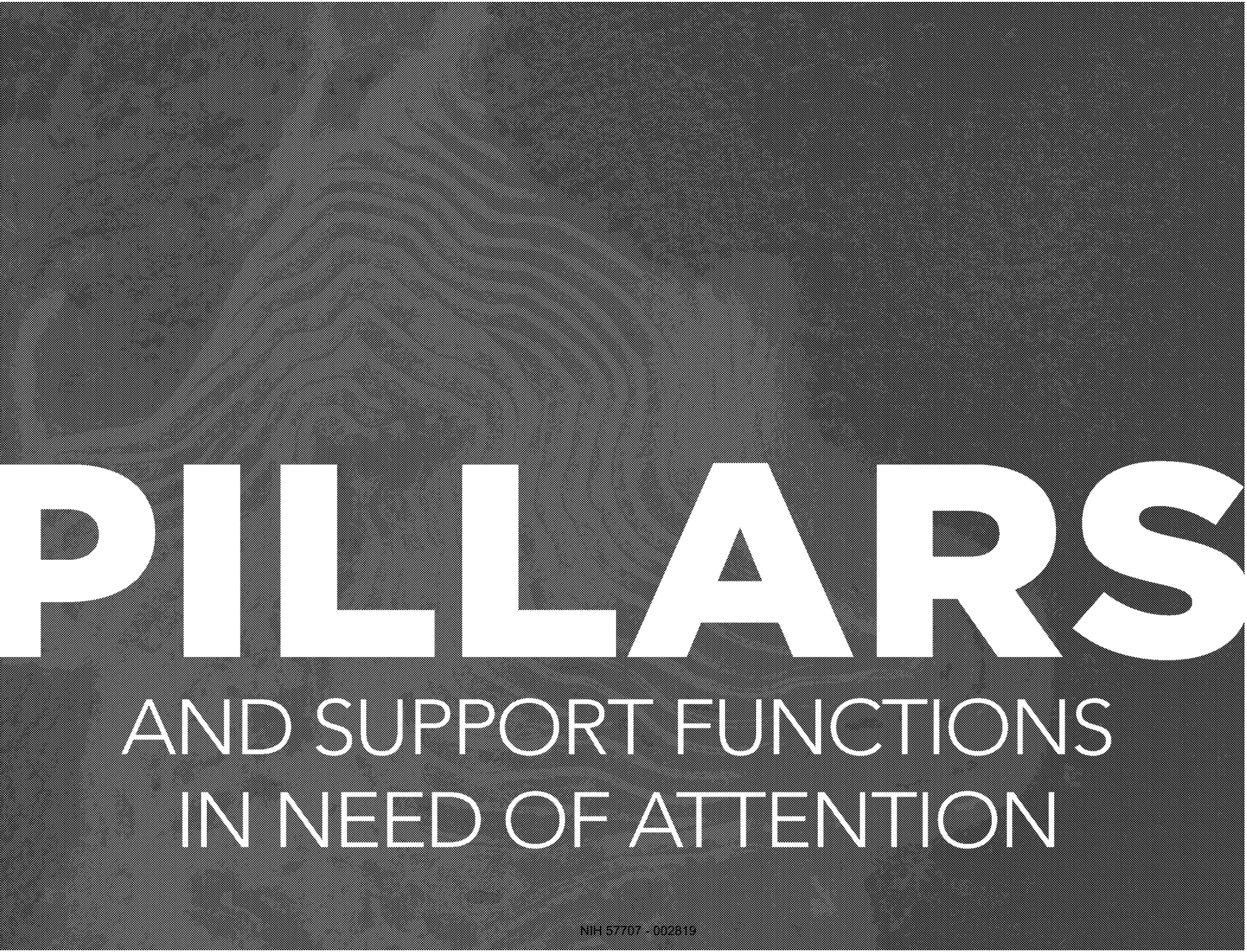
Liberia's context as a resource-limited, high-biodiversity country targeted for natural resource and economic development presents potential for intensifying contact with wildlife through changing forest access, modernized hunting techniques, movement of and contact with wildlife through wildlife trade, and agriculture without adequate biosecurity. At the same time, the country faces limited human and veterinary medical services (possibly as few as 50 medical doctors and five veterinarians) and poor electricity, supply chain, sanitation, and transport infrastructure.

Ebola revealed weaknesses in public health systems for both routine and emergency functions that left Liberia vulnerable to known and novel disease epidemics. Among these were chronic capacity gaps further identified during the country's JEE in 2016, including poor capacity for zoonotic disease surveillance, in part due to an extremely limited animal health workforce.

Liberia has subsequently embraced a One Health approach as part of its strong post-Ebola commitment to local, national, and global health security. The country has developed a national One Health Coordination Platform with strong leadership from the government of Liberia and support from WHO, USAID, U.S. CDC, and other partners. Under its associated Governance Manual, the Platform rotates host institutions on a time-specified basis. It is currently hosted at the National Public Health Institute of Liberia, with a designated Director and Coordinator. Signatories come from 36 agencies, ranging from the authorities responsible for animal health, education, and civil society organizations such as religious leaders. If fully implemented, the collaboration that could come from the participation of the 36 stakeholders may provide pathways to identify shared priorities and deliver clear and consistent information that can support optimal delivery of functions such as risk reduction and management, threat and disease detection, and risk communication. The vice president of Liberia serves as Chair, helping to convey its importance in the global landscape and promote an inclusive, equitable approach across sectors.



Country-level models like this can inform tailored approaches for the unique context of a given country and its stakeholder needs. The Platform has flexibility to convene needs-based Technical Working Groups on broad topics (e.g., surveillance) and disease-specific objectives (e.g., rabies). It also mobilizes participants in ways that encourage multisectoral approaches from the onset of assessments, priority setting, and implementation initiatives, including in its *National Action Plans for Health Security* and *Antimicrobial Resistance*. This may ultimately help to ensure that strategies are not biased to a limited set of conventional approaches. While limited familiarity or capacity in some sectors (notably, defense and environment) may be an initial barrier to complete implementation of the Platform's potential in Liberia, it holds significant promise for the promotion of alignment among sectors. One Health approaches are already being embedded into some national operations, including weekly Integrated Disease Surveillance and Response reporting for priority diseases in humans and animals from all of Liberia's 15 counties, and in building diagnostic capabilities for diseases notifiable to the OIE and WHO.


PILLARS
AND SUPPORT FUNCTIONS
IN NEED OF ATTENTION

This evaluation has revealed fundamental elements of global health security that remain unaddressed or under-addressed by the global community:

FINDING: GLOBAL INITIATIVES TO MANAGE BIOLOGICAL THREATS LARGELY OPERATE INDEPENDENTLY OF ONE ANOTHER

No governance effort nor strategic inter-institutional guiding framework attempts to align the global initiatives toward a commonly defined objective or set of goals. Implementation efforts and associated financing tend to tackle particular objectives—vaccine development incentivization; vaccine delivery; regional surveillance; diagnostics; training; reporting—and while such dedicated efforts are necessary, there is no overarching effort to coordinate them, ensure that they align with a designated set of goals, and see that they operate under a strategic framework to ensure all needed functions, regardless of sector, are in place to achieve them. This has both benefits and drawbacks. On one hand, a flexible structure leaves room for innovation, is not expressly limited by a specific set of priorities set by the judgement of only one authoritative group, and does not impede entry into working on pillars and functions. On the other, without it, the global health security landscape is highly fragmented, with disparate approaches and timelines, chronically under-resourced areas, and gaps in operational capacity. Without a shared framework, monitoring remains challenging and accountability limited.[45]

The Towards a Safer World initiative, a collaborative of experts established during the H5N1 avian influenza pandemic (2003–2011) through the UN System Influenza Coordination office and cutting across disciplinary and technical agencies, advocated for a whole-of-society and whole-of-government approach to prepare for pandemics and other major health disasters. It aimed to apply lessons learned from pandemic preparedness to other types of emergencies and threats. Following the H1N1 pandemic, the initiative took a light touch to keep the network of experts connected and up to date on global health security issues through a web-based platform. This inter-sector scope, however, was not formally adopted by UN agencies for the long term, despite strong support from many in the community. This is a testament to the predominance of the sector-specific approach and insufficient interest in financing coordination of prevention and preparedness efforts. Bill Gates has argued that the "world does not fund any organization to manage the broad set of coordinated activities required in an epidemic" and has suggested that the world needs a system coordinated by a global institution that is given enough authority and funding to be effective.[22] Whether the solution lies in a global institution or simply a mechanism for global alignment, we would extend this thought beyond those activities required "in an epidemic" to all the activities that should occur before it, and that must occur after it.

Conceptual and operational initiatives outside of formal UN-led structures are also emerging as a positive force in global health security planning. For example, the World Economic Forum (WEF) is working in partnership with over 80 corporate, technical, academic, donor, government, intergovernmental, and NGO partners to enhance public-private partnerships to effectively prepare for and respond to outbreaks. As part of this, the WEF's Epidemics Readiness Accelerator is strengthening essential public-private cooperation in five areas of work (travel and tourism, supply chain and logistics, data innovations, communications, and legal and regulatory); the WEF is also advancing other global health security activities, including helping companies understand the types and magnitudes of risks and impacts they may face from outbreaks. More such efforts will hopefully take hold through public-private cooperation.

FINDING: BIOTHREAT PLANNING AND IMPLEMENTATION ARE DOMINATED BY THE HUMAN HEALTH SECTOR

There seems to be a natural tendency to think about biothreats in terms of their consequences; and at that, of the single end consequence that worries us the most: our own health. This view then effectively drives the reverse engineering all of the structures and decisions that must occur before those human health consequences ensue, and the forward engineering of response actions tailored to that human health need. Areas like defense, environment, and animal health are often treated as needs outside of human health security frameworks, and direct partnerships are not often established. It is the central term "health" in the moniker "global health security" that has come to dominate the conversation around high-consequence pathogens, which is itself a symptom of this mindset, and which dramatically influences the nature of investment. This is true globally and, in many cases, nationally. While WHO has a valuable role in guidance and standard setting, we see a persistent gravitation toward holding WHO responsible as the sole organization for global health security planning and implementation, even though the myriad functions needed to do so reach beyond WHO's remit and, in some cases, technical and surge capacity. At a parallel U.S. level, the National Biodefense Strategy will be administered by a steering committee at the Department of Health and Human Services; and yet sixteen departments and agencies with wide-ranging responsibilities created that strategy.

Many initiatives are driven or owned by the health community rather than by multilateral partnerships (e.g., oversight of the JEE by ministries of health and WHO, and guidance of CEPI by WHO's R&D Blueprint). While this health sector leadership does not exclude potential inputs from other sectors, it does not promote their systematic inclusion. The IHR is a health framework, and as such the lead on its implementation naturally falls to ministries of health. The IHR and other health-oriented frameworks like it are typically developed only by the health sector. Absent the resources or empowerment to manage their existing mandates or be aware of the relevance of their own activities to other sectors, non-health sectors are not likely to come to the table.

For decades preceding the advent of the pandemic-inspired global health security push, there existed more traditional security-oriented activities in biowarfare and bioterrorism. These were first the superpower offensive bioweapons programs, followed by their cessation per the BWC and the concomitant development of threat reduction and counterproliferation policies and programs to thwart any future bioweapons development. These efforts were designed within the diplomacy and defense spheres of influence, wherein the rhetorical triad was not "prevent, detect, respond" but more akin to "counterproliferation, nonproliferation, and consequence management."[46]

The approach that has largely come to dominate U.S. federal policies with respect to biothreats—one that recognizes their sources in nature, in human intent, or in human error—was also built into the GHSA. GHSA was not about global health—it was about global health *security* which, while lacking a standardized definition, clearly differentiated it from other global health programs in areas like maternal-child health or malaria. The term "security" could be viewed in two lights in the GHSA: one with respect to securing human health from high-consequence pathogens, and the other with respect to securing the pathogens themselves from misuse. Both of these, but especially the latter, necessitate the involvement of other sectors that work in or toward security, such as defense, law enforcement, border control, customs, counterterrorism, and diplomacy.

Efforts to create bridges between the health and security communities should acknowledge that some in the health world will be wary of those from the defense world, and vice-versa. Building on initial military and health sector collaborations that were crucial in the response to the West Africa Ebola crisis, the Indonesian Government in collaboration with WHO hosted a meeting in 2017 to promote the sectors' collaboration to strengthen health security and advance implementation of the IHR. The meeting identified the need for development of guidance on national-level collaboration between military

and civilian health sectors, including the role WHO can play in supporting countries in their implementation. These advances should be promoted and sustained and also considered for other segments of the military beyond health services (and for other sectors), and should attend to both logistical coordination as well as tackling broader biothreats on the horizon (e.g., new developments in synthetic biology). Finding common ground to emphasize shared objectives for capacity and outcomes, and perhaps framing benefits in terms of securing human and global health, may help. The GHSA loosely provides a vision and associated frame for global health security through its dedicated action packages, though it leaves an overarching coordination piece to individual donors. Multiple national and global defense/security actors contribute in some fashion to the GHSA, for example under the Global Partnership, Interpol (a founding member of GHSA), and the many national-level funders from defense and related ministries. The equitable participation of the defense and security sectors was certainly the vision of the GHSA. But their presence has waned in international global health security fora according to experts. Although defense and security must be part of the global health security solution, "Around the world you don't often see ministers of foreign affairs or defense or their delegates at these meetings."[47] Yet the defense sector can contribute to many functions, regardless of the origin of the threat; it can similarly receive benefit to its own operations by collaborating with sectors like environment, agriculture, health, and finance. Such partnership can enable defense to better understand global threats, develop mitigation strategies, and inform risk analyses that ultimately inform what national and global biodefense priorities should be.

Actions and investments from many additional sectors are clearly needed. The engineering sector, for instance, is widely appreciated for improving sanitation to address water- and vector-borne disease risks. Engagement with sectors of trade, travel, and finance as well as with civil protection and disaster management authorities is similarly highly relevant. This can build on existing initiatives, especially as some sectors outside of health are already providing funding at significant levels; for example, an analysis of projects financed or undertaken by members of the Global Partnership under the BWC indicated that 13 country partners reported contributions totaling >$470 million for capacity building programs.[49] Ensuring investments are coordinated or considered with global health security targets in mind can help optimize their multisectoral impact. Governments could also capture revenues from multiple sectors, such as through taxation, to finance pandemic preparedness efforts.[19] The recently established multisectoral National Action Plans for Health Security, which help act on the findings of the JEE and other assessments toward implementation of IHR core capacities, recognize this potential for multi-sectoral resourcing and aim to bring finance ministers, agriculture, military, security, and other sectors to the table. Planned costing exercises, however, still remain largely in the health sector.

Finally, One Health is not yet an implementation reality. As discussed, the contributing causes of epidemics and pandemics span widely beyond the human health sector. Without systematically considering risks that contribute to disease emergence from livestock, other domestic animals, and wildlife, and the role of environmental factors as related risks, we will perpetually be left with limited options for disease prevention at the source of disease threats. The siloed approach to disease risk management contributes to the lack of accounting for these negative externalities; a more integrated approach could anticipate and reduce risks from the onset. The institutions that frequently bear the costs of responding to disease events, such as development banks and global foundations, are well placed to address this fundamental issue given their wide-ranging lending lines and technical expertise. This can be done through direct investments in One Health projects that build in dedicated mechanisms for collaboration and incentives for relevant sectors on specific objectives (e.g., REDISSE), as well as by applying a One Health approach to project design, implementation, and evaluation phases. Processes such as safeguard policies, which assess possible adverse impacts of projects, can be enhanced to include public health threats beyond their current scope of environmental and social risks to also help target the drivers of disease to identify risk factors and mitigate negative externalities.[16]

BOX 5. NEXUS OF INSECURITY: CONFLICT AND FRAGILITY IN THE KASAI REGION OF THE DEMOCRATIC REPUBLIC OF CONGO

Since late 2016, in response to the killing of a local chief by the Congolese armed forces and internal conflict along ethnic and political fault lines, 1.5 million people have been internally displaced in the Grand Kasai region of the Democratic Republic of Congo (DRC). Most of the displaced live in makeshift arrangements in their own or other communities, and they lack food and basic health and education services. Approximately 42% of households in this region are food insecure and, across the DRC, about 7.7 million face the risk of imminent famine; over one-third of those at risk are in Kasai.[48]

This crisis in southern DRC bookends the more limited but high-profile crisis that occurred in the north: on May 8, 2018, an outbreak of Ebola virus disease was declared in the Bikoro region of Equator province. Spread of the disease to Mbandaka, a city of almost 1.2 million, raised the specter of an uncontrolled epidemic that could spill into neighboring countries and markedly raise the death toll. Substantial funding was quickly mobilized, an experimental vaccine and 332 technical experts were deployed, and, on June 12, the last confirmed case was discharged from a treatment center. In total, 58 cases and 27 deaths were attributed to Ebola, but loss on the scale of the 2014 epidemic in West Africa was averted. As this report went to press, the virus had emerged again in DRC in other locations.

Though these crises—the Kasai conflict and the Ebola outbreak in Bikoro—occurred in distinct areas of the country, they represent on-the-ground challenges for national governments and indicate the need for resilience throughout the prevent-to-recover cycle.

Currently, much of the south and east of DRC is considered a "risk" or "deteriorated" area and, in addition to the 2018 Ebola outbreaks, there have been sporadic monkeypox cases and a recent widespread cholera epidemic, all with the risk of famine as a backdrop. These examples highlight the multiple simultaneous threats to security (i.e., food, health, and social and political) presently facing the DRC. Further, the disruption of agriculture, looting and destruction of health facilities and schools, and compromised access to water and sanitation due to conflict show that reinstating healthcare and establishing health security will require security support beyond that of the health sector alone.

FINDING: PREVENT IS SCARCELY ADDRESSED

The Prevent pillar is at once the most important and most under-appreciated. Only seven of 22 initiatives support our definition of prevention. This pillar is complicated by two sub-categories: unintentional (preventing spillover and spread in human populations by managing risk drivers, and preventing accidents with biological agents); and intentional (preventing development and use of bioweapons). Only four of 22 initiatives address prevention of unintentional release.

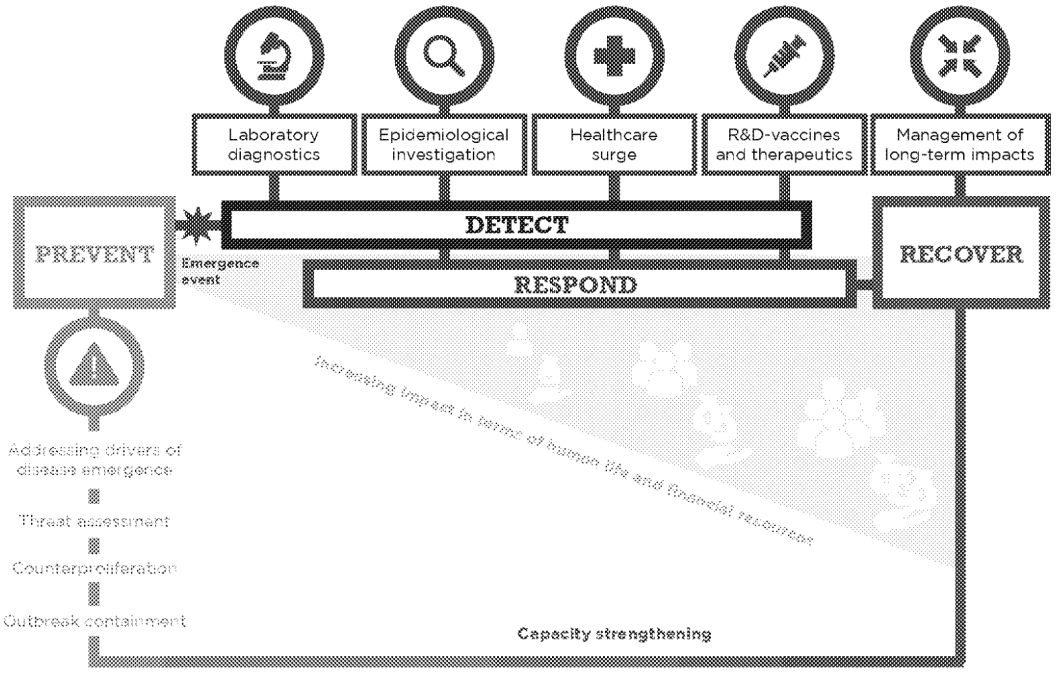
The counterterrorism-oriented functions of this pillar are far better addressed than those that are EID- or accident-oriented. This to some extent reflects the reality that counterterrorism efforts are relatively well defined and approachable through existing diplomatic and defense channels. Preventing EID events is perhaps perceived as less defined or less approachable, but perhaps only because we have not been willing to systematically identify and address the drivers of spillover, develop the research base to anticipate spillover events, and proscribe interventions. *In our construct, Prevent is not about limiting outbreaks before they become epidemics or pandemics. Such containment during response efforts to reduce potential for spread and impact is indeed critical when outbreaks do happen. But also important is reducing the likelihood and frequency that outbreaks happen in the first place by preventing the emergence of pathogens at their source. It is this prevention of initial emergence—essentially, the containment of pathogens to their natural hosts—that is so needed to shift the paradigm from one of response to one of prevention* (Figure 2).

Despite repeated lessons from HIV/AIDS, SARS, H7N9 avian influenza, Ebola, Zika, and many other infectious diseases, there is surprisingly little attention to diseases on the horizon as compared to other threats to the health and well-being of people and the planet. Ebola in West Africa was unexpected because it had never been reported there before, but reports published after the West Africa Ebola outbreak began showed that Ebola virus antibodies were present in suspected Lassa fever patients in Sierra Leone as early as 2006–2008, suggesting previous circulation of Ebola viruses in the region.[50] Upstream detection and prediction may be technically challenging, but how many opportunities to do so have been missed simply because we did not try? If paired with subsequent risk reduction, these offer real potential to curb the frequency of outbreaks. We acknowledge that some activities that begin with outbreak response—such as biosurveillance, laboratory diagnostics, and emergency operations management—may indeed work toward prevention or containment of future outbreaks if they are sustained. This reality to some extent, then, blurs the line between response and prevention. But even if these activities were sustained, other areas of prevention remain in need of support.

One of these is R&D. The WHO R&D Blueprint priority pathogens all have close environmental or animal health links, but efforts to develop countermeasures for these pathogens are typically targeted to humans. Even while livestock health is becoming increasingly integrated into health security, and the OIE PVS tool helps identify capacity gaps therein, most livestock development assistance is not optimized for reinforcing functions for health security (such as those that target risk reduction in areas like land use planning or animal husbandry). Investment and standards in environmental health have primarily been focused on reducing pollutant and other chemical exposures. Capacity and resources in environment/forestry sectors are typically severely under-developed at the country level. As a result, wide gaps remain related to wildlife and vector-borne diseases, as well as the environmental factors that may be associated with risks.[19,27]

FIGURE 2: EXAMPLES OF ACTIVITIES AND TRAJECTORY OF IMPACTS ALONG THE PREVENT-DETECT-RESPOND-RECOVER SPECTRUM.

The security community uses the term "left of boom" to describe the entry point at which it is optimal to intercede with respect to major security breaches like bombings. We do this on the intentional side of biothreats as well—but prevention of spillover is not yet the prevailing paradigm in managing outbreaks that originate from animal and environmental exposures.



Epidemics and pandemics are often spoken of as inevitable. It is true that we usually cannot know what we have prevented from happening, but this truth does not obviate the need for prevention research and implementation. The value of prevention is well recognized in other sectors, such as reduced speed limits to prevent traffic fatalities, fire-resistant building materials and sprinklers to prevent and slow the spread of fires, earthquake-proof building codes in high-risk fault lines to prevent building collapse, and building restrictions in high flood-risk zones to prevent the loss of homes and other assets. Incentives, too, exist for risk reduction practices in other mission spaces; for example, lower car insurance rates are offered to drivers without accident and speeding histories.

Some promising prevent-oriented programs have been funded by individual countries, such as those supported by USAID (the Emerging Pandemic Threats program and in particular the PREDICT project) and the U.S. Department of Defense (through the Defense Threat Reduction Agency and the Defense Advanced Research Projects Agency). Analysis reveals that certain species are more common sources of viral zoonoses than others (i.e., bats, rodents, non-human primates) and that habitat loss and exploitation of wildlife are convergent drivers of both species declines and viral spillover risk along with other drivers including agriculture intensification and food industry changes.[51,52] In addition, environmental factors like rainfall anomalies are positive predictors of climate-sensitive disease outbreaks such as Rift Valley fever.[53] Climate and weather systems maintained and financed by other sectors can be leveraged by the health security community to anticipate places and people and other animals at greatest risk for spillover events.

BOX 6. CONVERGENT RISK DRIVERS: POTENTIAL IMPACTS OF CLIMATE CHANGE AND URBANIZATION ON VECTOR-BORNE DISEASES IN MAURITANIA

Mauritania faces two critical risk factors for vector-borne disease: climate change and urbanization. While intensifying drought and desertification present threats to health and livelihoods in the central Sahel region, coastal erosion and the potential for flooding increase pressure on the growing coastal cities of this second most rapidly urbanizing country on the African continent.

Vector-borne diseases—those caused by pathogens transmitted through mosquito and tick hosts, primarily—are highly responsive to environmental change, including local changes in temperature, humidity, and precipitation, as well as larger-scale changes in land use due to agriculture and urbanization. Recent cases suggest three vector-borne diseases that may respond to climate change and urbanization: Rift Valley fever (RVF), Crimean-Congo hemorrhagic fever (CCHF), and dengue fever. RVF, which causes abortions in livestock and fever, eye damage and, rarely, death in humans, has shown both range expansion and an increase in the number of cases in Mauritania over the last decade. CCHF, which can emerge from a tick-livestock cycle, has a high case-fatality rate (>30%) and has been reported in Mauritania as recently as late 2017. Dengue, transmitted to people through mosquito bites, is present throughout tropical and subtropical regions of the world; it was first reported in Mauritania in 2014.

While these diseases present problems primarily for local communities, the recent cases highlight the broader threat of these diseases to Mauritania and to the region. After the 2014 Ebola epidemic, WHO heightened its monitoring of hemorrhagic diseases, and RVF and CCHF both figure prominently in emergency response plans and are included in the WHO R&D blueprint. The distribution and frequency of both diseases are likely to change as livestock move in response to the availability of food and water in a changing climate. Further, the potential for introduction of these diseases into cities and for altered routes of transmission (e.g., hospital-associated) should be considered in the context of routine movement into cities, including the provision of food products for these burgeoning populations. Finally, with the recent introduction of dengue into the capital city of Nouakchott, an increasing burden of disease in this and other growing cities is a near-term challenge that should be proactively managed.

Urban margins—areas of cities with dense human populations, inadequate infrastructure, and irregular access to water and sanitation—are fertile breeding grounds for vectors and the diseases they transmit, and monitoring and possible prevention mechanisms for introductions (particularly of RVF, CCHF, and dengue) into large- and intermediate-sized cities of Mauritania should be considered as a disease surveillance priority. A comprehensive development approach to urban and water infrastructure, coupled with increased human resources for health and agriculture, including entomological surveillance, will be needed to mitigate the vector-borne disease risks posed by climate change and urbanization in Mauritania.

Recovery

Systems, policies, and procedures to restore and strengthen normal operations

- **Needs assessment**
- **Health consequence management**
- **Economic and societal consequence management**
- **Socio-cultural sequela management**
- **Health system (re)establishment**
- **Decontamination**
- **Remediation**
- **Mental health**
- **Bioweapons disposal and decommissioning**

FINDING: RECOVERY IS ALL BUT MISSING

Initiatives to meaningfully and systematically advance recovery planning and implementation are extremely limited. The entire pillar of Recover is not captured by the major extant frameworks, nor are its functional areas nested within Prevent-Detect-Respond. They thus remain the most significantly overlooked.

Disaster recovery efforts are a mainstay for management of many natural hazards such as floods and earthquakes. Post-disaster recovery in such situations tends to emphasize rapid rehabilitation and reconstruction. But for epidemics, prior capacity is typically limited, with little existing platform on which to build. A true focus on building capacity in ways that "build back better" is generally missing for recovery from disasters that result from biological hazards.

Addressing the long-term burden of disease is the most obvious need for recovery efforts, as seen with the Ebola Survivors projects in West African nations, which focus on issues like healthcare services and research on long-term complications, skills retraining, and stipends to address livelihood impacts and social marginalization. Their very existence is a testament to the lasting impacts of outbreaks, but outside of these programs, support for disease survivors of infectious disease outbreaks is not routine. Nor is health system recovery in the aftermath of bio-disasters, including rebuilding the health workforce which may have suffered huge loss of lives of personnel, reactivation of health services which may have suffered as a result of the emergency, and addressing the overall weaknesses of the system. By effectively addressing lessons learned, investments in recovery could prevent repetitive spending on response reflected in activities like construction of short-term treatment centers, ad hoc animal and ecological surveillance, and the medical supply and healthcare worker influx that often accompany large outbreaks but are frequently not sustained long-term at national levels post-crisis.

The global health security governance community must decide whether recovery is a priority for them and if it is, it should be built into the frameworks, and initiatives in turn must be developed to address it. Recovery has high potential to leverage and optimize investments from other sectors (e.g., energy, education, supply chain development) in ways that benefit future emergency and routine operations. It is also crucial that recovery reinforce functions in the other pillars to address hazards, exposures, and vulnerability in order to avoid repeated devastation.[54] As with other functions, resilient recovery requires coordinated action from a range of sectors in preparation for, during, and following biothreats. Recovery must not merely be based on the return to "normal" but must include prevention activities that prevent future outbreaks or at least mitigate their effects.

BOX 7. CLOSING THE LOOP: FROM AN EFFECTIVE RESPONSE TO EPIDEMIC PLAGUE TO INFORMED RECOVERY AND PREVENTION IN MADAGASCAR

In 2017, an epidemic of plague hit the island of Madagascar. Although cases occur annually—Madagascar is a major focus of plague, routinely accounting for one-third of all cases worldwide—this epidemic represented a more than five-fold rise in the number of seasonal plague cases. In total, 2,348 cases and 202 deaths were attributed to the epidemic.

Agricultural communities in Madagascar are at highest risk of exposure to the bacterium Yersinia pestis, the etiologic agent of plague that cycles between fleas and rats and routinely spills over into humans in close contact. However, plague in the 2017 epidemic differed in important ways from seasonal plague. First, unlike the typical concentration of cases in the rural highlands at the center of the country, this epidemic was concentrated in urban areas, including the capital of Antananarivo. Second, rather than transmission through its usual flea-to-person route, the pathogen was transmitted person-to-person through the respiratory route. These two factors fueled the epidemic and posed the threat of wider transmission.

On November 25 of that year, the Madagascar Ministry of Health declared an end of the urban pneumonic plague outbreak, although rural bubonic cases continued to be detected. The epidemic was curtailed by an effective response that included contact tracing and free treatment, supported in part by $1.5 million in WHO emergency funds.[55] However, as noted by Bonds et al.,[56] international responses can quickly fade, without the needed pivot to stabilize the economy after fear-associated closures of businesses and reduction in transport and tourism, maintain essential healthcare capacity and risk awareness campaigns that were established during the epidemic, and scope long-term development investments in the health, agriculture, and urban resilience sectors.

Plague is an example of an endemic disease with pandemic potential, demonstrated by three high-mortality pandemics in the years 541, 1347, and 1894. Even though it is easily treated with currently effective antibiotics, pneumonic plague is highly contagious and invariably fatal without timely treatment. Investing in basic public health services, including urban sanitation and vector control programs, should be a priority to prevent the recurrence of a plague epidemic of this scale.

FINDING: CROSS-CUTTING FUNCTIONS PROVIDE UNDER-UTILIZED ENTRY POINTS FOR PARTICIPATION

The cross-cutting functions described in Table 3 are not relegated to the bottom of the table because they are unimportant—in fact, the opposite. They are architectural elements of the entire structure, without which it collapses. A few deserve special mention here as critically under-resourced.

While our analysis focused on global initiatives, the ultimate capacity for and return from the core functions is embedded within communities. This includes functions related to workforce, detection and reporting, and risk reduction opportunities. Functional approaches must therefore be designed with the motivations of the community and its wider constituents in mind (e.g., private sector entities, media, local government, and other leaders). The private sector has been relatively untapped by governments and major global efforts. The development of strategic public-private partnerships across all four pillars is in its infancy. Yet the areas that require public-private cooperation, as well as the benefits that the private sector could provide, are many, and are directly tied to communities. Business continuity helps each business but also society in general. Local businesses and large corporations alike have roles to play and a particular incentive to contribute to well-functioning societies to minimize business disruptions and may be engaged in novel ways to mobilize resources and convene sectors. Employers are a pivotal entry point for workforce development, risk communication, and pandemic prevention and preparedness. They are embedded in communities and often already involved in multi-sectoral initiatives in their own operations throughout a business's lifecycle.

Risk communication, both for operations within and between institutions and with the public, must underlie all decisions to support awareness of risks and needs and to build the trust of all stakeholders. It also can provide entry points for relevant sectors to ensure correct and consistent messaging and practical solutions. In terms of workforce development and sustainment, the intensive resources required of international responses to epidemics provide a strong rationale for considering ahead-of-time investments in workforce-building for basic public health and medical capacity, including community health workers, that can prepare for and deliver both emergency and routine health services. This investment is generally far more limited than the intensive resources poured into international responses to epidemics, which themselves do not typically support the building of long-term workforces. Global R&D initiatives are largely focused on biosurveillance, biodetection, and medical countermeasure development, omitting an important evidence basis for all of the other functions, notably among upstream prevention and recovery. Finally, information sharing is still deficient across sectors and disciplines and often among different levels of reporting (e.g., from point of care to national and international levels). Optimizing these, especially the latter, is now a major focus of Integrated Disease Surveillance and Response reporting for implementation of the IHR by countries in the African region (and is being expanded to other regions).[57] However, in general, multisectoral data sharing and interpretation, particularly for diseases before they appear in humans, are not routinely conducted for pandemic threats.

BOX 8: WHERE DOES THE PRIVATE SECTOR FIT IN?

The private sector has suffered significant losses from recent epidemics and pandemics.[27] Declines in tourism following disease-related travel advisories or disruptions to supply chains and workforce threaten business continuity and have considerable impacts on businesses. Companies thus have an incentive to invest in and promote healthy populations and the functions that support stable operations.

New channels are being formed for the private sector to link in to pandemic resilience efforts, such as the GHSA's Private Sector Roundtable. The private sector represents a diverse group of entities in terms of industries and scale. Viewing private entities beyond their role in corporate and social responsibility can provide new pathways for their participation at local, national, and regional levels. The human resources required to build and sustain both basic and surge functions are not yet addressed in a sustainable way, particularly at the national level, and the inputs of the private sector are clearly situated to help address this. Further, employers can implement risk reduction policies such as providing reliable food sources to alleviate wildlife hunting pressures, providing education to workers on zoonotic disease risks, and requiring use of personal protective equipment in high-risk settings to prevent disease transmission and spread to employees. As zoonotic and non-zoonotic diseases can both impose high economic and health security impacts, there are important incentives for many industries to reduce risks. The predominance of the informal or "gig" economy and other aspects of changing workforce paradigms will require new ways for disseminating risk communication and management approaches; links between the private and public sectors can help enable the tools needed to do so which, in turn, can reach countless numbers of people.

Multilateral development banks have committed to mobilizing upwards of 35% increased financing from the private sector within three years, and the World Bank has launched an initiative to maximize private sector financing by considering private financing options, and encourages use of public sector finance to provide an enabling environment. This has great potential to strengthen capacity for some aspects of health security (e.g., private networks of veterinarians), though financing incentives must be in place to engage with the public sector to ensure ongoing contribution to public good. The PEF is facilitating new public-private partnerships through the development of pandemic risk itself as a market, with pandemic catastrophe bonds being assumed by private insurers, with premiums financed by donor governments.

CONCLUSIONS
AND RECOMMENDATIONS

"The global health community should address future threats to health security comprehensively based on deeper understanding of prevention and remediation of human security. Simply taking the International Health Regulations to a next step would be too weak and too narrow an adjustment."

– Chen and Takemi 2015 [59]

The global commitment to building the capabilities needed for an optimal state of global health security is strong. Yet the system in place is not yet at the point where the capabilities—the foundation—fully support the pillars, which in turn do not yet fully support a ready and resilient global health security structure. In general, the system still tends toward reactivity rather than proactivity, toward response rather than prevention. Efforts to counter global biological threats can be characterized largely as ad hoc responses to known diseases, with limited attention to horizon scanning and drivers of emergence of new and unknown diseases (what WHO calls "Disease X").

Despite the reality that pandemic readiness is a function of the strength of all pillars, globally-organized efforts are primarily directed toward response, with 16 of 22 initiatives notionally or actually addressing this pillar. After-action reviews tend to target response failures, perpetuating this response-oriented mindset. Some might argue that global initiatives are naturally better suited to response than to prevention or recovery, and therefore that limiting our study to global initiatives unsurprisingly biased the results toward response. We strongly question this notion. Global institutions shape priority setting, investment incentives, and best practices that inform where countries emphasize their capacity and activities. That prevent and recovery implementation approaches may require context-specific tailoring, and require participation from and in some cases reliance on some sectors not currently involved in global health security efforts, should not preclude the global community from putting its weight behind efforts to aggressively address and invest in them if global health security is a development goal that extends beyond the health sector.

The global community has regularly generated response initiatives in reaction to outbreaks, and it was our intent to ask, what opportunities to address other fundamental areas might it be missing? The response bias precludes emphases on the other pillars that could provide encouragement, guidance, and cover for countries to take on activities toward those pillars at the national level. It also results in resource-intensive measures to contain outbreaks once an emergency has occurred, in many cases costing lives and leading to widespread societal and economic disruption. Most resources are mobilized downstream once emergencies occur. New major financing mechanisms—notably the WHO CFE and the World Bank PEF—allow resources to be mobilized when a certain trigger is activated. These mechanisms are important for assisting countries in outbreak response to avoid large-scale, international epidemics and potential pandemics or to provide insurance against their economic impacts; the CFE, specifically, provides resources for response to disease outbreaks as well as health emergencies that result from other disasters. However, response infrastructure should build on or lead to investments for resilience across prevent-detect-respond-recover. It should capitalize on opportunities for risk mitigation and early threat detection. In the long run, as demonstrated by the high costs of the recent Ebola and Zika outbreaks, relying on response results in huge loss of lives and damages, poses unsustainable financial costs, and represents missed opportunities for cost-saving risk reduction upstream. The imbalance would naturally be mitigated in a relative sense by a greater emphasis on addressing the other pillars. More importantly, the required investment levels would in absolute numbers go down in the long run if preventive efforts were the fundamental

priority for global health security efforts. Initiatives should also be in place to capture prevention and early warning inputs and celebrate success stories of outbreak prevention.

The gaps and limitations described in this report may provide a roadmap for choosing and prioritizing additional areas of investment of human and fiscal capital, ideally in concerted fashion. The work could take the form of designing a system of partnerships to meet the need, and ultimately implementing such a system. This would allow the community of stakeholders to move beyond ad hoc approaches, and instead operate as a more integrated and systematic global network dedicated to global health security capacity. This will require coordination across sectors, including in the design and tracking of assessment tools, action planning, investments, reporting, and promoting effective and efficient use of resources to ensure functions are sufficiently covered.

The global community can engage productively in all of the pillars. Indeed, the very *attention* of global entities to these pillars would be a huge step that could then support and create downstream activity from regional or national actors. The opportunity now waits in those areas of global health policy and implementation that are addressed insufficiently or not at all.

We believe this study provides a novel lens through which to view needs and opportunities for global health security. Our multidisciplinary findings, especially around the limited attention to date on systematic prevention and recovery, support a more comprehensive approach than is reflected by current health security efforts. We hope that the detail herein is a useful catalyst for further policy discussions and meaningful routes of entry into other sectors. This initial report can be followed up with expanded analyses to precisely map and track specific initiatives, new programs that will complement existing efforts and fill critical functional gaps, and new governance, implementation, and financing structures to ensure their coordination. These findings can be used to empower governments and international agencies to strengthen capacity for coverage of functions along the entire prevent, detect, respond, and recover spectrum of activity defined in the core functions framework. They can directly inform ongoing global initiatives to manage biothreats and future iterations of capacity assessments, as well as orient prospective initiatives to spaces in the global health security landscape for contributions with optimal impact. Between the relative calm after the West Africa Ebola outbreak and the appearance of the next major biothreat—all too certain a short window—lies opportunity to do so.

RECOMMENDATIONS

While additional research will help inform more precise evidence-based preventions and interventions, several activities can be implemented now to strengthen and reinforce global efforts for global health security.

1. Global biothreat initiatives should be more strategically aligned

Coordination and harmonization of dozens of parallel initiatives will help ensure coverage and synergy. While alignment with IHR is important for the health community and some have called for harmonization of multiple standards within it,[59] the relevance, entry points, incentives and ownership for other sectors must also be considered and made apparent. This is admittedly challenging without resources dedicated to coordination to establish working relationships between sectors at all levels, especially the sectors that may have limited capacity and resources (and thus may not be conducting the functions they are best served to address).

All of the needed sectors must be at the table to enable whole-of-society preparedness and promote independent thinking, monitoring, and accountability. One of the most important roles of the global community is to identify functional needs agnostic of sector and then create a framework that guides players to focus their initiatives in a way that is mutually beneficial and synergistic with the many other initiatives operating in the global health security mission space. At a country level, National Action Plans for Health Security offer a platform for integrating multisectoral inputs and identifying shared goals as well as integrating prevention of health emergencies into other sectors' national action plans, such as those for climate change, biodiversity, and urbanization. Related processes, such as WHO's recent multisectoral resource mapping and prioritization workshops, can also help bring stakeholders from various sectors together. However, the long-term success of implementing shared priorities will require new ways of working together and likely new mechanisms for financing multisectoral initiatives. The Global Pandemic Monitoring Board, taking shape now, could potentially bring all of these elements together to ensure coverage and coordination of core functions for health security. And the proposed GHSA 2024 Framework, in which more than 40 partners will reaffirm the need and set the stage for preparedness, could be upscaled to include additional nations or become a global compact. To support translation to country action, establishment of a Global Fund-like entity for global health security, which could be used to fund countries directly to implement their costed National Action Plans for Health Security, could help more systematically and sustainably provide a pathway for needed One Health capacity strengthening.

2. Multi-sectoral participation must be recognized as a requisite tenet of the entire global health security enterprise

The participation of many sectors and disciplines in the public and private spheres is vital to achieving a state of global health security. Yet the health sector dominates all others, despite the reality that preventing, detecting, responding to, and recovering from major biological events must employ the efforts of many public sector ministries and private sector industries. Our review has identified three glaring weaknesses that, if rectified and considered in the context of disaster risk reduction or management, perhaps through a renewed push per GHSA 2024 Framework development, could provide substantial benefit to the health security of global citizens:

Defense and security

Important investments in counterproliferation and counterterrorism have not yet been institutionalized as a co-equal in the fight for health security. Law enforcement, military, immigration control, and other entities can assist with core functions, including protection of critical infrastructure, bioforensics and attribution, logistics of essential services surge, and medical countermeasure distribution and dispensing. The GHSA "Biosafety and Biosecurity" action package is the most explicit in this purpose, with targets ensuring "that especially dangerous pathogens are identified, held, secured and monitored in a minimal number of facilities according to best practices; biological risk management training and educational outreach are conducted to promote a shared culture of responsibility, reduce dual use risks, mitigate biological proliferation and deliberate use threats, and ensure safe transfer of biological agents; and country-specific biosafety and biosecurity legislation, laboratory licensing, and pathogen control measures are in place as appropriate."[60] This acknowledgement of security is much less evident in the IHR and OIE regulations, and the effort to encourage partnerships among previously distinct sectors was therefore an important specific contribution of the GHSA. All of the action packages can, in fact, be implemented with security in mind if the defense and security sector is considered one among equals. Doing so will require complete engagement of this sector's representatives at the global and country levels. The GHSA could leverage regional security agreements, such as the North Atlantic Treaty Organization, to address biothreats through the 2024 Framework development process.

Environment

The close link between encroachment on wildlife and ecosystems and disease emergence makes the environment sector a critical partner that has yet to be integrated into health security efforts. This sector can be leveraged to contribute key information for threat detection and sentinel surveillance to enhance disease prevention, as well as intervention options to mitigate disease risks from wildlife and other environmental sources. For example, climate and weather systems and biodiversity monitoring financed by other sectors can be leveraged by the health security community to anticipate places, people, and animals at greatest risk for pathogen spillover events and address risk drivers upstream. In general, there is a continued need to apply (not just talk about) One Health approaches. Donors can more systematically coordinate with the environmental sector to ensure multisectoral approaches are built into programs prospectively. Working through existing channels and reinforcing dual capacities for emerging and endemic diseases may show immediate value and promote sustainability. These efforts can align with and advance many existing intergovernmental and non-governmental environmental organizations' efforts to explore biodiversity and ecosystem "mainstreaming" for health.

Private sector

We echo the call to "map the potential contributions of the nongovernmental sector to global health security and identify opportunities to catalyze multisectoral partnerships among the US government, private, and social sectors that will harness new allies, innovations, and investments to bolster pandemic preparedness."[61] Engagement of the private sector as a partner in preparedness is critical both for early detection and to minimize potential impacts of reported disease on trade and travel, as well as reduce disruption in other facets of society. Global initiatives with multi-national corporation participation, such as the Private Sector Roundtable, can be followed up with more local activities at country and community level where private sector entities are embedded and business continuity may be integral for both companies and wider society. Incentives to reduce risks, such as incorporating economic vulnerability from pandemic risks into country credit ratings, which has been proposed as a strategy to incentivize pandemic preparedness,[62] should be explored. Others have called on financing institutions to take steps to limit upstream risks to reduce potential liabilities. This can occur, for example, by incorporating emerging infectious disease risk in development project safeguards or partnering with industry to promote alternatives to high-risk practices to reduce risk and impact potential negative externalities.[63] Such approaches could tie into risk reduction efforts in the environment sector as well. We recommend the development of aggressive, early, and transparent partnerships between government agencies charged with global health security and the private sector. The private sector's unique health security functions should be defined, mapped to global health needs, and fiscally supported.

3. Strategic gaps at the margins must be aggressively addressed

Of the four pillars that define global health security in our construct, two are woefully under-addressed:

Prevent

Implementers should embrace Prevent as an area of need and target investments accordingly. Prevention programs could potentially tie into existing and sustained programs in place on the ground, such through Community Health Worker networks, which feature front-line public health workers with trusted relationships and strong understanding of the communities they serve, and by broadening the scope of other initiatives currently focused on specific communicable diseases (e.g., Roll Back Malaria partnerships). Some innovative approaches have been proposed to target gaps in Prevent, such as the Global Virome Project, which would enhance surveillance and characterize mammalian viral diversity to inform the global health community about potential risks and guide the development of preparedness measures in areas like spillover risk reduction and vaccine and therapeutic inputs.[64] The use of modeling and risk profiling and prioritization to predict disease emergence is still in its infancy, particularly with respect to incorporating elements of human behavior and risk drivers outside the health sector. Improved prediction and prevention science will require new approaches and financing to sectors that at present have limited health security engagement to address proximal and distal drivers of disease emergence. It will require factoring outbreak risk and risk reduction into land use planning, climate action, food production practices, anti-terrorism sanctions, and trade and travel. The GHSA's next iteration should include metrics that measure prevention of spillover not only in terms of surveillance efforts, but of other behaviors, policies, and practices that minimize that spillover.

Recover

Health threats should be managed as a continuum, from Prevent to Recover to Prevent. During Recover, the main focus should not only be to return to "normal" but to prioritize the instillation of policies, plans, and activities to Prevent. Best practices for recovery are extremely limited for biothreats. Granting these functions attention similar to that available with other types of disasters will promote a more systematic understanding of needs and should strengthen functions to prevent, detect, and respond to future risks and impacts. Financing must be sustained through the recovery phase, eliminating rapid shifts to the next outbreak that leave a debilitated country primed for another biothreat event. There is increasing recognition that humanitarian and development agencies must collaborate, recognizing the underlying vulnerabilities to hazards in conflict and fragile states and the need for sustained engagement to promote stability. Nascent programs in this area that contribute to global health security should be strongly supported.

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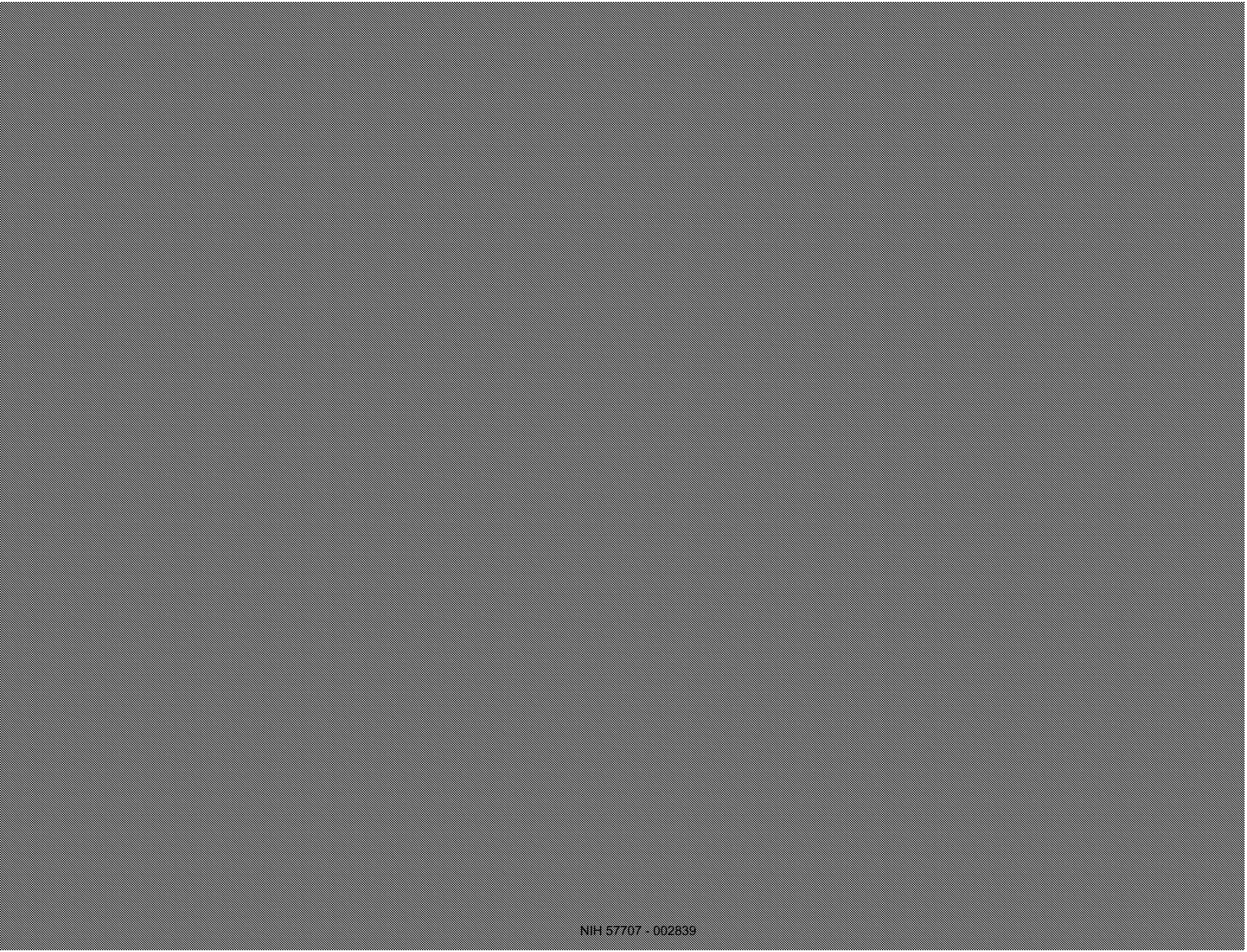

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NIH 57707 - 002840

From: Ellen Carlin [b6]
Sent: 1/31/2020 9:23:31 PM
To: Billy Karesh [b6]; Catherine Machalaba [b6]; Kanya Long [b6]; Franck Berthe [b6]; Morens, David (NIH/NIAID) [E] [b6] ([b6])
CC: Amanda Andre [b6]
Subject: Re: Action required: global health security manuscript
Attachments: Lancet GH author signatures.pdf

Sorry everyone—the form is attached now. It's a funny form so you may need to try opening in a Preview if you use a Mac. Let me know if any trouble.

Ellen

On Jan 31, 2020, at 3:44 PM, Ellen Carlin [b6] wrote:

Dear Team,

I hope your 2020 is off to a great start!

I'm writing to give an update on our global health security paper.[b6] which delayed things a bit, but we are ready to submit now. Attached is the version of the manuscript we will submit. Billy and I have updated the lead to reflect current events.

We're going to give *The Lancet Global Health* a try. **Please find attached an author contribution form that Kenya, Franck, and David need to sign electronically. Amanda is helping get signatures from Billy and Catherine. If you can please turn this around by Monday Feb 3, I can submit that day.** I have indicated that all authors contributed equally; if you prefer to word your contribution differently, please do so.

Some of you may not be aware that December 31 was my last day at EcoHealth Alliance. I am running my own consulting gig now and have a lot of exciting projects in store that I look forward to sharing with you as they develop. I am still affiliated with EHA as a Research Fellow.

Thanks again for all of your efforts!

Best wishes,
Ellen

<Carlin et al Building resilience Draft 1.31.19 v2.docx>

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Author statements

Please insert the relevant text under the subheadings below. A completed form must be signed by all authors. Please note that we will accept hand-signed and electronic (typewritten) signatures. Please complete multiple forms if necessary, and upload the signed copy with your submission, scan and email to: globalhealth@lancet.com, or fax to: +44 1865 853021.

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Authors' contributions

Please insert here the contribution each author made to the manuscript—eg, literature search, figures, study design, data collection, data analysis, data interpretation, writing etc. If all authors contributed equally, please state this. The information provided here must match the contributors' statement in the manuscript.

All authors contributed equally to this text.

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Role of the funding source

Please disclose any funding sources and their role, if any, in the writing of the manuscript or the decision to submit it for publication. Examples of involvement include: data collection, analysis, or interpretation; trial design; patient recruitment; or any aspect pertinent to the study. Please also comment whether you have been paid to write this article by a pharmaceutical company or other agency. If you are the corresponding author, please indicate if you had full access to all the data in the study and had final responsibility for the decision to submit for publication. The information provided here must match the role of the funding source statement in the manuscript.

The Smith Richardson Foundation funded the study on which this Comment is based (SRF Grant #2017-1534). The Foundation was not involved in the execution of the study nor in the drafting of this manuscript. Neither the Foundation nor any other agency has paid the authors to write this piece.

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I (Ellen P. Carlin) am the corresponding author and had full access to all data in the study and final responsibility to submit this manuscript for publication.

I (Ellen P. Carlin) am the corresponding author and had full access to all data in the study and final responsibility to submit this manuscript for publication.

Conflicts of interest

Please complete the ICMJE conflict of interest form, which is available at http://download.thelancet.com/flatcontentassets/authors/icjme-coi-form.pdf. Please ensure that a conflict of interest statement is included at the end of the manuscript, which matches what is declared on the ICMJE conflict of interest form.

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Please sign below to confirm that all necessary consents required by applicable law from any relevant patient, research participant, and/or other individual whose information is included in the article have been obtained in writing. **The signed consent form(s) should be retained by the corresponding author and NOT sent to *The Lancet Global Health*.**

I agree with: the plan to submit to *The Lancet Global Health*; the contents of the manuscript; to being listed as an author; and to the conflicts of interest statement as summarised. I have had access to all the data in the study (for original research articles) and accept responsibility for its validity.

Title and name: Ellen P. Carlin	Highest degree: DVM	Signature: b6	Date: 1/31/20
Title and name: Catherine Machalaba	Highest degree: MPH	Signature: SIGN HERE	Date:
Title and name: Kanya C. Long	Highest degree: PhD	Signature: SIGN HERE	Date:
Title and name: Franck C. J. Berthe	Highest degree: DVM	Signature:	Date:
Title and name: David Morens	Highest degree: MD	Signature: SIGN HERE	Date:
Title and name: William B. Karesh	Highest degree: DVM	Signature:	Date:
Title and name:	Highest degree:	Signature: SIGN HERE	Date:
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Corresponding author declaration

I [Signature], the corresponding author of this manuscript, certify that the contributors' and conflicts of interest statements included in this paper are correct and have been approved by all co-authors.

From: Ellen Carlin [b6]
Sent: 10/25/2019 3:53:14 PM
To: Morens, David (NIH/NIAID) [E] [b6]
b6
Subject: Re: Global health security gaps analysis

Ha yes— b6

I've basically only ever been to b6 and b6 —have never seen any of the rest of the state, and now you've sold me!
Ellen

From: "Morens, David (NIH/NIAID) [E]" b6
Date: Thursday, October 24, 2019 at 4:11 PM
To: Ellen Carlin b6
Subject: RE: Global health security gaps analysis

Wow, b6, eh? Have you ever been there? The b6 is arguably the priciest real estate in the whole US, running along several miles of gorgeousness with the b6 b6 on one side of the street, and the mega-mansions on the other, many of them millions and tens of millions of bucks worth. If you've never been there, just drive down the main drag in the summer: it's like a Hollywood fairy tale!

b6

Well, good for them! b6, which is also an enclave for the wealthy country club set, though not nearly as toney as b6.

One of the things I learned on my b6 – which I b6 and never really appreciated – is what a beautiful place it is. b6 b6 and she concluded that it has to be one of the most beautiful places in the US, if not the world. b6 – it's actually a huge state – except the b6 area, so that's still on my list. And I promised myself and b6 b6 that I will b6....

David

David M. Morens, M.D.
CAPT, United States Public Health Service
Senior Advisor to the Director
Office of the Director
National Institute of Allergy and Infectious Diseases
National Institutes of Health
Building 31, Room 7A-03
31 Center Drive, MSC 2520
Bethesda, MD 20892-2520

☎ b6 (assistants: Kimberly Barasch; Whitney Robinson)
301 496 4409
b6

From: Ellen Carlin b6
Sent: Thursday, October 24, 2019 3:46 PM

To: Morens, David (NIH/NIAID) [E] b6
Subject: Re: Global health security gaps analysis

Yes, sad but true! They've been considering it loosely for a while, nothing concrete, but the decision to really do it actually came up very quickly—I only learned about it a few weeks ago. Once they made the decision, they b6 b6. So everything has happened very quickly. They'll get b6 b6. They'll be b6. I have been invited to the b6 as well, and have yet to get there! Now I really must. Sounds like you have a good excuse to make it happen as well! b6 b6.

Thanks for your encouragement on the paper… I will work on it over the coming week and be back in touch soon!
Ellen

From: "Morens, David (NIH/NIAID) [E]" b6
Date: Wednesday, October 23, 2019 at 5:41 PM
To: Ellen Carlin b6
Subject: RE: Global health security gaps analysis

OMG! No, I didn't hear that b6? I know b6 b6 b6. (That's the way it works I'm afraid). b6 had again invited me to stop in but that wasn't possible. So many hits and misses in life, right?

I guess more b6. (5%+ of b6 is rural boondocks, beautiful though it is.

Funny, just a few months ago I b6 and b6 b6. This must have come up quickly….

I'll send her an email although b6 she won't have much time to do anything else except b6.

On the ms., yes, I still think it's a great idea and glad to help in whatever way you direct. You will definitely have to be the prime mover since it is YOUR knowledge and insight. Yes, Bob K would be great, and/or others who have this same sort of insight (which I don't).

As to specific journals, I'd have to think about that. I'm sure there would be many journals interested.

In any case, I say GO FOR IT!

David

David M. Morens, M.D.
CAPT, United States Public Health Service
Senior Advisor to the Director
Office of the Director
National Institute of Allergy and Infectious Diseases
National Institutes of Health
Building 31, Room 7A-03
31 Center Drive, MSC 2520
Bethesda, MD 20892-2520

☎ b6 (assistants: Meaghan Vance; Whitney Robinson)
301 496 4409
b6

From: Ellen Carlin b6
Sent: Wednesday, October 23, 2019 3:13 PM
To: Morens, David (NIH/NIAID) [E] b6
Subject: Re: Global health security gaps analysis

Hi David! How's everything going? Have you heard the b6 that our friend b6
b6

I've finally dug out of the manuscript backlog and am turning my attention to writing up the findings from the gaps analysis I presented on at Cosmos Club in April. Are you still game to co-author? I am happy to do the heavy lifting. We could also think about bringing on Bob Kadlec or another notable. I think my study co-investigators would also like to join.

You mentioned targeting a biomedical journal, and I'd be interested in your thoughts as to which might be best suited. Would be great to reach biomedical audiences that don't normally think in interdisciplinary fashion. If we kept it in a short form, we could aim high for The Lancet Global Health (their "Comment" articles are an easy drafting lift, at only a page or two), or the multi-disciplinary PNAS (which also has a "Commentary" form). A longer form could be suitable for PLOS Medicine's "Policy Forum," or perhaps Science & Diplomacy.

All thoughts welcome, and thanks again for your interest!

Ellen

From: Ellen Carlin b6
Date: Friday, April 12, 2019 at 3:41 PM
To: "Morens, David (NIH/NIAID) [E]" b6
Subject: Re: Global health security gaps analysis

I'm impressed—I never did receive that reply, and I don't know how you keep tabs on the vagaries of cyberspace!

I'm pretty (100%) certain that the policy stuff is not over your head. More to the point, credible scientists are needed to make worthwhile policy, which is why we included you on the project! I will get to work on an outline and a plan.

I saw b6 last week and we hatched a plan for her to have a Saturday night dinner party! Does that idea work for you? We can find an evening that works for all. That does not preclude getting together downtown as well. I can try to make the next OH meeting although I think I might be in b6 that week. Maybe we just find a good happy hour.

From: "Morens, David (NIH/NIAID) [E]" b6
Date: Friday, April 12, 2019 at 12:21 PM
To: Ellen Carlin b6
Subject: RE: Global health security gaps analysis

Hi Ellen, just doing my weekly check of correspondence and I found that my reply to you a few days ago isn't in my sent mail, so will re-reply just in case it went astray (yes, I can be a bit obsessive compulsive on occasion).

What I said was something like, of course, I'd be glad to work with you on this, with the caveat that I'm just a scientist and a lot of this policy stuff is over my head. But of course, important, which is why scientists and policy folks need to talk together and work together.

Let me know if you and b6 can get free some time, maybe at a One Health meeting downtown?

David

David M. Morens, M.D.
CAPT, United States Public Health Service
Senior Advisor to the Director
Office of the Director
National Institute of Allergy and Infectious Diseases
National Institutes of Health
Building 31, Room 7A-03
31 Center Drive, MSC 2520
Bethesda, MD 20892-2520

☎ b6 (assistants: Meaghan Vance; Whitney Robinson)
301 496 4409
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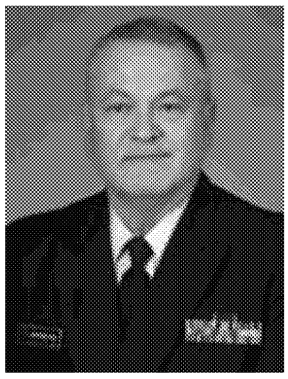

From: Ellen Carlin b6
Sent: Tuesday, April 9, 2019 12:45 PM
To: Morens, David (NIH/NIAID) [E] b6
Subject: Re: Global health security gaps analysis

Thank you, David! That means a lot. It's amazing how much work goes on behind the scenes for two years to culminate in a 15-minute presentation!

I am definitely interested in drafting something for a journal. Would you be interested in co-authoring a piece with us? You are after all a contributor to the report and it would be great to have you join us.
Ellen

From: "Morens, David (NIH/NIAID) [E]" b6
Date: Friday, April 5, 2019 at 1:07 PM
To: Ellen Carlin b6
Subject: RE: Global health security gaps analysis

Ellen, great talk last night. You should think about writing it up for some biomedical science journal, maybe centered around the 5 key points you had on a later slide. Maybe have someone like Dr. Kadlec as a coauthor, plus Billy or Peter.

David

David M. Morens, M.D.
CAPT, United States Public Health Service
Senior Advisor to the Director
Office of the Director
National Institute of Allergy and Infectious Diseases
National Institutes of Health
Building 31, Room 7A-03
31 Center Drive, MSC 2520
Bethesda, MD 20892-2520

☎ b6 (assistants: Meaghan Vance; Whitney Robinson)
301 496 4409
b6

From: Morens, David (NIH/NIAID) [E]
Sent: Tuesday, April 2, 2019 3:24 PM
To: 'Ellen Carlin' b6
Subject: RE: Global health security gaps analysis

Thanks, and I presume I can thank u also for the Eventbrite conformation that just came!

David

David M. Morens, M.D.
CAPT, United States Public Health Service
Senior Advisor to the Director
Office of the Director
National Institute of Allergy and Infectious Diseases
National Institutes of Health
Building 31, Room 7A-03
31 Center Drive, MSC 2520
Bethesda, MD 20892-2520

☎ b6 (assistants: Meaghan Vance; Whitney Robinson)
301 496 4409
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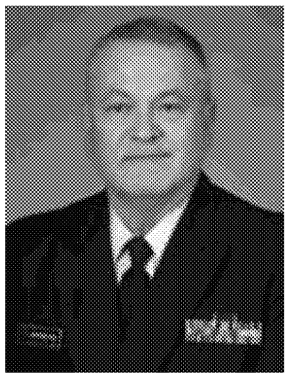


From: Ellen Carlin b6
Sent: Tuesday, April 2, 2019 1:54 PM
To: Morens, David (NIH/NIAID) [E] b6
Subject: Re: Global health security gaps analysis

I'll let them know you're coming! You can just show up. 6pm cocktails, 7pmm reception per usual!

Ellen P. Carlin, DVM
Senior Health and Policy Specialist

EcoHealth Alliance
b6 (direct)
(mobile)
b6
www.ecohealthalliance.org

Research Associate, Smithsonian Conservation Biology Institute
Adjunct Research Scientist, Columbia University National Center for Disaster Preparedness
Courtesy Lecturer, Cornell University College of Veterinary Medicine

EcoHealth Alliance leads cutting-edge scientific research into the critical connections between human and wildlife health and delicate ecosystems. With this science, we develop solutions that prevent pandemics and promote conservation.

From: "Morens, David (NIH/NIAID) [E]" b6
Date: Tuesday, April 2, 2019 at 10:45 AM
To: Ellen Carlin b6
Subject: RE: Global health security gaps analysis

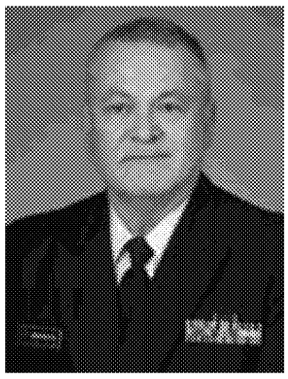
Ellen, I'm glad you ping'd me on this because although I am planning to go to the EcoHealth meeting I think I forgot to RSVP and now I can't find the invite letter. I have the hardcopy which I printed out, but misfiled or accidentally erased the original invite. If you still have it could you send? Otherwise I'll just email them "cold" to say I'm coming.

See ya then,

David

David M. Morens, M.D.
CAPT, United States Public Health Service
Senior Advisor to the Director
Office of the Director
National Institute of Allergy and Infectious Diseases
National Institutes of Health
Building 31, Room 7A-03
31 Center Drive, MSC 2520
Bethesda, MD 20892-2520

☎ b6 (assistants: Meaghan Vance; Whitney Robinson)
301 496 4409
b6



From: Ellen Carlin b6
Sent: Monday, April 1, 2019 7:26 PM
To: Morens, David (NIH/NIAID) [E] b6
Subject: Re: Global health security gaps analysis

Thanks, David! I'm just back from Panama, having attending a SOUTHCOM health security conference. I didn't get to see the canal… but I did see some tree sloths!

Looking forward to seeing you on Thursday. b6 told me that you b6 and that she'd love us to all get together. She's going to try to come late on Thursday, b6 b6. So hopefully we can look at our calendars then!

Enjoy LA,
Ellen

Ellen P. Carlin, DVM
Senior Health and Policy Specialist

EcoHealth Alliance
b6 (direct)
(mobile)
b6
www.ecohealthalliance.org

Research Associate, Smithsonian Conservation Biology Institute
Adjunct Research Scientist, Columbia University National Center for Disaster Preparedness
Courtesy Lecturer, Cornell University College of Veterinary Medicine

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From: "Morens, David (NIH/NIAID) [E]" b6
Date: Friday, March 22, 2019 at 11:48 AM
To: Ellen Carlin b6
Subject: RE: Global health security gaps analysis

Ellen, this looks so cool, thanks! I just scanned through it for a few minutes and I can see it was well thought out and researched. Kudos to you and the team.

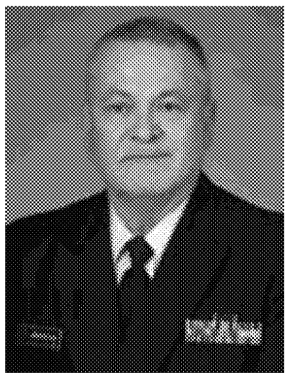
Yes, I plan to be there on the 4th, thanks!

Also, I spent the morning with b6 a few days ago! The context was she asked me to be a judge at the b6, which I did. Was fun! See you soon, I have to go to LA for a meeting but will be back before the 4th.

David

David M. Morens, M.D.
CAPT, United States Public Health Service
Senior Advisor to the Director
Office of the Director
National Institute of Allergy and Infectious Diseases
National Institutes of Health
Building 31, Room 7A-03
31 Center Drive, MSC 2520
Bethesda, MD 20892-2520

☎ b6 (assistants: Meaghan Vance; Whitney Robinson)
301 496 4409
b6



From: Ellen Carlin b6
Sent: Wednesday, March 20, 2019 7:25 AM
To: Morens, David (NIH/NIAID) [E] b6
Subject: Global health security gaps analysis

Dear David,

I am writing to let you know that my colleagues and I at EcoHealth Alliance have completed the high-level gaps analysis of global health security efforts that you helped us with last year. Your comments at the roundtable at the World Bank very much helped informed our assessment and the way we think about the problem. Please find the report attached!

We invite you to join us at the Cosmos Club on April 4 where we will discuss our findings. Our invited guest that evening will be Assistant Secretary for Preparedness and Response Bob Kadlec. You probably already received an invitation, but just in case, you can RSVP here.

Looking forward to seeing you at Cosmos hopefully… I am going to try to get b6 to come. If she can't, I will bug her for a proper happy hour for the three of us!

Ellen

Ellen P. Carlin, DVM
Senior Health and Policy Specialist

EcoHealth Alliance
b6 (direct)
(mobile)
b6
www.ecohealthalliance.org

Research Associate, Smithsonian Conservation Biology Institute
Adjunct Research Scientist, Columbia University National Center for Disaster Preparedness
Courtesy Lecturer, Cornell University College of Veterinary Medicine

From: Ellen Carlin [b6]
Sent: 12/11/2019 8:02:06 PM
To: Morens, David (NIH/NIAID) [E] [b6]
[b6]]
Subject: Journal contact?
Attachments: Carlin et al Building resilience Draft 10.31.19.docx

Hi David! I hope all is well.

I wanted to ask if you know any editors at The Lancet who might be receptive to an email from you about our paper (attached)? Billy tried an editor he knows there but has received no response. We thought a pre-submission inquiry would be better than a cold submission.

I also thought if The Lancet is a no-go, perhaps you might have a contact at NEJM or another high-impact journal? NEJM has a Commentary article type. I figure we should go big if we can!

Thanks!!
Ellen

Ellen P. Carlin, DVM
Senior Health and Policy Specialist

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(mobile)
b6
www.ecohealthalliance.org

Research Associate, Smithsonian Conservation Biology Institute
Adjunct Research Scientist, Columbia University National Center for Disaster Preparedness
Courtesy Lecturer, Cornell University College of Veterinary Medicine

Title
Global health security: targeting investments toward unmet needs

Authors
Ellen P. Carlin, DVM
EcoHealth Alliance, 460 West 34th Street, New York, NY 10001

b6

Catherine Machalaba, MPH
EcoHealth Alliance, 460 West 34th Street, New York, NY 10001

Kanya C. Long, PhD
University of California San Diego, 6304 Atkinson Hall, La Jolla, CA 92093
Dr. Long was a fellow at the World Bank at the time of the study.

Franck C. J. Berthe, DVM
World Bank, 1818 H Street, NW, Washington, DC 20433

David Morens, MD
National Institutes of Allergy and Infectious Diseases, 5601 Fishers Lane, Bethesda, MD 20892

William B. Karesh, DVM
EcoHealth Alliance, 460 West 34th Street, New York, NY 10001

As the second largest Ebola outbreak in history finally appears to be waning in the Democratic Republic of the Congo, a global reckoning is due. Understanding why especially dangerous pathogens are emerging with increasing frequency continues to take a back seat to response and response preparedness. This crisis-centered approach is bound to keep us trapped in a perpetual cycle of panic and neglect.[1]

To document this dynamic and reveal its extent, we collated the functions needed for effective defenses against major biological incidents and assessed which areas are receiving insufficient attention.[2] Our organizing construct included four "pillars"—prevent, detect, respond, and recover. Through extensive review of the scientific and gray literature, and with expert input via roundtable discussions, interviews, and peer review, we identified 60 functions that undergird these four pillars and to which countries must have sufficient access to optimize their health security. We also identified 22 major initiatives global in architecture or oversight and designed to support the development of local, country, or regional capacities. We then mapped the initiatives to the pillars to reveal areas of global neglect (Figure 1).

[Insert Figure 1 here]

As the figure shows, activities directed at prevention are minimal in number. We defined prevention as a multi-dimensional concept that captures prevention of 1) epidemics at pre-initiation (*before* pathogens emerge into people); 2) bioweapons development and deployment; and 3) accidental releases of pathogens, such as from laboratories. The majority of funded efforts do not address prevention at all, and even fewer deal with the underlying risk factors that lead to epidemic emergence. Most programs view epidemic prevention narrowly (i.e., preventing small outbreaks from growing) rather than addressing what drives outbreaks to occur in the first place. The latter entails politically challenging decisions about societal priorities ranging from land use and agricultural practices to urbanization and climate change.

Few efforts address recovery, and the very inclusion of recovery as a core pillar in our construct is novel among frameworks. (A recent World Bank publication on which some of the authors worked, which is designed to strengthen human, animal, and environmental public health systems at their interface, is one of the only examples and has not yet been adopted into global efforts.[3]) Since strong recovery from one epidemic event can pre-empt future outbreaks, systematic and sustained attention to this pillar is badly needed.

We also found two strategic points of concern. One is that, by current design, global health security implementation efforts and their attached financing tackle particular objectives—vaccine development, regional surveillance, training—while no governance effort or strategic inter-institutional guiding framework aligns them toward a commonly defined set of goals. The other is that there seems to be a tendency to view biothreats in terms of the single end consequence that worries people the most: our own health. The problem with this approach is that it drives reverse engineering of structures and decisions to deal with only human health consequences, and forward engineering of response activity tailored to human health needs. Defense, environment, and animal health are often treated as needs outside of human health security frameworks, even though their full inclusion would restore the breadth of the health *security* concept. Ebola in DRC exists at this nexus: viral circulation in an ecological

environment that supports spillover and a fragile, violent, and conflict-ridden setting that hampers both prevention and response.

The international community's approaches diverge from what may be fundamentally needed to grapple with the new epidemic threat reality and ultimately stave off its worst consequences. Some of the functions we identified require less investment than others to achieve great benefit—addressing drivers of epidemics is a case in point. The World Bank estimates that an annual expenditure of ~$3.4 billion to prevent one in every eight severe pandemics will save $30 billion.[4] Assessing cost-benefits and returns on investment of particular activities is precisely what a unifying strategic framework could do. The release of the 2019 Global Health Security Index, which finds among 195 countries assessed an average preparedness score of 40·2 out of a possible 100, may provide new impetus to act.[5] A substantial but feasible rethinking of the orientation of global and national investment is achievable within the major guiding frameworks and efforts that are already underway. As the Global Health Security Agenda embarks on its second five years, this is a timely opportunity to strengthen neglected lines of effort and support a holistic approach to dealing with the global health challenge of epidemic disease.

Acknowledgements
This work was funded by the Smith Richardson Foundation, which had no other role in the development of the study.

References

1. World Bank. *From panic and neglect to investing in health security: Financing pandemic preparedness at a national level.* Washington, DC: World Bank;2017.
2. Carlin EP, Machalaba C, Berthe FCJ, Long KC, Karesh WB. *Building resilience to biothreats: An assessment of unmet core global health security needs.* New York, NY: EcoHealth Alliance;2019.
3. World Bank. *Operational framework for strengthening human, animal and environmental public health systems at their interface.* Washington, DC: World Bank Group;2018.
4. World Bank. *People, pathogens, and our planet: The economics of one health, volume 2.* Washington, DC: World Bank;June 2012.
5. Nuclear Threat Initiative. *Global health security index: Building collective action and accountability.* Washington, DC: Nuclear Threat Initiative;2019.

Figure 1: Mapping of global health security initiatives to core needs

Initiative	
Australia Group	
CEPI*	
CP3	
Gavi†	
GLASS	
GLEWS‡	
Global Financing Facility	
Global Fund	
GHSA§	
GHSI	
Global Partnership	
International Reagent Resource	
OIE WAHIS	
Proliferation Security Initiative	
World Bank PEF‖	
World Bank Pandemic Preparedness Plan	
WEF Epidemics Readiness Accelerator	
WHO CFE	
WHO Global Influenza Programme	
WHO GOARN	
WHO Health Emergencies Program	
WHO R&D Blueprint	

Major global health security initiatives were mapped to four pillars of global health security activity: prevent, detect, respond, and recover, revealing a predominance of focus on detection and response. Figure reprinted from Carlin EP, Machalaba C, Berthe FCJ, et al. *Building Resilience to Biothreats: An assessment of unmet core global health security needs*. EcoHealth Alliance. 2019.

*Committed to funding through Phase 2 investigational stockpiles; not funded for Phase 3 or linked to a system for procurement, distribution, or dispensing. †To the extent that Gavi covers Prevent it is for the specific prevention of yellow fever spillover through vaccination in high-risk areas; does not address drivers. ‡Predominantly focused on risk monitoring and information alerts for Rift Valley fever in livestock. §Addresses prevention in the sense of containing outbreaks; attention to and capacity for spillover risk management is extremely limited. ‖Disbursement of funds only applies to select viruses.

From: Morens, David (NIH/NIAID) [E] [b6 b6]
Sent: 2/25/2020 10:22:15 PM
To: William B. Karesh [b6]
CC: Ellen Carlin [b6]; Catherine Machalaba [b6]; b6; Franck Berthe [b6]
BCC: Morens, David (NIH/NIAID) [E] [b6 b6]
Subject: Re: BMJ-2020-055182 Manuscript Decision Editorials

Ellen, my input is don't be discouraged, this is how things often go. It is absolutely a good piece and WILL be published, but it's just that many journals develop lanes and cross-cutting broad pieces like this never fit perfectly. I won't guess your next steps on this but am happy to help think it through WHEN/IF this corona craziness backs off. Actually, this paper is really timely in that regard. Not suggesting you do so, but a thought is to slightly reorient to emphasize that at the very beginning, we need to think down the long road if pandemic response, not just the short one. david

Sent from my iPhone
David M Morens
OD, NIAID, NIH

On Feb 25, 2020, at 16:47, William B. Karesh b6 wrote:

Hi Ellen,

Totally up to you on how much time you have to re-write something quickly to capture the news hook, but if not, I would completely support sending it to Health Affairs as is, maybe with a short but strong cover letter referring to the timeliness of this work.

BK

William B. Karesh, D.V.M
Executive Vice President for Health and Policy

EcoHealth Alliance
460 West 34th Street - 17th Floor
New York, NY 10001 USA

b6 (direct)
+1.212.380.4465 (fax)
www.ecohealthalliance.org

President, OIE Working Group on Wildlife

Co-chair, IUCN Species Survival Commission - Wildlife Health Specialist Group

EPT Partners Liaison, USAID Emerging Pandemic Threats - PREDICT-2 Program

EcoHealth Alliance develops science-based solutions to prevent pandemics and promote conservation.

On Feb 25, 2020, at 4:37 PM, Ellen Carlin [b6] wrote:

Hi everyone,

This was nice of the editor to give us this kind of feedback. We took a chance on submitting our piece as an Editorial to BMJ because the Analysis is a longer piece at 1800-2000 words, and Original Research more involved still. Our paper is about 750 words. We did this as a short-form piece to begin with so it would be done quickly, alas…!

Let me propose a few options, in no particular order, and get your feedback:

1. **Expand the paper** into a longer form analysis, suitable for submitting to BMJ or another journal as a more involved research/analysis piece.

2. **Keep the paper as is**, and submit elsewhere. I would suggest Health Affairs as a good next option; their "DataWatch" article type is 2000 words or less, up to 6 exhibits; these are short papers that highlight data that "speak for themselves" relative to important policy issues or topics. They should shed light on some important question and be "worth knowing." They do not typically test hypotheses, rely on sophisticated statistical methods, or include lengthy policy discussions. We aim to present new data or new analyses of existing data that are reliable and credible and that promote understanding among nonexperts on important, policy-relevant topics. We encourage work based on underused or new data sources.

If you want to submit as it but not to Health Affairs, please suggest a journal and article type.

3. **Take BMJ's suggestion to redraft into a rapid response** to their coronavirus coverage.

All comments welcome.
Thank you,
Ellen

On Feb 24, 2020, at 10:48 AM, BMJ <onbehalfof@manuscriptcentral.com> wrote:

24-Feb-2020
BMJ-2020-055182 entitled "Global health security: targeting investments toward unmet needs"

Dear Dr. Carlin,

Thank you for sending us your editorial. We read it with interest but decided against publication and I'm sorry to disappoint you.

The piece falls somewhere between research (you report methods) and Analysis (a long form article type that includes some data), but doesn't in its current form fit either. BMJ editorials don't report original findings.

Your bottom line message is clear however, and you might consider writing a rapid response to any recent content about covid - 19, discussing the lack of preventive initiatives globally. On line rapid responses are well read and a selection are published in full as letters. I'm sure you appreciate that I can't prejudge that selection

You'll find all our coverage of the covid - 19 outbreak here:
https://www.bmj.com/coronavirus

Sorry once again that I can't offer you an editorial, and thank you for your interest in the BMJ.

Yours sincerely,

Alison Tonks
Clinical Editor, BMJ
b6

If you elected during submission to send your article on to another journal the article will be transferred in 5 working days. If you intend to appeal against this decision please notify us before then.
The journal(s) (if any) you have selected at submission are: BMJ Global Health
If you want to speed up or stop this onward transmission please email the editorial office: papersadmin@bmj.com

From: Morens, David (NIH/NIAID) [E] [/ b6 (b6]
Sent: 7/21/2021 11:00:38 PM
To: Keusch, Gerald T [b6]
CC: Peter Daszak (b6) [b6]
BCC: Morens, David (NIH/NIAID) [E] [/ b6 (b6]]
Subject: Re: Bulletin of the Atomic Scientists/ W. Ian Lipkin: The known knowns, known unknowns, and unknown unknowns of COVID-19 https://bit.ly/3xZBrZ0

Well said! Perfectly said! d

Sent from my iPhone
David M Morens
OD, NIAID, NIH

On Jul 21, 2021, at 18:16, Keusch, Gerald T b6 wrote:

And one of the reasons it is extraordinarily safe is because people are trained in the basic principles of biosafety and are aware of the fact that the better their technique is the safer they are as there are limited engineering safeguards available to them other than a biosafety hood. When I was actively at the bench working on virulent Shigella (with a very low infectious inoculum) and Vibrio cholerae (with a higher infectious inoculum), or for my techs or fellows, we never had a lab acquired infection simply because we used proper technique and remained aware of what we were doing. We also didn't have the added burden of PPE, the dexterity limiting multiple barriers to the samples or equipment being used, and the time consuming entry and exit protocols which all add to the fatigue burden that impacts the likelihood of errors. I would say to Ian that one could be totally naked working on the open bench with no PPE and if you are really good at what you are doing you are not at risk of accidental infection. But then again I don't want to think about encountering a stark naked Ian Lipkin in a lab or for that matter anywhere else.

My take on the issue.

From: Morens, David (NIH/NIAID) [E] b6
Sent: Wednesday, July 21, 2021 5:59 PM
To: Keusch, Gerald T [b6]; Peter Daszak (b6 b6)
Subject: RE: Bulletin of the Atomic Scientists/ W. Ian Lipkin: The known knowns, known unknowns, and unknown unknowns of COVID-19 https://bit.ly/3xZBrZ0

There is a certain "snobbism" which you must have seen in your capacity, that people who work in BSL-3 and -4 often look down on those who work in BSL-2 as being duffers, if not wildly unsafe. In fact that's untrue. Work done in BSL-2 is done in BSL-2 because there is no need to be at a higher level, and if you look at it as serious risk per man-hour of work, BSL-2 work is extraordinarily safe. I think a lot of people don't get that.

David

David M. Morens, M.D.
CAPT, United States Public Health Service
Senior Advisor to the Director
Office of the Director
National Institute of Allergy and Infectious Diseases
National Institutes of Health
Building 31, Room 7A-03
31 Center Drive, MSC 2520
Bethesda, MD 20892-2520

☎ b6 (assistant: Whitney Robinson)
301 496 4409
b6

From: Keusch, Gerald T < b6
Sent: Wednesday, July 21, 2021 4:02 PM
To: Morens, David (NIH/NIAID) [E] b6 ; Peter Daszak
(b6) < b6

Subject: RE: Bulletin of the Atomic Scientists/ W. Ian Lipkin: The known knowns, known unknowns, and unknown unknowns of COVID-19 https://bit.ly/3xZBrZ0

Thanks David,

At least he takes the stance that pathogenesis studies are important and he disagrees with the anti-GOF'ers that it all needs to be shut down. But then he implies unsafe work at BSL-2 at WIV. Baric has said the same thing. That's where he opens the door for the others to stick their foot in the door and to try to kick it wide open.

But, I'll take even this piece from Ian in a positive way.

Jerry

From: Morens, David (NIH/NIAID) [E] b6
Sent: Wednesday, July 21, 2021 3:36 PM
To: Peter Daszak (b6) b6 ; Keusch, Gerald T b6
Subject: FW: Bulletin of the Atomic Scientists/ W. Ian Lipkin: The known knowns, known unknowns, and unknown unknowns of COVID-19 https://bit.ly/3xZBrZ0

David

David M. Morens, M.D.
CAPT, United States Public Health Service
Senior Advisor to the Director
Office of the Director
National Institute of Allergy and Infectious Diseases
National Institutes of Health
Building 31, Room 7A-03
31 Center Drive, MSC 2520
Bethesda, MD 20892-2520

☎ b6 (assistant: Whitney Robinson)
301 496 4409
b6

From: Folkers, Greg (NIH/NIAID) [E] b6
Sent: Wednesday, July 21, 2021 11:02 AM
Subject: Bulletin of the Atomic Scientists/ W. Ian Lipkin: The known knowns, known unknowns, and unknown unknowns of COVID-19 https://bit.ly/3xZBrZ0

The known knowns, known unknowns, and unknown unknowns of COVID-19

By W. Ian Lipkin | July 21, 2021


A nurse cares for a patient on a US Navy hospital ship during the COVID-19 pandemic. Credit: US Navy.

In 2002, while making the case for the US invasion of Iraq to those who asked for evidence of what we now know to be nonexistent weapons of mass destruction, Donald Rumsfeld referred to known knowns, known unknowns, and unknown unknowns. Nearly two decades later, we are in similar territory in discussing the

origin of SARS-CoV-2, the virus that causes COVID-19. Then, as now, we should be wary that incomplete data and strong opinions not determine high-impact decisions.

The known knowns are that SARS-CoV-2 is a new, highly transmissible virus that has the capacity to evolve rapidly. Genetic analyses indicate that closely related viruses existed in wildlife before human disease was detected in the Chinese city of Wuhan in 2019. We also know that despite promises to shut down wild animal markets in the aftermath of the first SARS outbreak in 2003, thousands of animals were sold in such markets in Wuhan. Many of these species are known to be infected and/or infectable with SARS-like coronaviruses. These animals could have been vectors for carrying SARS-CoV-2 to humans and for adaptation to growth in humans.

We also know that the Wuhan Institute of Virology and the Wuhan Center for Disease Control and Prevention collected specimens from wildlife that typically carry coronaviruses and pursued gain-of-function experiments. The level of biocontainment for these experiments may have been inappropriate. Nonetheless, there is no evidence that SARS-CoV-2 was deliberately created. Indeed, the features of SARS-CoV-2 that have resulted in at least four million deaths, lingering disease in millions more, and an estimated $22 trillion loss in output through 2025, could not have been predicted even had someone wanted to engineer a highly transmissible and pathogenic coronavirus and had the tools to do so.

There are many known unknowns. Unlike smallpox, Ebola, or other potentially lethal infectious diseases that announce themselves with a distinctive clinical syndrome, SARS-CoV-2 has the capacity to infect people and cause no or only mild disease. Furthermore, even people who ultimately develop severe disease may be infectious before they have symptoms. This insidious aspect of SARS-CoV-2 biology makes it difficult to track its spread and to determine when, where, and how it first emerged. One clue to the advent of SARS-CoV-2 might have been a spike in the number of cases of respiratory disease or in the use of prescription or over-the-counter medications to treat them. However, there is no evidence of either in Wuhan in the weeks prior to the first documented cases of COVID-19 in November 2019. Wuhan is also a major transportation hub. The first cases may have been imported from other regions in China or throughout the Asian continent where related viruses were reported.

A resource that epidemiologists frequently use for determining the origin and timing of the introduction of a new infectious agent is serially collected samples that can be tested for the presence of viral proteins or genetic material (in this case, RNA), or for antibodies that are produced in response to infection. While investigating the origin of MERS-CoV in 2012, a team of expert researchers of which I was a member found large amounts of viral RNA in young dromedary camels. Additionally, we found high

levels of antibodies in blood of more than 75 percent of contemporary adult camels and in blood from camels that had been collected annually and stored for a period of more than 10 years. These findings—plus the presence of viral RNA in camel meat in abattoirs—were helpful in implicating camels as important sources of human infection and in dating the incursion of MERS-CoV into the Arabian Peninsula.

RELATED:
Essential reading on lab leaks and gain-of-function research

To date, we have not succeeded in similar studies in searching for the origins of the COVID-19 pandemic. The presence of SARS-CoV-2 RNA would be considered unequivocal evidence of the presence of the causative agent. We are rapidly closing in on two years since the beginning of the Wuhan outbreak. The challenge in looking for RNA in archived materials is that it rapidly degrades unless samples are stored at ultralow temperatures. Proteins and antibodies are less labile but are also less specific. Through a mechanism known as cross reactivity, infection with a different, but related coronavirus (like SARS-CoV-1, the causative agent of the 2002-2003 SARS outbreak) can yield results that are mistaken to represent COVID-19. This was not a problem in Saudi Arabia, because no similar MERS-like viruses were circulating in camels or people. However, in the context of the COVID-19 pandemic, we must have assays that distinguish between SARS-CoV-2, SARS-CoV-1, and other coronaviruses.

There is considerable uncertainty about when SARS-CoV-2 first appeared both inside and outside of China. The *South China Morning Post* has reported the retrospective diagnosis of infection in a 55-year-old man in Hubei province on November 17, 2019. A US Centers for Disease Control and Prevention study of more than 7,000 routine blood donations collected from December 13, 2019 through January 17, 2020 revealed the presence of antibodies to SARS-CoV-2 in at least 84 people in nine US states. Given that an antibody response cannot be detected until two to three weeks after infection, we can only conclude the virus was circulating in the United States for several weeks before the first case of COVID-19 was diagnosed on January 19, 2020. Even more compelling evidence of early infection outside of China was found in a skin biopsy obtained in November 2019 from a woman in Milan, Italy with an inflammatory rash that was found to contain both SARS-CoV-2 viral RNA and proteins. Mathematical models based on studies of viral sequences and evolutionary rates suggest that SARS-CoV-2 emerged in China in early October to mid-November. We do not have the samples needed to search for evidence of infection in humans, wildlife, or domestic animals in China prior to November 2019. We also do not know whether such samples exist or whether the problem is lack of access.

Let us return to what we do know. Three quarters of emerging infectious diseases originate in wildlife. Over the past 40 years, I have personally been involved in addressing several: HIV/AIDS, West Nile encephalitis, SARS, MERS, Lujo, Lassa, Nipah,

Dandenong, Ebola, Marburg, dengue, monkeypox, Zika, influenza, and COVID-19. Estimates of numbers of unknown viruses lurking in mammals range from 320,000 to 1,000,000. If even 1 percent of them can infect humans or domestic animals, we may be ignorant of thousands of potential threats to human health and food security. In an increasingly interconnected world, diseases that might once have been contained to a region are now global. Accordingly, the international community can have zero tolerance for wildlife markets and wildlife trafficking for food, medicinal, or pet trade purposes. Our current focus in on China. However, trafficking in wildlife is a global threat and should be banned everywhere. It may have contributed to the emergence of HIV/AIDS and to outbreaks of Ebola and Marburg. France plays a central role in wildlife trafficking, with more than 28 million specimens imported between 2008 and 2017, including 4,000 seizures of illegal transport during that time period totaling two million specimens. Confiscated items included live mammals, birds, and reptiles along with bodies, parts, and products. In 2012, we received and analyzed tissues from primates smuggled into JFK airport in the United States. These contained sequences of human pathogens, including four strains of simian foamy virus (an agent closely related to HIV) and two herpes viruses.

A law enforcement officer in Puerto Rico displays illegally trafficked wildlife. Such trade can increase the risk of a disease spilling over from animals to people. Credit: US Fish and Wildlife Service.

This brings us to discussion of the lab-leak speculation. Some of my colleagues believe that research with infectious agents—particularly gain-of-function research, where a virus or other microbe is genetically manipulated to alter its ability to infect cells or cause disease—should also be banned. I disagree. This type of research is needed to understand how viruses infect us and thwart our immunological defenses. It is also essential to identifying and validating effective countermeasures. However, it should only be pursued in accordance with an internationally approved standard for biocontainment, project review that considers risk/benefit analysis, rigorous training, and continuous monitoring of personnel that includes antibody testing for evidence of laboratory-acquired infections.

After 9/11 and the anthrax attacks that followed, President George W. Bush established a National Biosurveillance Advisory Subcommittee to review infectious threats. A second subcommittee was established by President Barack Obama. Both committees issued reports (see the first report and the second report) that recommended investments in new technologies and personnel for national and global surveillance of and response to emerging infectious diseases. The committees endorsed the WHO International Health Regulations of 2005 that mandated building infrastructure for detecting microbial threats in the developing world.

Neither report gathered much traction until the film "Contagion" was released in 2011. "Contagion" was developed to call attention to pandemic risks originating in wildlife. It introduced audiences worldwide to epidemiology, biosafety laboratories, the process of vaccine development, false panaceas, and the term "R naught"—which describes how many people on average someone with an infectious disease will infect. It also led *The New York Times* to invite me to write an editorial that laid out what was needed to prevent a pandemic. There is much that the film got right; however, we did not predict the potential for asymptomatic transmission, promiscuous infection of multiple organ systems, or the impact of poor leadership.

What would good leadership entail now? The common elements in the several roadmaps proposed since the COVID-19 pandemic began (see *Foreign Affairs*, The Independent Panel, and the G20 Action Plan) include a stronger World Health Organization and global investment in the research and public health resources needed for effective surveillance, along with drug and vaccine development, production, and distribution. As understood in the context of the current pandemic, it is impossible to overstate the importance of surveillance and vaccines. We would not have been caught flat-footed if we knew that a novel coronavirus was circulating in the autumn of 2019. Early access to accurate diagnostic assays and track tracing would have enabled early containment. Similarly, if effective vaccines had been distributed globally, we might never have allowed SARS-CoV-2 the opportunity to evolve into the delta variant. The virus is still adapting and new variants will continue

to emerge that will challenge us. At an estimated cost of $25 billion, vaccinating the world is a bargain and an ethical imperative.

SARS-CoV-2 is now endemic worldwide in people, wildlife, and domestic animals; it is unlikely that we can eradicate it. I am nonetheless optimistic that we will ultimately bring it under control. The question is the durability of what we learn from this experience. As damaging as COVID-19 has been to humankind, there are other pathogens lurking worldwide—antibiotic-resistant bacteria, fungi, and threats to food security. Our commitment to a shared vision for global health must therefore continue even after the current pandemic recedes.

From: Morens, David (NIH/NIAID) [E] [b6 b6]
Sent: 7/21/2021 10:07:31 PM
To: Peter Daszak [b6]; Keusch, Gerald T [b6]
Subject: RE: Bulletin of the Atomic Scientists/ W. Ian Lipkin: The known knowns, known unknowns, and unknown unknowns of COVID-19 https://bit.ly/3xZBrZ0

Yes, I too have known Ian for years, b6

b6

b6. Human beings are complex. Ian has been wrong, but he is always able to change if new facts appear.

David

David M. Morens, M.D.
CAPT, United States Public Health Service
Senior Advisor to the Director
Office of the Director
National Institute of Allergy and Infectious Diseases
National Institutes of Health
Building 31, Room 7A-03
31 Center Drive, MSC 2520
Bethesda, MD 20892-2520

☎ b6 (assistant: Whitney Robinson)
301 496 4409
b6

From: Peter Daszak b6
Sent: Wednesday, July 21, 2021 5:04 PM
To: Keusch, Gerald T b6 ; Morens, David (NIH/NIAID) [E] b6
Subject: RE: Bulletin of the Atomic Scientists/ W. Ian Lipkin: The known knowns, known unknowns, and unknown unknowns of COVID-19 https://bit.ly/3xZBrZ0

I agree, at least he's not on the attack like Jeff Sachs. I've known Ian for years, b6
b6

I see this as Ian lipkin trying to thread the needle between him previously saying that a lab leak is plausible and they had unsafe biocontainment, but at the same time him knowing that's a disingenuous argument because he uses the same level of biocontainment in his own lab. He's criticized GoF during the original arguments a decade + ago, and now is supporting it.... b6
b6

Maybe, like David Relman, we should view these articles and appearances as submissions of their resume's for the WHO next phase, a future US Govt Covid Commission panel, or the NASEM consensus study (or all 3). I know Ian applied to be on the original WHO mission to Wuhan, b6
b6

Cheers,

Peter

Peter Daszak
President

EcoHealth Alliance
520 Eighth Avenue, Suite 1200
New York, NY 10018-6507

USA

Tel.: b6
Website: www.ecohealthalliance.org
Twitter: @PeterDaszak

EcoHealth Alliance develops science-based solutions to prevent pandemics and promote conservation

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From: Keusch, Gerald T b6
Sent: Wednesday, July 21, 2021 4:02 PM
To: Morens, David (NIH/NIAID) [E] b6; Peter Daszak (b6)
b6
Subject: RE: Bulletin of the Atomic Scientists/ W. Ian Lipkin: The known knowns, known unknowns, and unknown unknowns of COVID-19 https://bit.ly/3xZBrZ0

Thanks David,

At least he takes the stance that pathogenesis studies are important and he disagrees with the anti-GOF'ers that it all needs to be shut down. But then he implies unsafe work at BSL-2 at WIV. Baric has said the same thing. That's where he opens the door for the others to stick their foot in the door and to try to kick it wide open.

But, I'll take even this piece from Ian in a positive way.

Jerry

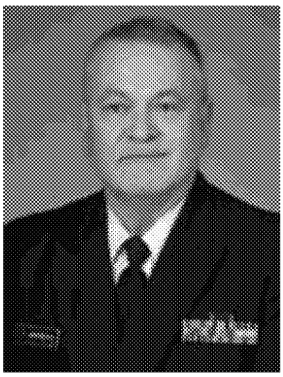
From: Morens, David (NIH/NIAID) [E] b6
Sent: Wednesday, July 21, 2021 3:36 PM
To: Peter Daszak (b6) b6; Keusch, Gerald T b6
Subject: FW: Bulletin of the Atomic Scientists/ W. Ian Lipkin: The known knowns, known unknowns, and unknown unknowns of COVID-19 https://bit.ly/3xZBrZ0

David

David M. Morens, M.D.
CAPT, United States Public Health Service
Senior Advisor to the Director
Office of the Director
National Institute of Allergy and Infectious Diseases
National Institutes of Health
Building 31, Room 7A-03

31 Center Drive, MSC 2520
Bethesda, MD 20892-2520

☎ b6 (assistant: Whitney Robinson)
301 496 4409
b6



From: Folkers, Greg (NIH/NIAID) [E] b6
Sent: Wednesday, July 21, 2021 11:02 AM
Subject: Bulletin of the Atomic Scientists/ W. Ian Lipkin: The known knowns, known unknowns, and unknown unknowns of COVID-19 https://bit.ly/3xZBrZ0

The known knowns, known unknowns, and unknown unknowns of COVID-19

By W. Ian Lipkin | July 21, 2021


A nurse cares for a patient on a US Navy hospital ship during the COVID-19 pandemic. Credit: US Navy.

In 2002, while making the case for the US invasion of Iraq to those who asked for evidence of what we now know to be nonexistent weapons of mass destruction, Donald Rumsfeld referred to known knowns, known unknowns, and unknown unknowns. Nearly two decades later, we are in similar territory in discussing the origin of SARS-CoV-2, the virus that causes COVID-19. Then, as now, we should be wary that incomplete data and strong opinions not determine high-impact decisions.

The known knowns are that SARS-CoV-2 is a new, highly transmissible virus that has the capacity to evolve rapidly. Genetic analyses indicate that closely related viruses existed in wildlife before human disease was detected in the Chinese city of Wuhan in 2019. We also know that despite promises to shut down wild animal markets in the aftermath of the first SARS outbreak in 2003, thousands of animals were sold in such markets in Wuhan. Many of these species are known to be infected and/or infectable with SARS-like coronaviruses. These animals could have been vectors for carrying SARS-CoV-2 to humans and for adaptation to growth in humans.

We also know that the Wuhan Institute of Virology and the Wuhan Center for Disease Control and Prevention collected specimens from wildlife that typically carry coronaviruses and pursued gain-of-function experiments. The level of biocontainment for these experiments may have been inappropriate. Nonetheless, there is no evidence that SARS-CoV-2 was deliberately created. Indeed, the features of SARS-CoV-2 that have resulted in at least four million deaths, lingering disease in millions more, and an estimated $22 trillion loss in output through 2025, could not have been predicted even had someone wanted to engineer a highly transmissible and pathogenic coronavirus and had the tools to do so.

There are many known unknowns. Unlike smallpox, Ebola, or other potentially lethal infectious diseases that announce themselves with a distinctive clinical syndrome, SARS-CoV-2 has the capacity to infect people and cause no or only mild disease. Furthermore, even people who ultimately develop severe disease may be infectious before they have symptoms. This insidious aspect of SARS-CoV-2 biology makes it difficult to track its spread and to determine when, where,

and how it first emerged. One clue to the advent of SARS-CoV-2 might have been a spike in the number of cases of respiratory disease or in the use of prescription or over-the-counter medications to treat them. However, there is no evidence of either in Wuhan in the weeks prior to the first documented cases of COVID-19 in November 2019. Wuhan is also a major transportation hub. The first cases may have been imported from other regions in China or throughout the Asian continent where related viruses were reported.

A resource that epidemiologists frequently use for determining the origin and timing of the introduction of a new infectious agent is serially collected samples that can be tested for the presence of viral proteins or genetic material (in this case, RNA), or for antibodies that are produced in response to infection. While investigating the origin of MERS-CoV in 2012, a team of expert researchers of which I was a member found large amounts of viral RNA in young dromedary camels. Additionally, we found high levels of antibodies in blood of more than 75 percent of contemporary adult camels and in blood from camels that had been collected annually and stored for a period of more than 10 years. These findings—plus the presence of viral RNA in camel meat in abattoirs—were helpful in implicating camels as important sources of human infection and in dating the incursion of MERS-CoV into the Arabian Peninsula.

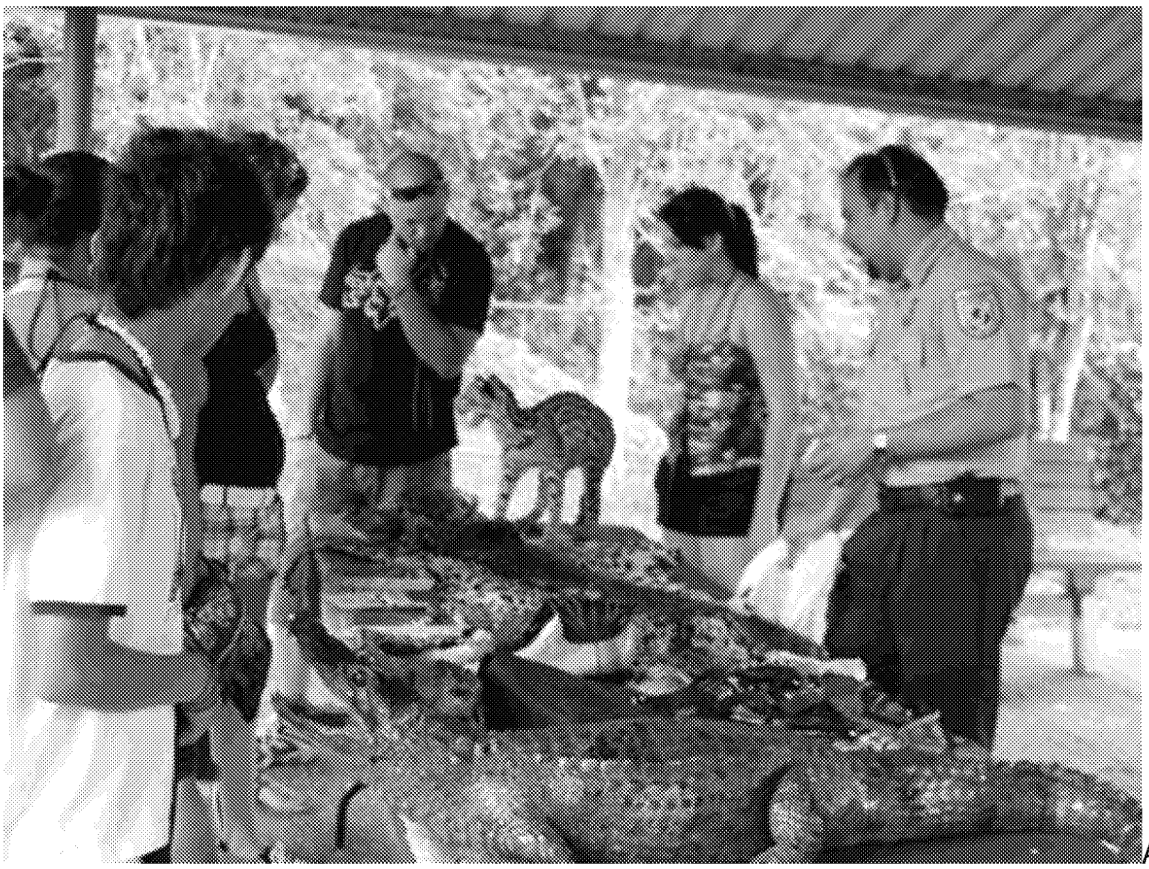
RELATED:
Essential reading on lab leaks and gain-of-function research

To date, we have not succeeded in similar studies in searching for the origins of the COVID-19 pandemic. The presence of SARS-CoV-2 RNA would be considered unequivocal evidence of the presence of the causative agent. We are rapidly closing in on two years since the beginning of the Wuhan outbreak. The challenge in looking for RNA in archived materials is that it rapidly degrades unless samples are stored at ultralow temperatures. Proteins and antibodies are less labile but are also less specific. Through a mechanism known as cross reactivity, infection with a different, but related coronavirus (like SARS-CoV-1, the causative agent of the 2002-2003 SARS outbreak) can yield results that are mistaken to represent COVID-19. This was not a problem in Saudi Arabia, because no similar MERS-like viruses were circulating in camels or people. However, in the context of the COVID-19 pandemic, we must have assays that distinguish between SARS-CoV-2, SARS-CoV-1, and other coronaviruses.

There is considerable uncertainty about when SARS-CoV-2 first appeared both inside and outside of China. The *South China Morning Post* has reported the retrospective diagnosis of infection in a 55-year-old man in Hubei province on November 17, 2019. A US Centers for Disease Control and Prevention study of more than 7,000 routine blood donations collected from December 13, 2019 through January 17, 2020 revealed the presence of antibodies to SARS-CoV-2 in at least 84 people in nine US states. Given that an antibody response cannot be detected until two to three weeks after infection, we can only conclude the virus was circulating in the United States for several weeks before the first case of COVID-19 was diagnosed on January 19, 2020. Even more

compelling evidence of early infection outside of China was found in a skin biopsy obtained in November 2019 from a woman in Milan, Italy with an inflammatory rash that was found to contain both SARS-CoV-2 viral RNA and proteins. Mathematical models based on studies of viral sequences and evolutionary rates suggest that SARS-CoV-2 emerged in China in early October to mid-November. We do not have the samples needed to search for evidence of infection in humans, wildlife, or domestic animals in China prior to November 2019. We also do not know whether such samples exist or whether the problem is lack of access.

Let us return to what we do know. Three quarters of emerging infectious diseases originate in wildlife. Over the past 40 years, I have personally been involved in addressing several: HIV/AIDS, West Nile encephalitis, SARS, MERS, Lujo, Lassa, Nipah, Dandenong, Ebola, Marburg, dengue, monkeypox, Zika, influenza, and COVID-19. Estimates of numbers of unknown viruses lurking in mammals range from 320,000 to 1,000,000. If even 1 percent of them can infect humans or domestic animals, we may be ignorant of thousands of potential threats to human health and food security. In an increasingly interconnected world, diseases that might once have been contained to a region are now global. Accordingly, the international community can have zero tolerance for wildlife markets and wildlife trafficking for food, medicinal, or pet trade purposes. Our current focus in on China. However, trafficking in wildlife is a global threat and should be banned everywhere. It may have contributed to the emergence of HIV/AIDS and to outbreaks of Ebola and Marburg. France plays a central role in wildlife trafficking, with more than 28 million specimens imported between 2008 and 2017, including 4,000 seizures of illegal transport during that time period totaling two million specimens. Confiscated items included live mammals, birds, and reptiles along with bodies, parts, and products. In 2012, we received and analyzed tissues from primates smuggled into JFK airport in the United States. These contained sequences of human pathogens, including four strains of simian foamy virus (an agent closely related to HIV) and two herpes viruses.

 A law enforcement officer in Puerto Rico displays illegally trafficked wildlife. Such trade can increase the risk of a disease spilling over from animals to people. Credit: US Fish and Wildlife Service.

This brings us to discussion of the lab-leak speculation. Some of my colleagues believe that research with infectious agents—particularly gain-of-function research, where a virus or other microbe is genetically manipulated to alter its ability to infect cells or cause disease—should also be banned. I disagree. This type of research is needed to understand how viruses infect us and thwart our immunological defenses. It is also essential to identifying and validating effective countermeasures. However, it should only be pursued in accordance with an internationally approved standard for biocontainment, project review that considers risk/benefit analysis, rigorous training, and continuous monitoring of personnel that includes antibody testing for evidence of laboratory-acquired infections.

After 9/11 and the anthrax attacks that followed, President George W. Bush established a National Biosurveillance Advisory Subcommittee to review infectious threats. A second subcommittee was established by President Barack Obama. Both committees issued reports (see the first report and the second report) that recommended investments in new technologies and personnel for national and global surveillance of and response to emerging infectious diseases. The committees endorsed the WHO International Health Regulations of 2005 that mandated building infrastructure for detecting microbial threats in the developing world.

Neither report gathered much traction until the film "Contagion" was released in 2011. "Contagion" was developed to call attention to pandemic risks originating in wildlife. It introduced audiences worldwide to epidemiology, biosafety laboratories, the process of vaccine development, false panaceas, and the term "R naught"—which describes how many people on average someone with an infectious disease will infect. It also led *The New York Times* to invite me to write an editorial that laid out what was needed to prevent a pandemic. There is much that the film got right; however, we did not predict the potential for asymptomatic transmission, promiscuous infection of multiple organ systems, or the impact of poor leadership.

What would good leadership entail now? The common elements in the several roadmaps proposed since the COVID-19 pandemic began (see *Foreign Affairs*, The Independent Panel, and the G20 Action Plan) include a stronger World Health Organization and global investment in the research and public health resources needed for effective surveillance, along with drug and vaccine development, production, and distribution. As understood in the context of the current pandemic, it is impossible to overstate the importance of surveillance and vaccines. We would not have been caught flat-footed if we knew that a novel coronavirus was circulating in the autumn of 2019. Early access to accurate diagnostic assays and track tracing would have enabled early containment. Similarly, if effective vaccines had been distributed globally, we might never have allowed SARS-CoV-2 the opportunity to evolve into the delta variant. The virus is still adapting and new variants will continue to emerge that will challenge us. At an estimated cost of $25 billion, vaccinating the world is a bargain and an ethical imperative.

SARS-CoV-2 is now endemic worldwide in people, wildlife, and domestic animals; it is unlikely that we can eradicate it. I am nonetheless optimistic that we will ultimately bring it under control. The question is the durability of what we learn from this experience. As damaging as COVID-19 has been to humankind, there are other pathogens lurking worldwide—antibiotic-resistant bacteria, fungi, and threats to food security. Our commitment to a shared vision for global health must therefore continue even after the current pandemic recedes.

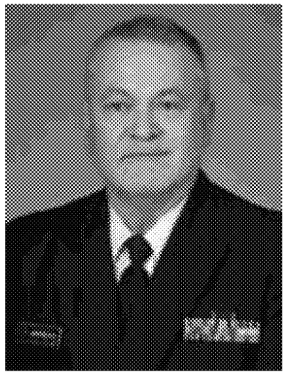
From: Morens, David (NIH/NIAID) [E] [b6 b6]
Sent: 11/22/2021 4:56:10 PM
To: William B. Karesh [b6]
CC: Catherine Machalaba [b6]; Daniel Mira-Salama [b6]
Subject: RE: figure for World Bank report

Yes, that would work, thanks

David

David M. Morens, M.D.
CAPT, United States Public Health Service
Senior Advisor to the Director
Office of the Director
National Institute of Allergy and Infectious Diseases
National Institutes of Health
Building 31, Room 7A-03
31 Center Drive, MSC 2520
Bethesda, MD 20892-2520

☎ b6 (assistant: Whitney Robinson)
301 496 4409
b6



From: William B. Karesh b6
Sent: Monday, November 22, 2021 11:54 AM
To: Morens, David (NIH/NIAID) [E] b6

Cc: Catherine Machalaba [b6]; Daniel Mira-Salama [b6]
Subject: Re: figure for World Bank report

Yes, both received.

If we use the more recent one (post 2020 publication) should we cite "Morens and Fauci, NIH, 2021" ?

BK

William B. Karesh, D.V.M
Executive Vice President for Health and Policy

EcoHealth Alliance
520 Eighth Avenue, Suite 1200
New York, NY 10018 USA

[b6] (direct)
+1.212.380.4465 (fax)
www.ecohealthalliance.org

President, OIE Working Group on Wildlife

Co-chair, IUCN Species Survival Commission - Wildlife Health Specialist Group

EcoHealth Alliance develops science-based solutions to prevent pandemics and promote conservation.

On Nov 22, 2021, at 11:49 AM, Morens, David (NIH/NIAID) [E] [b6] wrote:

Billy, Did you get both? You are free to use either one, just cite us as the source.

<image001.gif>

David M. Morens, M.D.
CAPT, United States Public Health Service
Senior Advisor to the Director
Office of the Director
National Institute of Allergy and Infectious Diseases
National Institutes of Health
Building 31, Room 7A-03
31 Center Drive, MSC 2520
Bethesda, MD 20892-2520

☎ b6 (assistant: Whitney Robinson)
301 496 4409
b6

<image002.jpg>

From: William B. Karesh b6
Sent: Monday, November 22, 2021 11:48 AM
To: Morens, David (NIH/NIAID) [E] b6
Cc: Catherine Machalaba b6 ; Daniel Mira-Salama
b6
Subject: Re: figure for World Bank report

Beautiful!! Thanks so much.

BK

On Nov 22, 2021, at 11:23 AM, Morens, David (NIH/NIAID) [E]
b6 wrote:

Billy, this is our updated version of what I just sent, made in June 2021. Let me know if this big file gets through to all.

<image001.gif>

David M. Morens, M.D.
CAPT, United States Public Health Service
Senior Advisor to the Director
Office of the Director
National Institute of Allergy and Infectious Diseases
National Institutes of Health
Building 31, Room 7A-03
31 Center Drive, MSC 2520
Bethesda, MD 20892-2520

☎ b6 (assistant: Whitney Robinson)
301 496 4409
b6

From: William B. Karesh b6
Sent: Monday, November 22, 2021 7:27 AM
To: Morens, David (NIH/NIAID) [E] b6
Cc: Catherine Machalaba b6 ; Daniel Mira-Salama b6
Subject: Re: figure for World Bank report

Thanks David !!!

If you could share the original with the three of us, Daniel can check to see if it will serve the purpose.

Thanks again,

Billy

On Nov 22, 2021, at 7:21 AM, Morens, David (NIH/NIAID) [E] b6 wrote:

Billy, this map was reconstructed from our original by the graphics department at the journal Cell. They did this purely so they could copyright it.

You could contact Cell, abd they will charge you. Or else we can give you the original with you can have for free. The original has all the same info and the same color code, but is less spread out vertically and differs in other minor ways

Let me know. My best to Peter and the gang. David

Sent from my iPhone
David M Morens
OD, NIAID, NIH

On Nov 22, 2021, at 06:46, William B. Karesh
b6 wrote:

Dear David,

Hope this finds you well.

We are in the final stages of printer's proofs of a report on EID's in Asia we did for the World Bank. We want to include your EID map from 2020 (attached), but the printer's tell us that our version is not high enough resolution. Would you happen to have high resolution version that could be used?

Hope you have a great Thanksgiving, all the best,

Billy

William B. Karesh, D.V.M
Executive Vice President for Health and Policy

EcoHealth Alliance
520 Eighth Avenue, Suite 1200
New York, NY 10018 USA

b6 (direct)
+1.212.380.4465 (fax)
www.ecohealthalliance.org

President, OIE Working Group on Wildlife

Co-chair, IUCN Species Survival Commission - Wildlife Health Specialist Group

EcoHealth Alliance develops science-based solutions to prevent pandemics and promote conservation.

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From: Peter Daszak [b6]
Sent: 7/9/2021 4:18:09 PM
To: Morens, David (NIH/NIAID) [E] [b6 b6]; Keusch, Jerry [b6]
Subject: RE: Politico: POLITICO-Harvard poll: Most Americans believe Covid leaked from lab

Bring on the Witchfinder-General! This shows how little we've improved in the public understanding of science since Medieval times..

It also demonstrates what a disastrous thing it was for David Relman and others to sign that letter to Science. It's fine to claim that as scientists we need to be honest about our doubt, but to give credence to the lab leak theory and place it on equal status to the wildlife farms is a heinous act as a scientist and a citizen.

Cheers,

Peter

Peter Daszak
President

EcoHealth Alliance
520 Eighth Avenue, Suite 1200
New York, NY 10018-6507
USA

Tel.: b6
Website: www.ecohealthalliance.org
Twitter: @PeterDaszak

EcoHealth Alliance develops science-based solutions to prevent pandemics and promote conservation

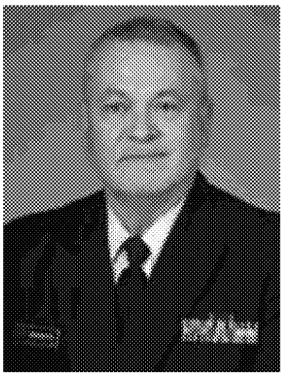
From: Morens, David (NIH/NIAID) [E] b6
Sent: Friday, July 9, 2021 10:32 AM
To: Peter Daszak (b6) b6; Keusch, Jerry (b6) b6
Subject: FW: Politico: POLITICO-Harvard poll: Most Americans believe Covid leaked from lab

Sad….. Most small children believe in Santa Claus….. Not so sad….

David

David M. Morens, M.D.
CAPT, United States Public Health Service
Senior Advisor to the Director
Office of the Director
National Institute of Allergy and Infectious Diseases
National Institutes of Health
Building 31, Room 7A-03
31 Center Drive, MSC 2520
Bethesda, MD 20892-2520

☎ b6 (assistant: Whitney Robinson)
301 496 4409
b6



From: Folkers, Greg (NIH/NIAID) [E] b6
Sent: Friday, July 9, 2021 8:52 AM
Subject: Politico: POLITICO-Harvard poll: Most Americans believe Covid leaked from lab

POLITICO-Harvard poll: Most Americans believe Covid leaked from lab

Opinion on the lab leak scenario, once seen as a fringe theory, has shifted dramatically.

By ALICE MIRANDA OLLSTEIN
07/09/2021 06:00 AM EDT

Most Americans now believe that the coronavirus leaked from a laboratory in China, according to a new POLITICO-Harvard poll that found a dramatic shift in public perception of Covid-19's origins over the last year.

U.S. adults were almost twice as likely to say the virus was the result of a lab leak in China than human contact with an infected animal, which many scientists believe is the most likely scenario. The poll's findings show what was once a fringe belief held mainly among some on the political right has become accepted by most Republicans, as well as most Democrats, amid heightened scrutiny of the lab leak theory.

In March 2020, a Pew Research Center poll found 29 percent of Americans believed the virus was made in a Chinese lab and released either accidentally or intentionally. The new survey shows 52 percent believe the virus came out of a lab, including 59 percent of Republicans and 52 percent of Democrats, while 28 percent said it was from an infected animal.

The absence of a large partisan gap on the issue is particularly striking, said Bob Blendon, a professor of health policy and political analysis at the Harvard T.H. Chan School of Public Health who designed the poll.

"Usually, our polls find a big split between Republicans and Democrats, so this is unique," he said. "More conservative media have been carrying the 'lab leak' issue, and it's been a Trump talking point from the beginning, so we expected people who lean Democratic would say either 'It's not true' or 'I don't know.' But the belief is bipartisan."

Blendon said Democrats likely became more receptive to the idea after President Joe Biden's recent order that intelligence agencies investigate the virus' origin and comments from Anthony Fauci, the White House chief medical officer, that it's worth digging into. Fauci and other scientists have cautioned the answer may never be known definitively.

"That the president thought there was enough evidence to ask intelligence agencies to put together a report sends a signal to Democrats that there might be something there," Blendon said.

Democratic lawmakers have also faced pressure to look more closely at the lab leak scenario, though they worry Republicans will stoke uncertainty about the virus origin for political gain. Several congressional committees have launched inquiries, and the House Science Committee plans to hold its first hearing on the issue next week.

The POLITICO-Harvard poll, which will be released next week, also found there's a high level of public interest in investigating Covid-19's origin, with almost two-thirds of Democrats and Republicans calling the issue "extremely" or "very" important. The finding also surprised Blendon, who said the public isn't typically invested in such a scientific inquiry.

The broad attention on the issue underscores the stakes for the Biden administration's upcoming report on the virus origin, due in August. Even if the report concludes the virus came from nature, it could be hard to move public opinion, lawmakers and researchers like Blendon have noted.

The poll surveyed 1,009 adults from June 22-27. The margin of error was plus or minus 3.8 percentage points.

From: Peter Daszak [b6]
Sent: 8/10/2021 6:49:37 PM
To: Morens, David (NIH/NIAID) [E] [b6] ([b6]); Robert Kessler [b6]; Keusch, Jerry [b6]
Subject: RE: Bulletin of the Atomic Scientists: COVID-19 lab-leak theory: Gain-of-function is a hot topic, but a bad explanation https://bit.ly/3yDCUnZ

Good article, finally…

Cheers,

Peter

Peter Daszak
President

EcoHealth Alliance
520 Eighth Avenue, Suite 1200
New York, NY 10018-6507
USA

Tel.: b6
Website: www.ecohealthalliance.org
Twitter: @PeterDaszak

EcoHealth Alliance develops science-based solutions to prevent pandemics and promote conservation

From: Morens, David (NIH/NIAID) [E] b6
Sent: Monday, August 9, 2021 3:03 PM
To: Peter Daszak (b6) b6; Kessler, Robert (b6) b6; Keusch, Jerry (b6) b6
Subject: FW: Bulletin of the Atomic Scientists: COVID-19 lab-leak theory: Gain-of-function is a hot topic, but a bad explanation https://bit.ly/3yDCUnZ

David

David M. Morens, M.D.
CAPT, United States Public Health Service
Senior Advisor to the Director
Office of the Director
National Institute of Allergy and Infectious Diseases
National Institutes of Health
Building 31, Room 7A-03
31 Center Drive, MSC 2520
Bethesda, MD 20892-2520

☎ b6 (assistant: Whitney Robinson)
301 496 4409
b6

From: Folkers, Greg (NIH/NIAID) [E] b6
Sent: Monday, August 9, 2021 2:14 PM
Subject: Bulletin of the Atomic Scientists: COVID-19 lab-leak theory: Gain-of-function is a hot topic, but a bad explanation https://bit.ly/3yDCUnZ

"COVID-19 is scary. Gain-of-function experiments can be scary. But not all scary things are related. It is unlikely that COVID-19 is the result of a lab escape. But even if was, there is little reason to believe that this lab escape was the result of a gain-of-function experiment. There's nothing in particular about gain-of-function experiments that make them more likely to cause a lab escape than any other kind of experiments on pathogens."

COVID-19 lab-leak theory: Gain-of-function is a hot topic, but a bad explanation

By Nicholas G. Evans, Anna Muldoon | August 9, 2021

The Wuhan Institute of Virology in Wuhan, China. Credit: Ureem2805 via Wikimedia Commons. CC BY-SA 4.0.

For the second time in recent months, Sen. Rand Paul, a conservative Republican from Kentucky, sparred with Anthony Fauci, the director of the National Institute of Allergy and Infectious Disease, during a heated Congressional hearing on the coronavirus pandemic in July. By then, Fauci had already become a pandemic bogeyman for the American right, in part for undercutting former President Donald Trump's rosy assessments of the COVID-19 situation and also for supposedly covering up alleged Chinese culpability in the pandemic's origins. Pushing what has become a key assertion in the conservative case against Fauci, Paul accused the senior US infectious disease expert—along with government science funders—of financing so-called gain-of-function pathogen research in China, a type of experimentation in which researchers enhance the transmissibility, virulence, or host range of microbial agents. During the confrontation, the senator wove together the

reputation of the research method with a controversial idea: that the pandemic could have been caused by a lab incident in Wuhan, China.

Fauci, for his part, told Paul, "officially," that the senator didn't know what he was talking about.

The idea that a lab accident could be responsible for the worst year-and-a-half the world has experienced in recent decades gained serious traction after prominent scientists rebuffed a World Health Organization investigation and subsequent report that found that a natural origin of the virus is the most likely explanation. This report led to a group of scientists calling for further review of lab research in Wuhan. But the so-called "lab escape theory" is really more a collection of theories that claim SARS-CoV-2, the virus that causes COVID-19, began its trajectory towards a global pandemic somewhere in a research facility. The typical culprit lab is the Wuhan Institute of Virology, China's only biosafety level 4 laboratory. And an increasingly popular move in lab escape theories is to reference, as Paul did, so-called gain-of-function studies.

While the US government did in fact fund experiments that manipulated coronaviruses at the Wuhan Institute of Virology, officials like Fauci say those experiments don't qualify as gain-of-function research, and, furthermore, that the manipulated pathogens involved didn't spark the pandemic, a point that Paul acknowledged. "No one is alleging that those viruses caused the pandemic. What we're alleging is that gain-of-function research was going on in that lab and [National Institutes of Health] funded it," he said. Researchers in Wuhan were manipulating coronaviruses with US money, but not viruses that were known to affect people. Gain-of-function has nonetheless been incorporated into the COVID-19 origins debate.

It's a linkage that has made a sound debate on both the potentially risky research method and on the origins of COVID-19 more difficult. As with any knot, to understand how gain-of-function and the lab escape theory have gotten so tangled up, it's worth starting at the beginning.

The origins of gain-of-function. Some attempted definitions of gain-of-function are expansive, including claims that microbial agents in nature can "gain" a "function." But in terms of US government policy and the debate over the lab escape theory, gain-of-function means something quite specific: an experiment conducted by researchers in which a microbial organism is engineered such that it gains a function that may enhance its ability to infect, cause disease, or kill its host. Of most concerning is gain-of-function research resulting in potential pandemic pathogens.

Avian influenza surveillance in Bangkok, Thailand. Researchers in 2011 used gain-of-function experiments to show the virus could be made to more readily transmit among mammals. Credit: Richard Nyberg / USAID. CC BY-NC 2.0.

Gain-of-function involving the creation of potential pandemic pathogens emerged into public consciousness in 2011 with the controversy over two papers on influenza: one led by Ron Fouchier, of the Erasmus Medical Center in Rotterdam, the other by Yoshihiro Kawaoka of the University of Wisconsin-Madison and the University of Tokyo. These studies, funded by the US National Institutes of Health, examined the potential mutations that might allow H5N1, or avian influenza, to become a human-transmissible pandemic pathogen under the right circumstances by creating a virus with the right characteristics. In other words, the studies described the creation of exactly the kind of virus the public health community had been fearing for years. Their publication caused intense concern and a firestorm of criticism.

The debate in 2011 led to the creation of the "Framework for Guiding U.S. Department of Health and Human Services Funding Decisions about Research Proposals with the Potential for Generating Highly Pathogenic Avian Influenza H5N1 Viruses that are Transmissible among Mammals by Respiratory Droplets."

The framework didn't deal with all gain-of-function experiments, which are common. Scientists continue to alter the function of organisms in ways that arguably benefit humanity, such as enabling the study of coronaviruses through the development of a strain of Middle East respiratory virus (MERS) that can infect mice—animals typically used to study viral disease but that are resistant to the MERS coronavirus—allowing researchers to better study the human disease.

Gain-of-function research involves many different types of experiments on microbes that pose a wide-range of risks—from entirely benign *e. coli*, for instance, to potential pandemic pathogens.

As the name suggests, the 2011 policy only covered influenza research. It wouldn't stay that way.

A veterinarian collects samples from a dromedary after a case of Middle East Respiratory Syndrome (MERS) was found in Yemen in 2014. Credit: Awadh Mohammed Ba Saleh / CDC Global . CC BY 2.0.

In 2014, a series of biosafety scares—involving anthrax, avian influenza, and smallpox—led the US government to impose a moratorium on gain-of-function experiments dealing with research that could potentially enhance the virulence or transmissibility of influenza, or the SARS coronavirus responsible for the 2002-2003 outbreaks and the MERS coronavirus. The government put in place a deliberative process between the National Academies of Science, Engineering, and Medicine and the National Science Advisory Board for Biosecurity to develop a series of policy recommendations on assessing the risks and benefits of gain-of-function research in these viruses. The policy is known as the "HHS Framework for Guiding Funding Decisions about Proposed Research Involving Enhanced Potential Pandemic Pathogens." Its implementation over that year led to the retraction of the gain-of-function funding moratorium in late 2017.

The framework has eight components that must be satisfied to justify US government funding of gain-of-function research. First, the project must be independently reviewed and determined to be scientifically sound. Second, the pathogen to be created must be reasonably judged to be a credible source of a potential future human pandemic. Third, an assessment of the overall potential risks and benefits associated with the project has to determine that the potential risks as compared to the potential benefits to society are justified. Fourth, there must be no feasible, equally efficacious alternative methods to address the same question in a manner that poses less risk than does the proposed approach.

The project must also satisfy three procedural steps and have a lab with an appropriate record of safety, a responsible communication plan for results, and a funding mechanism with appropriate oversight for safety and security. And finally, the project must be "ethically justified," though what this means beyond the first seven steps is unclear.

What's happened since? After the new review policy and the lifting of the moratorium, the gain-of-function world largely went quiet. It's not clear if this was because there were no experiments of concern, or new developments. Certainly, there was some debate around the properties of the new policy. But it is possible, though not definitive, that the Trump administration did not care about gain-of-function, and equally possible that no one in an oversight role of the policy was particularly enthusiastic about making it an issue unless necessary during that time.

This changed in 2020. Officials on the federal biosecurity advisory board raised concerns about the transparency of the gain-of-function review process. The debate centered around concerns that the body that was set up to evaluate research did not release its findings publicly, the membership of that body was unknown, and the number of items it reviewed (and approved or denied) were likewise unknown. Proponents of increased transparency pointed to its value in building trust and in providing scholars who studied biosafety information on the decision-making process applied to the gain-of-function funding reviews.

Opponents of increased transparency noted that review bodies at that level of government are rarely transparent in the way proponents desired, and Christian Hassell at the Department of Health and Human Services has claimed that making this body open might deter individuals from serving on it. (Though that has never stopped, to our knowledge, anyone serving on the National Science Advisory Board for Biosecurity, the committee that recommended this new oversight body). Kenneth Bernard, who currently serves on the board, has noted that there were potential scientific and security risks associated with revealing information about the kinds of research being reviewed, including making the United States appear like it was running a covert biological weapons program. But at a time when Chinese officials are raising questions about what goes on in US government labs like Fort Detrick in Maryland, a lack of transparency has arguably made that problem worse in 2021—not better.

Then COVID-19 happened. And like much else in biosecurity, experts re-focused from the gain-of-function debates to the pandemic. Few continued to debate the gain-of-function reviews and the research has remained largely undiscussed since, with the exception of the theory that SARS-CoV-2 is, itself, a product of a gain-of-function experiment.

What do COVID-19 and gain-of-function have to do with one another? As assertions that COVID-19 must have leaked from the Wuhan Virological Institute have gained support from the public and some members of Congress, the long-standing debates about gain-of-function research have been drawn into the conversation. From Paul's assertion that the National Institutes of Health funded gain-of-function research at the Wuhan lab to debates about whether a location on the SARS-CoV-2 virus—called the furin cleavage site—shows signs of genetic engineering, conversations about the lab escape theory and gain-of-function have become utterly intertwined.

But this connection is, frankly, spurious. There is no reason a hypothetical lab leak would have to be the result of a gain-of-function experiment. Many proponents of the theory simply assume enhancement rather than show any evidence of it. They forget that laboratory safety doesn't need gain-of-function experiments to be important.

This conflation of all laboratory research with gain-of-function research muddies the waters around the origins of COVID-19. It also leads to debates that misunderstand the risks of life sciences research, and the risks that bad-faith arguments like Paul's pose in the context of this pandemic. Any discussion of the lab escape theory should in fact be divided into two separate issues: first, whether the virus emerged from a laboratory; second, what kind of experiment it could be.

It seems unlikely on its face—though, of course, not strictly impossible—that a gain-of-function experiment is to blame for the COVID-19 pandemic. There have been a number of papers published that have gone into considerable details to show that the possibility of engineering is very low. A recent review of these arguments by University of Sydney evolutionary biologist Edward Holmes and colleagues includes a positive argument for zoonotic (natural) origins of the SARS-CoV-2 virus and an argument against gain-of-function having played a role. Holmes' report notes that the basic building blocks of SARS-CoV-2 aren't consistent with the limited gain-of-function research conducted at the Wuhan Institute of Virology, meaning that even the existence of that research doesn't connect to COVID-19. Things are rarely absolutely certain in science, especially in the life sciences, but it seems that gain-of-function research is not to blame for the pandemic.

For researchers to have engaged in a gain-of-function experiment at the Wuhan Institute of Virology that led to a lab escape, one would have to accept that a cover-up had occurred—the plentiful details that Holmes and colleagues, among others, have described about Wuhan Institute of Virology would have to disguise a secret, highly technical experiment that was important enough to spend resources on but not so important that the scientists left any record of it and never sought to publish any of their results.

Nonetheless, the gain-of-function theory seems to have become the darling of some scientists and many political commentators in recent weeks. Despite ongoing scientific uncertainty and debate, some authors have already gone so far as to apportion blame to scientific communities for a potential lab leak. At times, some people simply want or need COVID-19 to be anything but natural, because otherwise society would have to accept that occasionally nature is downright nasty. But wanting to believe natural pathogens are not so deadly or wanting someone to blame for this maddening 18 months is no reason to assume only humans could have created this virus.

While the world has not yet seen a pandemic caused by an altered virus, there has been a human pandemic and an animal outbreak likely caused by lab escape of natural viruses. It is likely the 1977 flu pandemic escaped from a lab, possibly during vaccine development. A 2007 foot-and-mouth disease outbreak was caused by a faulty pipe at the Pirbright Institute, a disease research center in England, leading to 278 infected cattle on 8 farms. In the first case, the genetics of the flu strain showed that it was most closely related to strains circulating in 1949-50, rather than contemporary strains. In the case of foot-and-mouth disease, genetic analysis also quickly identified the Pirbright Institute as the likely source of the outbreak, even as investigations and response continued. The two cases show that natural viruses held in laboratories for study, reference samples, and basic disease research can pose risks worth discussing. Since the Wuhan Institute of Virology was a centralized collection point for coronavirus samples for study, in many

ways this type of lab escape would be more likely than a gain-of-function experiment, though still unproven.

Two important things arise from this. The first is that even if there were definitive evidence of a lab escape of some kind, all other things being equal it seems much less likely that this lab escape was a result of gain-of-function experiments, and more likely that it was the result of normal laboratory functions in collecting pathogens form animal hosts for analysis. This is a primary function of the Wuhan Institute of Virology; it is a laboratory built close to a known reservoir for coronaviruses and other emerging infectious disease. One can only imagine how the risk profile would increase if researchers were always mailing those samples thousands—or tens of thousands—of miles further for analysis. It makes sense to have a lab in Wuhan, but it is not a riskless activity.

A second question that we have both asked about the lab escape theory is "so what"? A lab escape would be bad. But gain-of-function experiments were already a concern—this pandemic doesn't and won't change that. Pandemics were already a concern—a lab escape wouldn't and won't change that. And the oversight of both of these health security concerns remains fragmented, and historically so.

COVID-19 is scary. Gain-of-function experiments can be scary. But not all scary things are related. It is unlikely that COVID-19 is the result of a lab escape. But even if was, there is little reason to believe that this lab escape was the result of a gain-of-function experiment. There's nothing in particular about gain-of-function experiments that make them more likely to cause a lab escape than any other kind of experiments on pathogens.

In the end, scientific and policy communities have a strong interest in continuing calm, evidence-based conversations about both the origins of COVID-19 and gain-of-function experiments. Understanding the origins of COVID-19 will help us detect and prepare for future pandemics. Agreeing to international guidelines around gain-of-function would encourage safe, responsible, and publicly acceptable research. However, in order to continue either conversation, researchers, officials, and others must disentangle the two from each other and from other forms of laboratory research. Conflating the two helps no one, and arguably makes fixing either more difficult.

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From: Morens, David (NIH/NIAID) [E] [b6]
Sent: 7/8/2021 5:36:13 PM
To: Keusch, Gerald T [b6]; Peter Daszak [b6]
Subject: RE: BMJ: The covid-19 lab leak hypothesis: did the media fall victim to a misinformation campaign?

I don't know him, or of him….

David

David M. Morens, M.D.
CAPT, United States Public Health Service
Senior Advisor to the Director
Office of the Director
National Institute of Allergy and Infectious Diseases
National Institutes of Health
Building 31, Room 7A-03
31 Center Drive, MSC 2520
Bethesda, MD 20892-2520

☎ b6 (assistant: Whitney Robinson)
301 496 4409
b6

From: Keusch, Gerald T [b6]
Sent: Thursday, July 8, 2021 1:33 PM

To: Peter Daszak [b6]; Morens, David (NIH/NIAID) [E] [b6]
Subject: RE: BMJ: The covid-19 lab leak hypothesis: did the media fall victim to a misinformation campaign?

Do any of you know what has become of [b6]? I would like to contact him about what has happened to a formerly quality journal, in fact more highly regarded than the Lancet.

Jerry

From: Peter Daszak [b6]
Sent: Thursday, July 8, 2021 1:17 PM
To: Morens, David (NIH/NIAID) [E] [b6]; Keusch, Gerald T [b6]
Subject: RE: BMJ: The covid-19 lab leak hypothesis: did the media fall victim to a misinformation campaign?

Really disappointed they gave space to this scheister – he's been trolling the internet darkweb with lab leak theories for at least a year.

[b6] commented that BMJ has been putting out anti-vaxx articles too recently…

Cheers,

Peter

Peter Daszak
President

EcoHealth Alliance
520 Eighth Avenue, Suite 1200
New York, NY 10018-6507
USA

Tel.: [b6]
Website: www.ecohealthalliance.org
Twitter: @PeterDaszak

EcoHealth Alliance develops science-based solutions to prevent pandemics and promote conservation

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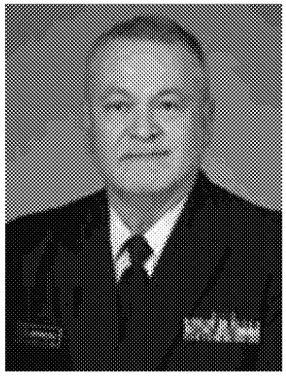
From: Morens, David (NIH/NIAID) [E] [b6]
Sent: Thursday, July 8, 2021 11:03 AM
To: Peter Daszak ([b6]) [b6]; Keusch, Jerry ([b6]) [b6]
Subject: FW: BMJ: The covid-19 lab leak hypothesis: did the media fall victim to a misinformation campaign?

David

David M. Morens, M.D.
CAPT, United States Public Health Service
Senior Advisor to the Director
Office of the Director
National Institute of Allergy and Infectious Diseases
National Institutes of Health
Building 31, Room 7A-03
31 Center Drive, MSC 2520
Bethesda, MD 20892-2520

☎ b6 (assistant: Whitney Robinson)
301 496 4409
b6



From: Folkers, Greg (NIH/NIAID) [E] b6
Sent: Thursday, July 8, 2021 10:43 AM
Subject: BMJ: The covid-19 lab leak hypothesis: did the media fall victim to a misinformation campaign?

The covid-19 lab leak hypothesis: did the media fall victim to a misinformation campaign?

BMJ 2021; 374 doi: https://doi.org/10.1136/bmj.n1656 (Published 08 July 2021) Cite this as: BMJ 2021;374:n1656 Paul D Thacker, investigative journalist
1. *Madrid*

1. thackerpd{at}gmail.com
Twitter @thackerpd

The theory that SARS-CoV-2 may have originated in a lab was considered a debunked conspiracy theory, but some experts are revisiting it amid calls for a new, more thorough investigation. **Paul Thacker** explains the dramatic U turn and the role of contemporary science journalism

For most of 2020, the notion that SARS-CoV-2 may have originated in a lab in Wuhan, China, was treated as a thoroughly debunked conspiracy theory. Only conservative news media sympathetic to President Donald Trump and a few lonely reports dared suggest otherwise. But that all changed in the early months of 2021, and today most outlets across the political spectrum agree: the "lab leak" scenario deserves serious investigation.

Understanding this dramatic U turn on arguably the most important question for preventing a future pandemic, and why it took nearly a year to happen, involves understanding contemporary science journalism.

A conspiracy to label critics as conspiracy theorists

Scientists and reporters contacted by *The BMJ* say that objective consideration of covid-19's origins went awry early in the pandemic, as researchers who were funded to study viruses with pandemic potential launched a campaign labelling the lab leak hypothesis as a "conspiracy theory."

A leader in this campaign has been Peter Daszak, president of EcoHealth Alliance, a non-profit organisation given millions of dollars in grants by the US federal government to research viruses for pandemic preparedness.1 Over the years EcoHealth Alliance has subcontracted out its federally supported research to various scientists and groups, including around $600 000 (£434 000; €504 000) to the Wuhan Institute of Virology.1

Shortly after the pandemic began, Daszak effectively silenced debate over the possibility of a lab leak with a February 2020 statement in the *Lancet*.2 "We stand together to strongly condemn conspiracy theories suggesting that covid-19 does not have a natural origin," said the letter, which listed Daszak as one of 27 coauthors. Daszak did not respond to repeated requests for comment from *The BMJ*.

"It's become a label you pin on something you don't agree with," says Nicholas Wade, a science writer who has worked at *Nature*, *Science*, and the *New York Times*. "It's ridiculous, because the lab escape scenario invokes an accident, which is the opposite of a conspiracy."

But the effort to brand serious consideration of a lab leak a "conspiracy theory" only ramped up. Filippa Lentzos, codirector of the Centre for Science and Security Studies at King's College, London, told the *Wall Street Journal*, "Some of the scientists in this area very quickly closed ranks."3 She added, "There were people that did not talk about this, because they feared for their careers. They feared for their grants."

Daszak had support. After he wrote an essay for the *Guardian* in June 2020 attacking the former head of MI6 for saying that the pandemic could have "started as an accident," Jeremy Farrar, director of the Wellcome Trust and co-signer of the *Lancet* letter, promoted Daszak's essay on Twitter, saying that Daszak was "always worth reading."4

Daszak's behind-the-scenes role in orchestrating the statement in the *Lancet* came to light in November 2020 in emails obtained through freedom of information requests by the watchdog group US Right To Know.

"Please note that this statement will not have EcoHealth Alliance logo on it and will not be identifiable as coming from any one organization or person," wrote Daszak in a February email, while sending around a draft of the statement for signatories.5 In another email, Daszak considered removing his name from the statement "so it has some distance from us and therefore doesn't work in a counterproductive way."6

Several of the 27 scientists who signed the letter Daszak circulated did so using other professional affiliations and omitted reporting their ties to EcoHealth Alliance.3

For Richard Ebright, professor of molecular biology at Rutgers University in New Jersey and a biosafety expert, scientific journals were complicit in helping to shout down any mention of a lab leak. "That means *Nature*, *Science*, and the *Lancet*," he says. In recent months he and dozens of academics have signed several open letters rejecting conspiracy theory accusations and calling for an open investigation of the pandemic's origins.789

"It's very clear at this time that the term 'conspiracy theory' is a useful term for defaming an idea you disagree with," says Ebright, referring to scientists and journalists who have wielded the term. "They have been successful until recently in selling that narrative to many in the media."

The *Lancet*'s editor in chief, Richard Horton, did not respond to repeated requests for comment but, after *The BMJ* had sent him questions, the *Lancet* expanded Daszak's conflicts of interest on the February statement and recused him from working on its task force looking into the pandemic's origin.1011

The *Lancet* letter ultimately helped to guide almost a year of reporting, as journalists helped to amplify Daszak's message and to silence scientific and public debate. "We're in the midst of the social media misinformation age, and these rumours and conspiracy theories have real consequences," Daszak told *Science*.12 Months later in *Nature*, he again criticised "conspiracies" that the virus could have come from the Wuhan Institute of Virology and complained about "politically motivated organisations" requesting his emails.13

That summer *Scientific American*, one of the oldest and best known popular science magazines in America, published a complimentary profile of Daszak's colleague, Shi Zhengli, a centre director at the Wuhan Institute of Virology, which has been funded by EcoHealth Alliance.14

EcoHealth Alliance and the Wuhan Institute of Virology earned additional sympathetic reporting after the US National Institutes of Health (NIH) cancelled its grant to EcoHealth Alliance in April last year—allegedly on President Trump's order—because of its ties to Wuhan, a decision protested by 77 Nobel laureates and 31 scientific societies.15 (The NIH has subsequently awarded EcoHealth Alliance new funding.)

Efforts to characterise the lab leak scenario as unworthy of serious consideration were far reaching, sometimes affecting reporting that had first appeared well before the covid-19 pandemic. For example, in March 2020 *Nature Medicine* added an editor's note ("Scientists believe that an animal is the most likely source of the coronavirus") to a 2015 paper on the creation of a hybrid version of a SARS virus, co-written by Shi.16

Wade explains, "Science journalists differ a lot from other journalists in that they are far less sceptical of their sources and they see their main role as simply to explain science to the public." This, he says, is why they began marching in unison behind Daszak.

The U turn

By the end of 2020, just a handful of journalists had dared to seriously discuss the possibility of a lab leak. In September, *Boston* magazine reported on a preprint that found the virus unlikely to have come from the Wuhan seafood market, as Daszak has argued, and that it seemed too well adapted to humans to have arisen naturally. However, the story failed to garner much attention, similarly to a little noticed investigative report by the Associated Press in December that exposed how the Chinese government was clamping down on research into covid-19's origins.

In January this year, *New York* magazine ran a sprawling story detailing how the pandemic could have started with a leak from the lab in Wuhan. The hypothetical scenario: "SARS-CoV-2, the virus that causes covid-19, began its existence inside a bat, then it learned how to infect people in a claustrophobic mine shaft, and then it was made more infectious in one or more laboratories, perhaps as part of a scientist's well-intentioned but risky effort to create a broad-spectrum vaccine." Scientists and their media allies swiftly criticised the article.

But mainstream outlets from the *New York Times* to the *Washington Post* are now treating the lab leak hypothesis as a worthy question, one to be answered with a serious investigation. In a recent interview with the *New York Times*, Shi denied that her lab was ever involved in "gain of function" experiments (box 1) that enhance a virus's virulence. But the newspaper reported that her lab had been involved in experiments that altered the transmissibility of viruses, alongside interviews with scientists who said that far more transparency was necessary to determine the truth of SARS-CoV-2's origins.17

Box 1

What is "gain of function" research?

After two teams genetically tweaked the H5N1 avian flu virus in 2011 to make it more transmissible in mammals, biosafety experts voiced concerns about "gain of function" research—experimental research that involves altering microbes in ways that change their transmissibility, pathogenicity, or host range.

In the *Bulletin of the Atomic Scientists* in 2012, Lynn Klotz predicted an 80% chance that a leak of a potential pandemic pathogen would occur sometime in the next 12 years. Two years later a Harvard epidemiologist, Marc Lipsitch, founded the Cambridge Working Group to lobby against such experiments.

At that time, three safety lapses involving dangerous pathogens led to a safety crackdown at the US Centers for Disease Control and Prevention. Lipsitch later argued in 2018 that the release of such a pathogen would "lead to global spread of a virulent virus, a biosafety incident on a scale never before seen."

Gain of function research was briefly paused because of these concerns, although critics debate as to when it restarted. For more than a decade, scientists at the Wuhan Institute of Virology have been discovering coronaviruses in bats in southern China and bringing them back to their lab for gain of function research, to learn how to deal with such a deadly virus should it arise in nature.

The closest known relative of the SARS-CoV-2 virus was found in a region of China almost 1000 miles from the Wuhan Institute of Virology—yet the pandemic apparently started in Wuhan. Biosafety experts have noted that lab leaks are common but rarely reported, as hundreds of lab accidents had happened in the US alone.27

RETURN TO TEXT

Two major events are probably responsible for the media's change in tune. First, Trump was no longer president. Because Trump had said that the virus could have come from a Wuhan lab, Daszak and others used him as a convenient foil to attack their critics. But the framing of the lab leak hypothesis as a partisan issue was harder to sustain after Trump left the White House.

Second, after months of negotiation the Chinese government finally allowed the World Health Organization to come to Wuhan and investigate the pandemic's origin. But in January 2021 WHO, which included Daszak on the team, returned with no evidence that the virus had arisen through natural spill-over.18 More worryingly, members were allowed only a few hours of supervised access to the Wuhan Institute of Virology.

The White House then released a statement making clear that it did not trust China's propaganda denying that the virus could have come from one of the country's labs. "We have deep concerns about the way in which the early findings of

the covid-19 investigation were communicated and questions about the process used to reach them," said the statement. "It is imperative that this report be independent, with expert findings free from intervention or alteration by the Chinese government."

The following month the *Washington Post* editorial board called for an open and transparent investigation of the virus's origins, highlighting Shi's experiments with bat coronaviruses that were genetically very similar to the one that caused the pandemic.19 It asked, "Could a worker have gotten infected or inadvertent leakage have touched off the outbreak in Wuhan?" The *Wall Street Journal*, citing a US intelligence document, recently reported that three Wuhan Institute of Virology researchers were admitted to hospital in November 2019.20

To follow any US financial ties and to better understand how the pandemic started, Republicans have launched investigations of government agencies that fund coronavirus research, and one investigative committee has sent a letter to Daszak at EcoHealth Alliance demanding that he turn over documents. Meanwhile, Senate Republicans and Democrats have started to discuss an independent investigation of the virus's origins.

A hard truth to swallow

The growing tendency to treat the lab leak scenario as worthy of serious investigation has put some reporters on the defensive. After Robert Redfield, former director of the Centers for Disease Control and Prevention, appeared on CNN in March, *Scientific American*'s editor in chief, Laura Helmuth, tweeted, "On CNN, former CDC director Robert Redfield shared the conspiracy theory that the virus came from the Wuhan lab." The following day, *Scientific American* ran an essay calling the lab leak theory "evidence free." And a week later a *Nature* reporter, Amy Maxmen, labelled the idea that the virus could have leaked from a lab as "conjecture."

Helmuth did not respond to questions from *The BMJ*.

Some media outlets have attempted to justify their past reporting about the lab leak hypothesis as simply a matter of tracking a "scientific consensus" which, they say, has now changed. *Vox* posted an erratum noting, "Since this piece was originally published in March 2020, scientific consensus has shifted."

The "scientific consensus" argument does not sit well with David Relman, a microbiologist at Stanford University, California. "We can't even begin to talk about a consensus other than a consensus that we don't know [the origins of SARS-CoV-2]," he recently told the *Washington Post*.21

A year lost

While the narrative took months to change in the media, several high profile intelligence sources had treated the lab leak theory seriously from early on. In April 2020, Avril Haines joined two other former deputy directors of the Central Intelligence Agency to write an essay in *Foreign Policy* asking, "To what extent did the Chinese government misrepresent the scope and scale of the epidemic?"22 A week later, one of the former intelligence officials who wrote that essay gave similar quotes to *Politico*.

Ignoring these early warnings led to a year of biased, failed reporting, says Wade. "They didn't question what their sources were saying," he says of the reporters who helped to sell the conspiracy theory narrative to the public. "That is the simple explanation for this phenomenon."

An impartial, credible investigation?

As the news media scramble to correct and reflect on what went wrong with nearly a year of reporting, the episode has also highlighted quality control issues at the ubiquitous "fact checking" services.

Prominent outlets such as *PolitiFact*23 and FactCheck.org24 have added editor's notes to pieces that previously "debunked" the idea that the virus was created in a lab or could have been bioengineered—softening their position to one of an open question that is "in dispute." For almost a year Facebook sought to control misinformation by banning stories suggesting that the coronavirus was man made. After renewed interest in the virus's origin, Facebook lifted the ban.25

Whether a credible investigation will be made into the lab leak scenario remains to be seen. WHO and the *Lancet* both launched investigations last year (box 2), but Daszak was involved in both, and neither has made significant progress.

Box 2

Timeline

2019

September Weeks before the pandemic erupts, Jeremy Farrar (Wellcome Trust) and Anthony Fauci (US National Institutes of Health; NIH) help oversee a World Health Organization report highlighting an "increasing risk of global pandemic from a pathogen escaping after being engineered in a lab"

November Three researchers from the Wuhan Institute of Virology are admitted to hospital, says a previously undisclosed US intelligence document reported by the *Wall Street Journal* on 23 May 2021

31 December China notifies WHO of "cases of pneumonia of unknown aetiology" in Wuhan City

2020

1 February Jeremy Farrar holds a teleconference with Anthony Fauci and others to discuss the outbreak's origins

6 February A commentary from Chinese researchers based in Wuhan, arguing that "the killer coronavirus probably originated from a laboratory in Wuhan," is posted and later removed from ResearchGate (the user account "Botao Xiao" is also deleted)

19 February An open letter is published in the *Lancet* from 27 scientists including Peter Daszak and Jeremy Farrar, who "strongly condemn conspiracy theories suggesting that covid-19 does not have a natural origin"

19 February*Science* magazine reports: "Scientists 'strongly condemn' rumors and conspiracy theories about origin of coronavirus outbreak," quoting Daszak as saying, "We're in the midst of the social media misinformation age, and these rumors and conspiracy theories have real consequences, including threats of violence that have occurred to our colleagues in China."

22 February*New York Post* publishes an article by a China scholar arguing that "coronavirus may have leaked from a lab"—subsequently censored by Facebook

6 March Kristian Andersen (Scripps Research Institute) thanks Jeremy Farrar (Wellcome), Anthony Fauci (NIH), and Francis Collins (NIH) "for your advice and leadership as we have been working through the SARS-CoV-2 'origins' paper." The paper is published on 17 March in *Nature Medicine* and states, "Our analyses clearly show that SARS-CoV-2 is not a laboratory construct or a purposefully manipulated virus."

24 April NIH abruptly cuts funding to EcoHealth Alliance, allegedly on President Trump's order

28 April Three former US intelligence agents write in *Foreign Policy* asking whether the virus emerged from nature or escaped from a Chinese lab

21 May*New York Times* depicts the Wuhan Institute of Virology as a victim of "conspiracy theories"

27 May*Nature* reports the lab leak hypothesis as "coronavirus misinformation" and "false information"

8 June The science magazine *Undark* reports that the lab leak is a conspiracy theory "that's been broadly discredited"

30 December Associated Press investigation finds documents from March 2020 showing how Beijing has shaped and censored research into the origins of SARS-CoV-2

2021

February Facebook places warning on an article by Ian Birrell about the origins of covid-19. Facebook says that these warnings reduce article viewership by 95%

13 February Jake Sullivan, US national security adviser, expresses "deep concerns" about WHO's covid-19 investigation, calling on China to be more transparent

March*Washington Post* calls for serious investigations of the lab leak hypothesis

30 March WHO releases a report on its investigation into the origins of covid-19, listing the lab leak as least likely of the possible scenarios considered. Hours earlier, WHO's director general, Tedros Adhanom Ghebreyesus, acknowledged that the lab leak hypothesis should "remain on the table" and called for a more extensive probe

30 March The US, Australian, Japanese, Canadian, UK, and other governments express concern over WHO's investigation and call for "transparent and independent analysis and evaluation, free from interference and undue influence"

26 May Facebook lifts its ban on posts referencing the lab leak hypothesis

RETURN TO TEXT

In recent weeks, several high profile scientists who once denigrated the idea that the virus could have come from a lab have made small steps into demanding an open investigation of the pandemic's origin.

The NIH's director, Francis Collins, said in a recent interview, "The Chinese government should be on notice that we have to have answers to questions that have not been answered about those people who got sick in November who worked in the lab and about those lab notebooks that have not been examined." He added, "If they really want to be exonerated from this claim of culpability, then they have got to be transparent."26

But the nature of this investigation has still not been decided.

Footnotes

- Competing interests: I am paid by various media outlets for journalism stories and consult part time for a non-profit institute focused on brain disorders. I run a newsletter called the *Disinformation Chronicle*.
- Provenance and peer review: Commissioned, not externally peer reviewed.

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From: Morens, David (NIH/NIAID) [E] [b6 b6]
Sent: 8/5/2021 9:42:12 PM
To: Edward Holmes [b6]
CC: Peter Daszak ([b6]) [b6]; Keusch, Jerry ([b6]) [b6]; Kessler, Robert ([b6]) [b6]; Rich Roberts ([b6]) [b6]
BCC: Morens, David (NIH/NIAID) [E] [b6 b6]
Subject: Re: CNN: Exclusive: Intel agencies scour reams of genetic data from Wuhan lab in Covid origins hunt https://protect-au.mimecast.com/s/xCyoCvl1rKi7NAywGIQWvWo?domain=cnn.it

I take some pleasure in knowing that in the end they will all kick themselves for having wasted their time.

Sent from my iPhone
David M Morens
OD, NIAID, NIH

On Aug 5, 2021, at 17:29, Edward Holmes [b6] wrote:

Yes, I hope that means we can put that particular issue to bed.

Professor Edward C. Holmes FAA FRS
The University of Sydney

On 6 Aug 2021, at 7:26 am, Morens, David (NIH/NIAID) [E] [b6] wrote:

<image001.gif>

David M. Morens, M.D.
CAPT, United States Public Health Service
Senior Advisor to the Director
Office of the Director
National Institute of Allergy and Infectious Diseases
National Institutes of Health
Building 31, Room 7A-03
31 Center Drive, MSC 2520
Bethesda, MD 20892-2520

☎ b6 (assistant: Whitney Robinson)
301 496 4409
b6

From: Folkers, Greg (NIH/NIAID) [E] b6
Sent: Thursday, August 5, 2021 4:18 PM
Subject: CNN: Exclusive: Intel agencies scour reams of genetic data from Wuhan lab in Covid origins hunt https://cnn.it/3fzBbsp

Exclusive: Intel agencies scour reams of genetic data from Wuhan lab in Covid origins hunt

By Katie Bo Williams, Zachary Cohen and Natasha Bertrand, CNN

Updated 9:02 AM ET, Thu August 5, 2021

*Washington (CNN)*US intelligence agencies are digging through a treasure trove of genetic data that could be key to uncovering the origins of the coronavirus -- as soon as they can decipher it.

This giant catalog of information contains genetic blueprints drawn from virus samples studied at the lab in Wuhan, China which some officials believe may have been the source of the Covid-19 outbreak, multiple people familiar with the matter tell CNN.

It's unclear exactly how or when US intelligence agencies gained access to the information, but the machines involved in creating and processing this kind of genetic data from viruses are typically connected to external cloud-based servers -- leaving open the possibility they were hacked, sources said.

Still, translating this mountain of raw data into usable information -- which is only one part of the intelligence community's 90-day push to uncover the pandemic's origins -- presents a range of challenges, including harnessing enough computing power to process it all. To do that, intelligence agencies are relying on supercomputers at the Department of Energy's National Labs, a collection of 17 elite government research institutions.

There's also a manpower issue. Not only do intelligence agencies need government scientists skilled enough to interpret complex genetic sequencing data and who have

the proper security clearance, they also need to speak Mandarin, since the information is written in Chinese with a specialized vocabulary.

"Obviously there are scientists who are (security) cleared," one source familiar with the intelligence told CNN. "But Mandarin-speaking ones who are cleared? That's a very small pool. And not just any scientists, but ones who specialize in bio? So you can see how this quickly becomes difficult."

Officials conducting the 90-day review hope this information will help answer the question of how the virus jumped from animals to humans. Unlocking that mystery is essential to ultimately determining whether Covid-19 leaked from the lab or was transmitted to humans from animals in the wild, multiple sources told CNN.

Investigators both inside and outside the government have long sought genetic data from 22,000 virus samples that were being studied at the Wuhan Institute of Virology. That data was removed from the internet by Chinese officials in September 2019, and China has since refused to turn over this and other raw data on early coronavirus cases to the World Health Organization and the US.

The question for investigators is whether the WIV or other labs in China possessed virus samples or other contextual information that could help them trace the coronavirus' evolutionary history.

Two scientists who study coronaviruses told CNN they are skeptical that there is any genetic data either in the tranche of 22,000 samples or any other database from the WIV that scientists don't already know about.

"Basically in [a 2020 research paper published in Nature], the WIV talked about all the sequences they had up until a certain point in time -- it's what most scientists virologists believe, that's pretty much what they had," said Dr. Robert Garry, a virologist at the Tulane University School of Medicine.

A source familiar with the US investigation would neither confirm nor deny that any of the data pertaining to those 22,000 samples is among what US intelligence agencies are currently analyzing.

No 'smoking gun'

Sources familiar with the effort say filling in that missing genetic link won't be enough to definitively prove whether the virus originated in the lab at Wuhan or first emerged naturally. Officials will still need to piece together other contextual clues to determine the true origins of the pandemic.

But it is a critical puzzle piece that the Biden administration has been prioritizing. "The most prized technical data in this context are genetic sequences, database entries and contextual information about the provenance of the samples and the time and context in which they were acquired -- information people would use to place them in a narrative of the origins of SARS, Covid," one source familiar with the investigation told CNN.

For now, senior intelligence officials still say that they are genuinely split between the two prevailing theories on the pandemic's origins, or some combination of both scenarios. CNN reported last month that senior Biden administration officials overseeing

the 90-day review now believe the theory that the virus accidentally escaped from a lab in Wuhan is at least as credible as the possibility that it emerged naturally in the wild -- a dramatic shift from a year ago, when Democrats publicly downplayed the so-called lab leak theory.

Multiple sources told CNN that absent an unexpected windfall of new information, officials don't expect to uncover a "smoking gun" -- like intercepted communications, for example -- that would offer definitive proof for either theory. The Biden administration's 90-day push is predicated on the expectation that science, not intelligence will be the key.

Intelligence officials are tasked with addressing several "scientific knowledge gaps" about the virus' evolution, according to the collection guidance governing the 90-day push, distributed to more than a dozen agencies on June 11 by the Office of the Director of National Intelligence and obtained by CNN.

The memo instructs the intelligence community to "expand its collection" and consider data already in its possession to identify both the initial host of the coronavirus and any species that it may have passed through as it adapted to humans -- or to find as "any progenitor virus and/or virus that could serve as backbone for genetic engineering purposes."

But former Director of National Intelligence John Ratcliffe told CNN that the US intelligence community already had sufficient collection on the topic of Covid origins.

"Obviously the more, the better. But we've had extraordinary insight into this topic for many months, much more than has been declassified. Pretending we didn't is political theater and a classic example of a politician trying to buy time by using the IC as a scapegoat," he told CNN in a statement.

Digging into the science

That's where the genomic data from the Wuhan lab could come in.

The genetic code of a given virus is the signature that allows scientists to tell the difference between the Delta and Beta variants of the coronavirus, for example. It can also offer clues as to how the virus has adapted or mutated over time, including whether it shows signs of human manipulation -- a kind of genetic history.

Many scientists continue to believe that the most likely scenario is that the virus jumped from animals to humans naturally. But despite testing thousands of animals, researchers still haven't identified the intermediate host through which the virus passed as it adapted to humans.

But some researchers, intelligence officials and Republican lawmakers believe that researchers at the WIV might have genetically altered a virus in the lab, using a controversial kind of research known as "gain of function" that could have infected researchers who then spread it in their community.

It's also plausible that the initial infection took place naturally outside of the lab, perhaps while a scientist was collecting a sample from an animal in the wild, and that scientist then spread the virus unknowingly when he returned to the lab with the samples, multiple sources familiar with the intelligence explained.

"If it was the latter, it was likely brought into a lab to study because someone got sick ... which means there were an unknowable number of other people who were already sick," the source familiar with the probe said.
Understanding exactly which viruses researchers at the WIV were working on could provide important evidence for any one of these theories. It's one of the reasons that investigators on Capitol Hill and elsewhere have been keenly focused on the database that was taken offline in 2019.

But it might not prove anything definitively, sources familiar with the intelligence say. Even if scientists in the intelligence community are able to use the data from the lab to stitch together a complete genetic history that shows how the virus mutated, they might not have enough information about how it was handled by the Chinese lab to determine with a high level of confidence that it leaked.

"Despite having that complete history of variants, [officials might] lack the contextual information to make sense of it in a narrative way," the source familiar with the investigation explained.
"Even a complete sequence history is difficult to obtain. And doesn't really tell us anything about the origins of the pandemic itself without the context," this person added.

Some Republicans on Capitol Hill have jumped into the uncertainty with their own report claiming that "the preponderance of evidence suggests" the coronavirus was "accidentally" released from a lab in Wuhan in 2019 -- an assertion that goes far beyond the intelligence community's current view of the matter.

90 days -- and then what?

It's possible that at the end of Biden's 90-day push, the intelligence community won't have reached what's known as a "high-confidence" assessment as to the pandemic's origins. Administration officials have previously suggested to CNN that it's possible a second review could be ordered at the end of the 90 days.

A bipartisan group of lawmakers on the Senate Intelligence and Foreign Relations Committees earlier this week sent a letter urging the administration to continue to prioritize the hunt until such a judgment can be made in order to prevent future pandemics.

But the lawmakers also zeroed in on a related focus for intelligence officials probing the pandemic's origins: China's "efforts to conceal the severity and scope of the outbreak of the SARS-CoV-2 virus that caused the COVID-19 pandemic."
"We also believe that the investigation should address PRC efforts to prevent international inquiries into the origins of SARS-CoV-2, and other actions PRC authorities have taken to obscure the nature of the virus and its transmission," the lawmakers said.

Republican lawmakers in the House, meanwhile, have latched onto the theory that the virus escaped from a lab. GOP lawmakers in a report released Monday by Rep. Michael McCaul of Texas have claimed that "the preponderance of evidence suggests" the coronavirus was "accidentally" released from a lab in Wuhan in 2019.

Intelligence officials say it's still far too soon to say.

From: b6 [b6]
Sent: 11/22/2021 12:21:22 PM
To: William B. Karesh [b6]
CC: Catherine Machalaba [b6]; Daniel Mira-Salama [b6]
BCC: Morens, David (NIH/NIAID) [E] [b6]
b6]
Subject: Re: figure for World Bank report
Attachments: PastedGraphic-1.tiff

Billy, this map was reconstructed from our original by the graphics department at the journal Cell. They did this purely so they could copyright it.

You could contact Cell, abd they will charge you. Or else we can give you the original with you can have for free. The original has all the same info and the same color code, but is less spread out vertically and differs in other minor ways

Let me know. My best to Peter and the gang. David

Sent from my iPhone
David M Morens
OD, NIAID, NIH

On Nov 22, 2021, at 06:46, William B. Karesh b6 wrote:

Dear David,

Hope this finds you well.

We are in the final stages of printer's proofs of a report on EID's in Asia we did for the World Bank. We want to include your EID map from 2020 (attached), but the printer's tell us that our version is not high enough resolution. Would you happen to have high resolution version that could be used?

Hope you have a great Thanksgiving, all the best,

Billy

William B. Karesh, D.V.M
Executive Vice President for Health and Policy

EcoHealth Alliance
520 Eighth Avenue, Suite 1200
New York, NY 10018 USA

b6 (direct)

+1.212.380.4465 (fax)
www.ecohealthalliance.org

President, OIE Working Group on Wildlife

Co-chair, IUCN Species Survival Commission - Wildlife Health Specialist Group

EcoHealth Alliance develops science-based solutions to prevent pandemics and promote conservation.

From: Morens, David (NIH/NIAID) [E] [b6] ([b6])
Sent: 10/19/2021 5:14:03 PM
To: Peter Daszak ([b6]) [[b6]]; Keusch, Jerry ([b6]) [[b6]]; Kessler, Robert ([b6]) [[b6]]; Rich Roberts ([b6]) [[b6]]; Taubenberger, Jeffery (NIH/NIAID) [E] ([b6]) [[b6]]; Eddie Holmes ([b6]) [[b6]]
Attachments: mBio.01864-21.pdf

David

David M. Morens, M.D.
CAPT, United States Public Health Service
Senior Advisor to the Director
Office of the Director
National Institute of Allergy and Infectious Diseases
National Institutes of Health
Building 31, Room 7A-03
31 Center Drive, MSC 2520
Bethesda, MD 20892-2520

☎ [b6] (assistants: Kimberly Barasch; Whitney Robinson)
301 496 4409
[b6]

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PERSPECTIVE

Rapid Proliferation of Pandemic Research: Implications for Dual-Use Risks

Sriharshita Musunuri,[a] Jonas B. Sandbrink,[b,c] Joshua Teperowski Monrad,[b,d,e] Megan J. Palmer,[f,g] Gregory D. Koblentz[h]

[a]Department of Chemistry, Stanford University, Stanford, California, USA
[b]Future of Humanity Institute, University of Oxford, Oxford, United Kingdom
[c]Medical Sciences Division, University of Oxford, Oxford, United Kingdom
[d]Faculty of Public Health and Policy, London School of Hygiene and Tropical Medicine, London, United Kingdom
[e]Department of Health Policy, London School of Economics, London, United Kingdom
[f]Department of Bioengineering, Stanford University, Stanford, California, USA
[g]Center for International Security and Cooperation (CISAC), Stanford University, Stanford, California, USA
[h]Schar School of Policy and Government, George Mason University, Fairfax, Virginia, USA

Sriharshita Musunuri, Jonas B. Sandbrink, and Joshua Teperowski Monrad made equal contributions. Author order was decided arbitrarily.

ABSTRACT The COVID-19 pandemic has demonstrated the world's vulnerability to biological catastrophe and elicited unprecedented scientific efforts. Some of this work and its derivatives, however, present dual-use risks (i.e., potential harm from misapplication of beneficial research) that have largely gone unaddressed. For instance, gain-of-function studies and reverse genetics protocols may facilitate the engineering of concerning SARS-CoV-2 variants and other pathogens. The risk of accidental or deliberate release of dangerous pathogens may be increased by large-scale collection and characterization of zoonotic viruses undertaken in an effort to understand what enables animal-to-human transmission. These concerns are exacerbated by the rise of preprint publishing that circumvents a late-stage opportunity for dual-use oversight. To prevent the next global health emergency, we must avoid inadvertently increasing the threat of future biological events. This requires a nuanced and proactive approach to dual-use evaluation throughout the research life cycle, including the conception, funding, conduct, and dissemination of research.

KEYWORDS COVID-19, dual-use research, biosecurity, biosafety, pandemic preparedness, preprints, zoonotic risk

The COVID-19 pandemic has revealed the world's vulnerability to biological threats and will shape pandemic preparedness efforts for decades to come. Recent discussions have particularly emphasized biosafety risks associated with gain-of-function experiments and accidental pathogen release (1). However, global health security leaders have also cautioned that the COVID-19 pandemic may increase the threat from deliberate biological events, i.e., biosecurity risks, by potentially inspiring malicious actors (2–4). These warnings come against the backdrop of existing global vulnerabilities to potential biosecurity risks, as both the WHO Joint External Evaluations and the inaugural 2019 Global Health Security Index have identified inadequate capacity and policies for biosecurity in the vast majority of countries (5, 6).

Additionally, biosecurity threats may be particularly concerning given that pathogens engineered for transmissibility or virulence may cause biological events of the largest magnitude, including global catastrophic biological risks (GCBRs) (7). Such engineering may be enabled by the misapplication of publicly available insights and tools from certain "dual-use" life sciences research, even when this research was conceived

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Editor Paul Keim, Northern Arizona University

Address correspondence to Sriharshita Musunuri, svmusu@stanford.edu.

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TABLE 1 Journal articles on SARS-CoV-2 published between 1 January 2020 and 5 July 2021 and GHS Index Dual-Use Indicator by country on a scale of 0 to 100 (low to high preparedness)[a]

Country	Research output (no. of articles)	GHS Index Dual-Use Indicator score (0–100)
United States	52,281	50
United Kingdom	21,600	33.3
China	19,389	0
Italy	15,093	0
India	12,896	0
Spain	8,862	0
Canada	8,203	33.3
Germany	7,977	0
France	7,410	0
Australia	7,039	33.3

[a]Articles were counted if they included "SARS-CoV-2" OR "COVID-19" OR "Coronavirus 2019" OR "novel coronavirus" OR "2019-nCoV," in title or abstract. The Indicator is determined by whether countries have (a) active oversight of potential dual-use research of concern and (b) screening of genetic synthesis orders against lists of known pathogens and toxins.

with beneficial intent. Research associated with the greatest misuse potential constitutes "dual-use research of concern" (DURC), which the U.S. National Institutes of Health defines as "life sciences research that, based on current understanding, can be reasonably anticipated to provide knowledge, information, products or technologies that could be directly misapplied to pose a significant threat with broad potential consequences to public health and safety" (8).

Determining what research exhibits dual-use risks is an ongoing challenge, and if national policies on this exist, they frequently fall short of establishing comprehensive, flexible, and nuanced oversight. In the United States, in addition to the review of risks from public funding of the enhancement of potential pandemic pathogens under the P3CO framework, federally funded institutions are required to assess dual-use risks for only research involving 7 classes of experiments on 15 biological agents, and individual investigators are encouraged to voluntarily raise concerns about research that falls outside these categories (8, 9). Currently, SARS and SARS-CoV-2 are not considered Select Agents under this classification. In contrast, in Canada all institutions working with pathogens and toxins, regardless of funding source, are required to assess dual-use risks of any conducted research (10). According to the Global Health Security Index (GHSI), only 1% of countries worldwide are equipped with adequate review processes for research with especially dangerous pathogens (11). This means that almost all research carried out in the wake of the pandemic will be both conducted and published without adequate dual-use oversight, underscoring the importance of improved guidance globally (Table 1). Moreover, even when review processes are nominally in place, worrying research may nevertheless be conducted in the absence of robust efforts to implement and evaluate the effectiveness of existing policies (12, 13).

The COVID-19 pandemic may exacerbate biological risks stemming from the misapplication of research. We highlight several types of research with dual-use potential associated with pandemic response and preparedness efforts and emphasize how changes to the life science research enterprise complicate oversight of research with dual-use potential. We then describe the need for dual-use frameworks suited for application in the midst of emergency situations, as well as the need to consider dual-use risks associated with pandemic countermeasures. Ongoing dual-use review throughout the research life cycle is necessary to address increasingly common dissemination of research before peer review.

COVID-19 RESPONSE EFFORTS HAVE CREATED DUAL-USE INSIGHTS

The vast majority of research that is being conducted and published related to the development of countermeasures against SARS-CoV-2 aims to contribute to global

pandemic response efforts. This research includes advances such as the identification of neutralizing monoclonal antibodies as therapeutics, genetic surveillance to rapidly characterize variants of concern, and immunogens that aim to elicit lasting protection against the disease (14, 15). However, some work may have dual-use potential that increases the risk of deliberate misuse alongside the potential for accidents, thereby endangering not only the current response but also preparedness efforts for future outbreaks.

For instance, certain research may inform the explicit identification of mutations to the genome of the virus to enhance its resistance to existing countermeasures (16), replicative fitness, or transmissibility. While such studies are often done to pinpoint exactly how current countermeasures, such as convalescent patient sera or monoclonal antibody therapeutics, are insufficient to address potential emerging variants of concern, they also offer a blueprint of changes to be made that could increase the virulence of the virus. Thus, a few of these studies constitute "gain-of-function" (GOF) experiments that have the potential to enhance the lethality and/or transmissibility of a virus. These types of experiments deserve additional review given the associated dual-use risks but may have received less scrutiny due to the urgency of the pandemic and already widespread circulation of the pathogen in question. Some of this information has been rapidly incorporated into countermeasures upon publication and dissemination, such as modification of vaccine formulations to reflect circulating variants (17, 18). However, we must still be wary of the risk that the availability of granular mutational data linked to viral phenotype poses in the long term. This is especially important if it enables the engineering of more concerning strains of SARS-CoV-2, or other viruses, by malicious actors for deliberate release or strategic stockpiling as a biological weapon. While accidental and intentional misuse scenarios may be associated with the same lines of research, the latter could be more catastrophic.

Instructions for the *de novo* reconstruction of replication-competent SARS-CoV-2 virus are another example of dual-use knowledge that has been created and disseminated as a result of the pandemic (19, 20), as they may lower tacit knowledge barriers to conducting risky research. While methods such as restriction enzyme digestion, cDNA fragment assembly, and polymerase chain reaction are staple biochemistry techniques, detailed protocols regarding the assembly of functional virus and its derivative mutants may increase the number of researchers capable of using reverse genetics, regardless of prior training. Therefore, the likelihood that a bad actor acquires the practical knowledge necessary to culture recombinant viruses without safeguards, including those engineered for properties such as immune evasion, increases.

It is important to recognize that transparent dissemination of protocols and reagents is a crucial aspect of accelerating pandemic response research among the scientific community. However, there may be specific tools or insights that pose greater risks than benefits and should require an additional screening step before being shared or should be replaced by a safer alternative. Similar to the practical use of pseudotyped viruses wherever possible to reduce biosafety risks, we should adopt approaches that minimize biosecurity risks. For instance, there are a number of available methods to obtain replication-competent virus other than through synthesis. Extraction of live virus from clinical isolates is not accompanied by straightforward methods of introducing mutations that accentuate certain viral properties in the way that reverse genetics approaches are (21). Another viable alternative may be the use of a transcomplementation system producing nonvirulent SARS-CoV-2 that is infectious for only a single round of replication (22). This approach is also attractive given that it duplicates authentic viral replication, can be implemented in biosafety level 2 (BSL-2) containment, and facilitates the development of countermeasures with fewer risks.

Evidently, only a small fraction of response efforts is associated with dual-use risks. However, we must ensure that such studies do not endanger the overall response and preparedness effort. While an ongoing pandemic warrants rapid dissemination and collaboration to develop countermeasures, maintenance and consideration of dual-use

concerns cannot be neglected either in order to avoid the possibility of an even larger crisis in the future.

COUNTERMEASURE RESEARCH IN THE WAKE OF THE PANDEMIC CAN POSE DUAL-USE RISKS

In addition to the potential dissemination of security-relevant insights during the direct pandemic response, increased infectious disease countermeasure research over the coming years may raise risks from deliberate and accidental biological events. To minimize biosecurity risks from deliberate events, conception and funding decisions regarding infectious disease countermeasure research need to consider how associated insights may inform pathogen engineering by malicious actors. For instance, research on viral vector platform-based vaccines may be associated with generating insights on engineering immune evasion could be translated to pathogens of concern (23). Previous natural exposure to the virus utilized as a vaccine vector may result in preexisting immunity that can limit the effectiveness of vaccination in certain individuals, and induction of antivector immunity through vaccine administration limits the reusability of a given vector platform (24). To overcome this limitation, chimeric vector viruses have been created which evade neutralization by preexisting antibodies (25). While most vaccine-related work focuses on less concerning viral families, such as *Adenoviridae*, researchers have also explored and engineered orthopoxviruses—related to variola virus, the agent that causes smallpox—like vaccinia virus. Less risky alternatives to solving antivector immunity include expanding the vector portfolio to include nonhuman viruses and focusing efforts on nongenetic modifications which are not passed onto viral progeny, such as PEGylation (26, 27). Especially promising may be preferential investment into mRNA-based vaccines which both exhibit excellent properties as fast response platforms and are associated with few dual-use risks (23, 28, 29).

Another example of potentially concerning countermeasure research is the creation of transmissible vaccines for eradicating zoonotic pathogens, which has been advocated for with increased urgency in the wake of the pandemic (30, 31). Despite some potentially useful applications, such research would be associated with substantial safety risks as well as ecological and ethical concerns about introducing a new transmissible agent into animal populations. Importantly, such research would also create unique incentives for engineering the transmissibility, genetic stability, and immune evasion of viruses and hence be associated with significant dual-use risks (32).

SAFETY AND SECURITY RISKS FROM EFFORTS TO UNDERSTAND ZOONOTIC SPILLOVER EVENTS

Beyond specific countermeasure research leading to dual-use insights on viral engineering, research conducted to investigate and predict zoonotic spillover events may also increase biosafety and biosecurity risks. Experiments that use a "gain-of-function" approach to determine the contribution of genotypic changes to the transmissibility or virulence of a virus could create enhanced potential pandemic pathogens (33), such as the controversial generation of mammalian transmissible H5N1 avian influenza virus (34, 35) as well as more recent work on coronaviruses (36). While this type of research should be conducted at facilities with the appropriate level of safety and security measures, even high-containment labs have an appreciable accident rate (33, 37). Moreover, making specific insights on concerning mutations publicly available can pose information hazards if this enables malicious actors to reconstruct or enhance pandemic pathogens (38, 39).

Systematic approaches to the characterization of viruses with potential for zoonotic spillover bear particular biosecurity risks. Large-scale efforts with the aim to collect hundreds of thousands of samples of viruses and investigate them in laboratories have been proposed and initiated (40). Such efforts are associated not only with accidental exposure and release risks (41) but also the potential of generating dual-use insights. Large-scale characterization of animal viruses may enable computational viral

engineering capabilities by creating large data sets which link genetic sequence and function for thousands of viruses. This may be leveraged to create more transmissible and virulent pathogens (42). In addition, broad genomic surveys and characterization of animal viruses have been suggested to be of little practical use to mitigate the emergence of biological events (43). Therefore, preferential investment into approaches which are associated with little biosecurity risk may more robustly reduce overall health security risk. For instance, the real-time surveillance of human populations for emerging pathogens does not involve large-scale collection and characterization of zoonotic viruses and has been highlighted as an effective approach to mitigating outbreaks (44).

Transmissible vaccine research, specific GOF experiments, and large-scale efforts to characterize animal viruses are examples of research aimed at reducing zoonotic risks that at the same time may increase the biological risk from other sources, including deliberate and accidental release. Table 2 summarizes the potential dual-use nature of research across pandemic response and preparedness efforts. Assessing pandemic preparedness research for associated risks should be of particular importance during the coming years, given increased funding for necessary efforts to prevent future pandemics as well as potentially heightened interest in weaponizing viruses by malicious actors, inspired by the havoc caused by the COVID-19 pandemic.

A CHANGING LANDSCAPE FOR DURC REVIEW

Changes to how scientific information is disseminated also pose new challenges for managing dual-use risks. From the rapid sharing of the SARS-CoV-2 genome by Chinese researchers (45) to the internationally coordinated vaccine development process, the swift dissemination of knowledge has been a cornerstone of the groundbreaking scientific advances since the beginning of the pandemic. Although this spread of information has been vital for efforts to curtail global outbreaks, the emergency conditions of the pandemic pose distinct challenges from the perspective of managing any emerging dual-use research of concern.

Though dual-use concerns are ideally identified earlier in the research life cycle, in practice many concerns arise or are made apparent when insights are codified for wider release via publication. Only a minority of life science research journals have written policies for assessing dual-use risks (46–48), but the role of journal review has featured prominently in historical controversies over DURC. In cases involving the reconstruction of the 1918 pandemic influenza virus (49), GOF research on avian influenza A/H5N1 (50–52) and A/H7N1 (53, 54) viruses, and the synthesis of horsepox virus (39, 55, 56), editors, journal DURC committees, and external bodies such as the U.S. National Science Advisory Board for Biosecurity (NSABB) ultimately decided in favor of publication of the manuscripts in question. In contrast, the *Journal of Infectious Diseases* decided in 2014 to redact information on key gene sequences from two manuscripts on the molecular characterization of a novel *Clostridium botulinum* toxin, following consultation between editors, authors, and various U.S. government agencies (57, 58), while another journal previously rejected manuscripts on smallpox and anthrax out of security concerns (59). Irrespective of each specific outcome, the discussions around these cases have emphasized the role of journal review in biosecurity. However, recent developments in publication practices as well as the unique circumstances of public health emergencies pose distinct challenges for this approach to managing dual-use risks.

One such challenge relates to the use of preprint servers such as bioRxiv, medRxiv, and SSRN, which has been steadily increasing in recent years and surged as the COVID-19 pandemic unfolded. Clearly, preprint publishing provides many benefits, including the rapid dissemination, evaluation, and discussion of academic work; open-access research; the facilitation of interdisciplinary collaborations; and benefits for early-career researchers (60–62). However, the discussion around preprints has primarily focused on scientific integrity (63), and scant attention has been given to the implications of preprint publishing for research with dual-use potential (64). While the effectiveness of

TABLE 2 Pandemic response and preparedness research related to SARS-CoV-2 associated with dual-use potential

Work	Proposed benefits	Potential risks	Reference(s)
Identification of mutations that make SARS-CoV-2 more transmissible, virulent, and immune evasive	Informing genomic surveillance and countermeasure design such as vaccines or monoclonal antibodies	May enable engineering of more concerning variants of SARS-CoV-2 or other viruses	Starr et al. (2021) (16)
Publication of detailed SARS-CoV-2 engineering protocols	Increased access to recombinant SARS-CoV-2 for response research	May inform malicious or careless actors on how to create SARS-CoV-2 variants	Xie et al. (2021) (20)
Engineering immune evasion for viral vectors	Improve effectiveness and reusability of viral vector vaccines	Can create transferable insights on engineering immune evasion for pathogens	Sandbrink and Koblentz (2021) (23), Roberts et al. (2006) (25)
Creation of transmissible vaccines	Use for vaccination of animal reservoirs for eradication of zoonotic viruses at risk of spillover	Safety risks; ethical and ecological concerns; may create insights on engineering transmissibility, genetic stability, and immune evasion	Nuismer et al. (2018) (31), Nuismer and Bull (2020) (30), Sandbrink et al. (2021) (32)
Increased gain-of-function work on future potential pandemic pathogens, not limited to coronaviruses	Prediction of zoonotic epidemics, possibility to inform biosurveillance targeting, and design of countermeasures	Risk of accidental exposure and lab release of engineered pathogens; risk of informing the creation of pathogens with enhanced lethality and transmissibility	Herfst et al. (2012) (34), Imai et al. (2012) (35), Casadevall and Imperiale (2014) (74)
Large-scale viral collection and characterization	Prediction of zoonotic epidemics, possibility to inform biosurveillance targeting, and design of countermeasures	Risk of accidental exposure and release; risk of informing viral engineering by creating large-scale data sets connecting sequence and function	Carroll et al. (2018) (40), Monrad and Katz (2020) (41), Carlson et al. (2021) (42)

any peer review, with or without guidance, to reliably identify and resolve dual-use risks remains uncertain, preprint publishing removes a safeguard against the dissemination of potential biosecurity information hazards that cannot be redacted once published on public servers. Therefore, scientists who choose to publish research with dual-use implications must assume a greater responsibility for reviewing the benefits and risks of their work before publication, including consulting with appropriate experts and authorities, and take measures as relevant to minimize the information hazards posed by their research.

Even when manuscripts are not posted to preprint servers, a public health emergency could influence the extent of scrutiny for dual-use risks, either due to accelerated review (65) or because the presence of a significant health threat—rather than a hypothetical or minor one—leads to a higher tolerance for potential risks than under usual circumstances. Consequently, it is critical that scientific journals and external committees are equipped to evaluate dual-use considerations swiftly and in a way that considers how the risks posed by some information hazards may persist longer than any given public health emergency (38).

THE PATH FORWARD

To safeguard global pandemic response and preparedness efforts, we need to proactively address dual-use risks. Certain elements of a pandemic response, such as the publication of detailed protocols or insights on immune evasion engineering, bear dual-use potential and may increase the risk from deliberate biological events for the foreseeable future alongside accidents in the near term. Therefore, despite the importance of a fast pandemic response, scientists, funders, and publishers should not blindly conduct or publish any and all research that might help with these efforts but still pause and examine individual approaches for risks and benefits. Importantly, deliberative frameworks must be established and incorporated in the life science research cycle now, so as to avoid becoming an unwelcome burden during the next public health emergency and as the life science enterprise grows. Moreover, steps must be taken to ensure that established guidance has the intended effects on shaping scientific efforts. Specifically, it is vital that implementation of the guidelines is continually evaluated in terms of whether the assumptions embedded in their design hold true in practice, including whether they are correctly interpreted and adhered to by laboratory scientists and where ambiguities arise. Realizing the full potential of dual-use policies requires a strong feedback loop between implementation, evaluation, and review (12, 13).

Pandemic preparedness efforts directed at mitigating risks from different sources of biological risks may interfere with each other (66). For instance, large-scale collection of viruses, GOF experiments, and research into acquisition of human transmissibility that is conducted to assess the risk of zoonotic spillovers may increase the pandemic risk from accidental or deliberate releases (67). Consequences of actions by individuals in this space may have global repercussions, necessitating a global dialogue on how to manage tradeoffs from different lines of preparedness. Key drivers of such a global dialogue should be international organizations and scientific bodies including the World Health Organization, the Biological Weapons Convention, and the InterAcademy Partnership. Moreover, commercial, philanthropic, and public funders will need to play a more active role in incentivizing researchers to consider dual-use tradeoffs. To withstand the test of time and future emergencies, such evaluation must consider dual-use risks beyond lists of specific pathogens and existing technologies (68).

The changing landscape for how scientific information is disseminated necessitates a modern approach to managing dual-use research. The growing role of preprint publishing accentuates the disadvantage of relying exclusively on the academic review stage as a filter for biosecurity risks and the importance of evaluating research early on and throughout its life cycle (56, 69). Enabling stakeholders to manage dual-use concerns in a rapidly evolving landscape will require strategies and incentives to increase

transparency, information sharing, and education about risk management (70). At the same time, scientific journals continue to have a critical role in shaping norms and incentives in the life sciences, as research typically receives considerably more attention once it is published in prestigious outlets. Consequently, more publishers should follow the example of pioneering journals in the field that already have robust policies for dual-use review (68). Successful efforts from academic journals will also influence the norms governing preprint servers, which could advance innovative practices. At the minimum, these may include providing guidance and conditions for submission of manuscripts including attesting to and disclosing reviews and moving toward implementing screening for biosecurity and biosafety risks in submitted manuscripts where needed. Given that a few prominent servers host the majority of life science preprints, such screening may be a high-leverage avenue for identifying and mitigating potentially concerning research.

Adequately addressing dual-use risks will require updating assessment frameworks, strengthening oversight of life science research from proposal to publication, educating scientists and other stakeholders who shape the scientific landscape about the importance of this topic, and further developing a culture of responsible science (71). The biosecurity community should also recognize that dual-use oversight is not just a scientific and technical matter but also has political and social dimensions, which must be taken into account when designing processes and systems designed to address dual-use concerns (72). Many of the assumptions underlying the effectiveness of our governance strategies for risk management remain untested, and despite calls for applied biosafety and biosecurity research, this work has received little support (9). In particular the social sciences can make an important contribution to designing institutions necessary to monitor, evaluate, and learn from dual-use governance measures (11). Moreover, oversight is only part of what must be a more comprehensive approach that addresses incentives for proactive risk management—including rewarding innovations and highlighting best practices and champions (73). COVID-19 continues to demonstrate the grave costs of pandemic events and that we cannot afford to wait to address dual-use risks until an inevitable, avoidable disaster strikes. The aftermath of this pandemic is an opportunity to proactively increase preparedness for a wide range of potential global catastrophic biological risks.

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From: b6 [b6]
Sent: 11/22/2021 12:23:41 PM
To: William B. Karesh [b6]
CC: Catherine Machalaba [b6]; Daniel Mira-Salama [b6]
BCC: Morens, David (NIH/NIAID) [E] [b6]
b6]
Subject: Re: figure for World Bank report
Attachments: PastedGraphic-1.tiff

PS, you might be able to get Cell to let you use it for free, as it is for a good cause, a non profit entity, and is good advertising for Cell. d

Sent from my iPhone
David M Morens
OD, NIAID, NIH

On Nov 22, 2021, at 07:21, Morens, David (NIH/NIAID) [E] b6 wrote:

Billy, this map was reconstructed from our original by the graphics department at the journal Cell. They did this purely so they could copyright it.

You could contact Cell, abd they will charge you. Or else we can give you the original with you can have for free. The original has all the same info and the same color code, but is less spread out vertically and differs in other minor ways

Let me know. My best to Peter and the gang. David

Sent from my iPhone
David M Morens
OD, NIAID, NIH

On Nov 22, 2021, at 06:46, William B. Karesh b6 wrote:

Dear David,

Hope this finds you well.

We are in the final stages of printer's proofs of a report on EID's in Asia we did for the World Bank. We want to include your EID map from 2020 (attached), but the printer's tell us that our version is not high enough resolution. Would you happen to have high resolution version that could be used?

Hope you have a great Thanksgiving, all the best,

Billy

William B. Karesh, D.V.M
Executive Vice President for Health and Policy

EcoHealth Alliance
520 Eighth Avenue, Suite 1200
New York, NY 10018 USA

+ b6 (direct)
+1.212.380.4465 (fax)
www.ecohealthalliance.org

President, OIE Working Group on Wildlife

Co-chair, IUCN Species Survival Commission - Wildlife Health Specialist Group

EcoHealth Alliance develops science-based solutions to prevent pandemics and promote conservation.

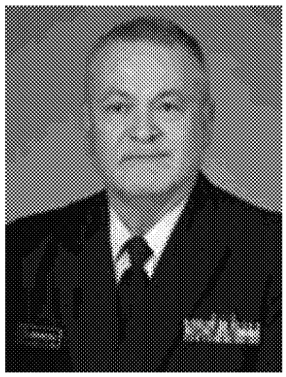
From: Morens, David (NIH/NIAID) [E] [b6 b6]
Sent: 7/9/2021 8:53:04 PM
To: Keusch, Gerald T [b6]; Peter Daszak [b6]
Subject: RE: Politico: POLITICO-Harvard poll: Most Americans believe Covid leaked from lab

In my experience these folks are bean counters but they know honest people when they see them. They don't go nuts over minor issues, which evberyone has. Not to worry…..

David

David M. Morens, M.D.
CAPT, United States Public Health Service
Senior Advisor to the Director
Office of the Director
National Institute of Allergy and Infectious Diseases
National Institutes of Health
Building 31, Room 7A-03
31 Center Drive, MSC 2520
Bethesda, MD 20892-2520

☎ b6 (assistant: Whitney Robinson)
301 496 4409
b6



From: Keusch, Gerald T [b6]
Sent: Friday, July 9, 2021 4:05 PM

To: Peter Daszak [b6]; Morens, David (NIH/NIAID) [E] [b6]
Subject: RE: Politico: POLITICO-Harvard poll: Most Americans believe Covid leaked from lab

There is only one response, bite your tongue and comply with their inspection.

Gerald T. Keusch, M.D.
Professor of Medicine
Associate Director
National Emerging Infectious Diseases Laboratory
Boston University, Boston MA 02118

From: Peter Daszak [b6]
Sent: Friday, July 9, 2021 12:19 PM
To: Morens, David (NIH/NIAID) [E] [b6]; Keusch, Gerald T [b6]
Subject: RE: Politico: POLITICO-Harvard poll: Most Americans believe Covid leaked from lab

By the way – we got our notice from the HHS Office of the Inspector-General today that they're going to audit us.

I'm not worried, we've done nothing wrong, but this is upsetting and a major waste of our time and of taxpayer funds.

Advice welcome, of course…

Cheers,

Peter

Peter Daszak
President

EcoHealth Alliance
520 Eighth Avenue, Suite 1200
New York, NY 10018-6507
USA

Tel.: [b6]
Website: www.ecohealthalliance.org
Twitter: @PeterDaszak

EcoHealth Alliance develops science-based solutions to prevent pandemics and promote conservation

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From: Morens, David (NIH/NIAID) [E] [b6]
Sent: Friday, July 9, 2021 10:32 AM
To: Peter Daszak ([b6]) [b6]; Keusch, Jerry ([b6])

b6

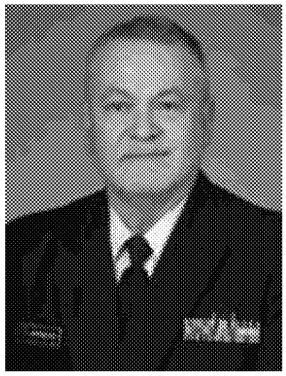
Subject: FW: Politico: POLITICO-Harvard poll: Most Americans believe Covid leaked from lab

Sad….. Most small children believe in Santa Claus….. Not so sad….

David

David M. Morens, M.D.
CAPT, United States Public Health Service
Senior Advisor to the Director
Office of the Director
National Institute of Allergy and Infectious Diseases
National Institutes of Health
Building 31, Room 7A-03
31 Center Drive, MSC 2520
Bethesda, MD 20892-2520

☎ b6 (assistant: Whitney Robinson)
301 496 4409
b6



From: Folkers, Greg (NIH/NIAID) [E] b6
Sent: Friday, July 9, 2021 8:52 AM
Subject: Politico: POLITICO-Harvard poll: Most Americans believe Covid leaked from lab

POLITICO-Harvard poll: Most Americans believe Covid leaked from lab

Opinion on the lab leak scenario, once seen as a fringe theory, has shifted dramatically.

By ALICE MIRANDA OLLSTEIN
07/09/2021 06:00 AM EDT

Most Americans now believe that the coronavirus leaked from a laboratory in China, according to a new POLITICO-Harvard poll that found a dramatic shift in public perception of Covid-19's origins over the last year.

U.S. adults were almost twice as likely to say the virus was the result of a lab leak in China than human contact with an infected animal, which many scientists believe is the most likely scenario. The poll's findings show what was once a fringe belief held mainly among some on the political right has become accepted by most Republicans, as well as most Democrats, amid heightened scrutiny of the lab leak theory.

In March 2020, a Pew Research Center poll found 29 percent of Americans believed the virus was made in a Chinese lab and released either accidentally or intentionally. The new survey shows 52 percent believe the virus came out of a lab, including 59 percent of Republicans and 52 percent of Democrats, while 28 percent said it was from an infected animal.

The absence of a large partisan gap on the issue is particularly striking, said Bob Blendon, a professor of health policy and political analysis at the Harvard T.H. Chan School of Public Health who designed the poll.

"Usually, our polls find a big split between Republicans and Democrats, so this is unique," he said. "More conservative media have been carrying the 'lab leak' issue, and it's been a Trump talking point from the beginning, so we expected people who lean Democratic would say either 'It's not true' or 'I don't know.' But the belief is bipartisan."

Blendon said Democrats likely became more receptive to the idea after President Joe Biden's recent order that intelligence agencies investigate the virus' origin and comments from Anthony Fauci, the White House chief medical officer, that it's worth digging into. Fauci and other scientists have cautioned the answer may never be known definitively.

"That the president thought there was enough evidence to ask intelligence agencies to put together a report sends a signal to Democrats that there might be something there," Blendon said.

Democratic lawmakers have also faced pressure to look more closely at the lab leak scenario, though they worry Republicans will stoke uncertainty about the virus origin for political gain. Several congressional committees have launched inquiries, and the House Science Committee plans to hold its first hearing on the issue next week.

The POLITICO-Harvard poll, which will be released next week, also found there's a high level of public interest in investigating Covid-19's origin, with almost two-thirds of Democrats and Republicans calling the issue "extremely" or "very" important. The finding also surprised Blendon, who said the public isn't typically invested in such a scientific inquiry.

The broad attention on the issue underscores the stakes for the Biden administration's upcoming report on the virus origin, due in August. Even if the report concludes the virus came from nature, it could be hard to move public opinion, lawmakers and researchers like Blendon have noted.

The poll surveyed 1,009 adults from June 22-27. The margin of error was plus or minus 3.8 percentage points.

compliance and other essential capabilities. Mimecast helps protect large and small organizations from malicious activity, human error and technology failure; and to lead the movement toward building a more resilient world. To find out more, visit our website.

From: Wang Linfa [b6]
Sent: 9/18/2021 3:56:48 PM
To: Morens, David (NIH/NIAID) [E] [b6]; Peter Daszak [b6]; Edward Holmes [b6]; Jason Gale [j.gale@bloomberg.net]
CC: Stephen Goldstein [b6]; [b6]; Garry, Robert F [b6]; [b6]; [b6]; [b6]; Robert Kessler [b6]; David Morens [b6]; [b6]
Subject: RE: Study from 2007 shows SARS-infected civets on farms in Hubei

Game changer, dynamite and …. basically we (the international scientific community) have now found the natural/bat origin of "the functional core of SARS-CoV-2". As we all know, RBD is the key for sarbecovirus to infect human.

Just to put this in perspective: after 18 years of intensive searching, we still have NOT found the bat origin of "the functional core of SARS-CoV-1". The closest we had was WIV1 which has 10 aa difference from SARS-CoV-1 in the RBD region. Here we have a bat sarbecovirus RBD which has only 1 aa difference and that change has NO impact on its ability to bind human ACE2. I am completely amazed with the rapid progress of the research ….. and it proved what we have been saying all along: pay more attention to SE Asia. There are more bats there, but with much less surveillance intensity than Southern China!

Case closed as far as I am concerned! Good night (morning) to all….

Linfa (Lin-Fa) WANG, PhD FTSE FAAM
Professor
Programme in Emerging Infectious Disease
Duke-NUS Medical School,
8 College Road, Singapore 169857
Tel: b6

From: Morens, David (NIH/NIAID) [E] b6
Sent: Saturday, 18 September 2021 11:44 PM
To: Peter Daszak b6; Wang Linfa b6; Edward Holmes b6; Jason Gale <j.gale@bloomberg.net>
Cc: Stephen Goldstein b6; Garry, Robert F b6; b6; Robert Kessler b6; David Morens b6
Subject: RE: Study from 2007 shows SARS-infected civets on farms in Hubei

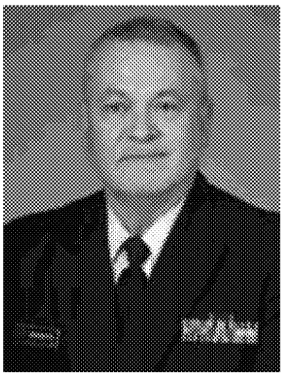
- External Email -

Yes, this is dynamite,. and all the more reason that more work needs to be done to characterize the bat sarbecovirus "universe" all over the region.

David

David M. Morens, M.D.
CAPT, United States Public Health Service
Senior Advisor to the Director
Office of the Director
National Institute of Allergy and Infectious Diseases
National Institutes of Health
Building 31, Room 7A-03
31 Center Drive, MSC 2520
Bethesda, MD 20892-2520

☎ b6 (assistant: Whitney Robinson)
301 496 4409
b6



From: Peter Daszak b6
Sent: Saturday, September 18, 2021 10:09 AM
To: Wang Linfa b6; Edward Holmes b6; Jason Gale <j.gale@bloomberg.net>
Cc: Stephen Goldstein b6; Garry, Robert F b6; b6; Morens, David (NIH/NIAID) [E] b6; Robert Kessler b6; David Morens b6
Subject: RE: Study from 2007 shows SARS-infected civets on farms in Hubei
Importance: High

Yes – saw that paper Jason – really interesting

I looked through the paper and it's yet another game changer. So far, in the last few weeks/months, we've got the following new evidence supporting emergence via bat-to-intermediate host-to-human origin for COVID-19 (I've probably missed something):

Multiple new, SARS-CoV-2 related CoVs in SE Asia (Cambodia, Thailand, Japan, China etc.). I know of other work in review describing other related viruses in SE Asia also. We're also finding further novel SARS-CoV-2 related bat viruses in Malaysia, Thailand.
New evidence that live animals of the type that carry CoVs were present in the Wuhan markets (including Huanan).
Evidence from other bat SARSr-CoVs that mutations occur where there FCS is found (eg. RmYN02) https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7211627/
a rat alpha-CoV with an FCS in wildlife farms, hotels and train stations in S. China, showing that FCS insertions are more common in nature than previously thought. https://journals.asm.org/doi/epdf/10.1128/JVI.01173-21
Epidemiological analysis of early cases supporting early origin close to Huanan market, not WIV https://www.cell.com/cell/fulltext/S0092-8674(21)00991-0
Phylogenetic analyses suggesting there may have been multiple introductions into the human population, supporting presence of a virus circulating in animals rather than a lab leak (@virology paper)
Our work showing a very large interface for bat SARSr-CoV spillover in a v. densly population region, and potential for large numbers of missing cases each year https://www.medrxiv.org/content/10.1101/2021.09.09.21263359v1
This paper showing ACE2 binding for bat SARS-CoV-2 related CoVs. https://www.researchsquare.com/article/rs-871965/v1

On the lab leak side, we have convoluted accusations based on interpretations of intent about how Chinese scientists submitted genomes, wrote the papers, or how me and other scientists had collaborations with Chinese scientists. But, as far as new evidence goes, I could only find this:

- None

Of course, the momentum on the lab leak side will continue, with books by Sharri Markison, Alina Chan/Matt Ridley, Op Eds that criticize scientists, 70+ FoIAs by one organization alone, many other FoIAs on their way, 900 pages of FoIA'd grants and reports from EHA/NIAID showing zero evidence of lab leak.

This rate of research even in a pandemic is remarkable and suggests that we'll pretty quickly have such overwhelming evidence for the 'natural' origins that most people will move on from the lab leak.

(Off-the-record) However, the damage they leave behind is already horrific and will be worse by the time they decide to find another issue to focus on.

Cheers,

Peter

Peter Daszak
President

EcoHealth Alliance
520 Eighth Avenue, Suite 1200
New York, NY 10018-6507
USA

Tel.: b6
Website: www.ecohealthalliance.org
Twitter: @PeterDaszak

EcoHealth Alliance develops science-based solutions to prevent pandemics and promote conservation

From: Wang Linfa b6
Sent: Friday, September 17, 2021 10:56 PM
To: Edward Holmes b6; Jason Gale <j.gale@bloomberg.net>
Cc: Stephen Goldstein b6
b6; Peter Daszak b6;
b6
Subject: RE: Study from 2007 shows SARS-infected civets on farms in Hubei

Almost identical SARS-CoV-2 RBD in several bat sarbecoviruses! This is as close as you can get for a natural RBD origin!

Also, the paper concluded that SARS-CoV-2 genome fragments are found in different sarbecoviruses, very similar to the PloS Path paper for SARS-CoV-1.

All we need is to find a sarbecovirus with a furin cleavage site and no more debate on the natural origin of SARS-CoV-2!

Linfa (Lin-Fa) WANG, PhD FTSE FAAM
Professor
Programme in Emerging Infectious Disease
Duke-NUS Medical School,
8 College Road, Singapore 169857
Tel: b6

From: Edward Holmes b6
Sent: Thursday, 16 September 2021 3:31 PM
To: Jason Gale <j.gale@bloomberg.net>
Cc: Stephen Goldstein b6;
b6; Peter Daszak b6;
b6; Wang Linfa b6
Subject: Re: Study from 2007 shows SARS-infected civets on farms in Hubei

[redacted]- External Email -

Dismantles one key argument of the leakers - how could a virus get from Yunnan to Wuhan - in one simple move.

PROFESSOR EDWARD C. HOLMES FAA FRS
ARC Australian Laureate Fellow

THE UNIVERSITY OF SYDNEY
Marie Bashir Institute for Infectious Diseases & Biosecurity,
School of Life & Environmental Sciences and School of Medical Sciences,
The University of Sydney | Sydney | NSW | 2006 | Australia

T
E
b6

On 16 Sep 2021, at 2:26 pm, Jason Gale (BLOOMBERG/ NEWSROOM:) <j.gale@bloomberg.net> wrote:

And there's this:
"The discovery of civet-CoVs in the Hubei province should not be a surprise as SARS-CoV-like viruses were recently found in a bat species in the same province"

From: b6 At: 09/16/21 14:24:33 UTC+10:00
To: Jason Gale (BLOOMBERG/ NEWSROOM:)
Cc: b6,
b6,
Subject: Re: Study from 2007 shows SARS-infected civets on farms in Hubei

Just stumbled across it reading the discussion of another paper honestly. It's been cited since - there are certainly people who remembered it but I did not know of it and clearly had not penetrated the public origins discussion.

Stephen

Sent from my iPhone

On Sep 15, 2021, at 10:22 PM, Jason Gale (BLOOMBERG/ NEWSROOM:) <j.gale@bloomberg.net> wrote:

Well done, Stephen for finding this: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1900161/

Jason Gale, MHlthSec
Senior editor & chief biosecurity correspondent | Bloomberg News
Level 30, 120 Collins St., Melbourne VIC 3000
Tel. (landline) +61-3-9228-8783 | Mobile b6
@jwgale | Linkedin: http://www.linkedin.com/pub/jason-gale/6/249/a56

Disclaimer

From: Edward Holmes [b6]
Sent: 9/18/2021 9:18:02 PM
To: Peter Daszak [b6]
CC: Garry, Robert F [b6]; Wang Linfa [b6]; Jason Gale [j.gale@bloomberg.net]; Stephen Goldstein [b6]; Kristian G. Andersen [b6]; Rasmussen, Angie [b6]; b6; Morens, David (NIH/NIAID) [E] [b6]; Robert Kessler [b6]; David Morens [b6]; b6
Subject: Re: Study from 2007 shows SARS-infected civets on farms in Hubei

Yes, very good summary Peter.

As you note, despite a seemingly endless stream of papers, grants, genome sequences, theses, FOIAs and intelligence reports there is not a single piece of evidence that SC2 was in the lab. The work needed for a virus to escape a lab leaves a footprint, but there is none to be found.

We're in lockdown here in Sydney but as soon as I'm allowed out a fully English "cholesterol heaven" is on the cards.

Cheers,

Eddie

PROFESSOR EDWARD C. HOLMES FAA FRS
ARC Australian Laureate Fellow

THE UNIVERSITY OF SYDNEY
Marie Bashir Institute for Infectious Diseases & Biosecurity,
School of Life & Environmental Sciences and School of Medical Sciences,
The University of Sydney | Sydney | NSW | 2006 | Australia
T
E b6

On 19 Sep 2021, at 2:05 am, Peter Daszak b6 wrote:

I put it all in a twitter thread while drinking coffee in my local diner (Saturday is "full English breakfast" day for me).

https://twitter.com/peterdaszak/status/1439236376776658945?s=21

No doubt ill be attacked by multiple lab leak aficionados but so be it - at least eddie, Garry and Kristian won't see. The horrors of that…

Cheers,

Peter

Peter Daszak
(Sent from my iPhone)

President
EcoHealth Alliance

460 West 34th Street, New York, NY10001, USA

www.EcoHealthAlliance.org

On Sep 18, 2021, at 10:26 AM, Garry, Robert F b6 wrote:

> Of course, the momentum on the lab leak side will continue, with books by Sharri Markison, Alina Chan/Matt Ridley, Op Eds that criticize scientists, 70+ FoIAs by one organization alone, many other FoIAs on their way, 900 pages of FoIA'd grants and reports from EHA/NIAID showing zero evidence of lab leak.

From: Taubenberger, Jeffery (NIH/NIAID) [E] [b6 b6]
Sent: 3/19/2020 5:06:46 PM
To: Howard Markel [b6]; Peter Daszak [b6]; Morens, David (NIH/NIAID) [E] [b6 b6]
CC: Taubenberger, Jeffery (NIH/NIAID) [E] [b6 b6]
Subject: Pandemic history manuscript, tracked
Attachments: HMPANDEMIC COVID draft 03 19 20 PD comments JKT.docx

Hi guys,

I did a read through with some additional tracked changes and saved a new version here. With tracked comments from Peter, Howard, and me, it is looking a bit messy. David, do you want to have the next go at it? It might be easiest to make an accepted version for the next round of edits.

We have all suggested references which are great. It will be easy to add those with endnote when we get to a closer to final draft. I am working from home today and do not have access to my endnote library.

Thanks all,

Jeff

PANDEMIC COVID-19 JOINS HISTORY'S PANDEMIC PANTHEON

Since ~~January~~December 201920, the world has watched the slow-motion birth of a new pandemic disease, Cov-Vid-19. As in Albert Camus' *The Plague*, the familiar rhythms of our very real lives have been shaken by an unfamiliar existential threat. Rising death and case numbers have changed every aspect of our work, school, recreation, travel, economic well-being, and interactions with friends and family.

Yet, oOurs is hardly the only era to face such tribulations. Deadly pandemics and large-scale epidemics have challenged human existence throughout history ~~Since January 2020, the world has watched the nightmarish slow-motion birth of a new pandemic disease. Life's familiar rhythms are suddenly being shaken by an unfamiliar existential threat. Escalating death counts force rethinking of~~us to ~~rethink every aspect of daily life: work, school, recreation, travel, economic well-being, relationships with friends and family. It is lucky, we think, that previous generations were spared such 21st century cataclysms.~~

~~But previous generations were not spared~~they were not. ~~Fatal pandemics and large-scale epidemics have challenged human existence throughout recorded history, and likely beforehand~~ [1]. ~~Some of them killed large percentages of humanity~~ (Table). ~~The Black Death is thought to have killed up to 25% of the European population, and smallpox around 50% of Aztec communities, and almost complete extinction of some tribal groups (e.g. in Tierra del Fuego). Though pandemics~~

Commented [PD1]: Added this to make up for deletion further down in section on "Early Pandemic History"

Commented [PD2]: In the text we say 'large percentages' – could we put in some figures here. Black death was around 25% of European population if I remember rightly

YEAR	NAME	DEATHS	
430 BCE	"Plague of Athens"	~ 100,000	First identified trans-regional pandemic
541	Justinian plague (*Yersinia pestis*)	30-50 million	Pandemic; killed half of world population
1340s	"Black Death" (*Yersinia pestis*)	~ 50 million (25%)	Pandemic; killed at least a quarter of world population
1494	Syphilis (*Treponema pallidum*)	>50,000	
c. 1500	Tuberculosis	High millions	Ancient disease; became pandemic in Middle Ages
1520	*Hueyzahuatl* (*Variola major*)	3.5 million (50%)	Pandemic brought to New World by Europeans
1793-1798	"The American plague"	~ 25,000	Yellow fever terrorized colonial America
1832	2nd cholera pandemic (Paris)	18,402	Spread from India to Europe/Western Hemisphere
1918	"Spanish" influenza	~ 50 million	Led to additional pandemics in 1957, 1968, 2009
1976-2020	Ebola	15,258	First recognized in 1976; 29 regional epidemics to 2020
1981	Acute hemorrhagic conjunctivitis	rare deaths	First recognized in 1969; pandemic in 1981
1981	HIV/AIDS	~ 32 million	First recognized 1981; ongoing pandemic

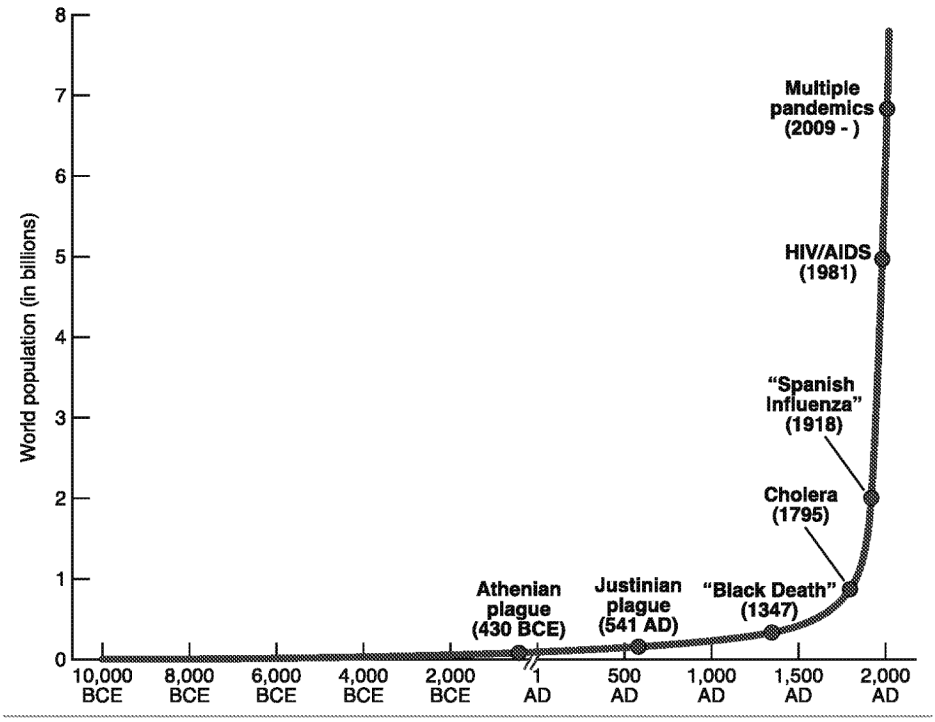
2002	**SARS**	**774**	**Near-pandemic**
2009	**H1N1 "swine flu"**	**284,000**	**5th influenza pandemic of the century**
2014	**Chikungunya**	**uncommon**	**Pandemic, mosquito-borne**
2015	**Zika**	**~ 1,000?***	**Pandemic, mosquito-borne**

Table. Some notable pandemic and epidemic diseases. For most historical pandemics, estimated deaths have varied widely, and figures cannot be considered accurate.

*Zika deaths occur mostly *in utero* or in newborns; death in older children and adults is extremely rare.

While these crises were once separated by centuries, or at least many decades, they are now becoming much more common. Since 2003 we have experienced SARS, an influenza pandemic (H1N1pdm in 2009), a chikungunya pandemic (2014), a Zika pandemic (2015), and widespread pandemic-like extension of Ebola over five African countries, with cases exported globally (2014-2015). We now live in an era of pandemics, newly emerging infectious diseases and the return of old contagious foes.~~were once separated by centuries, they are now becoming much more common. Since 2009 we have experienced an influenza pandemic (H1N1pdm in 2009), a chikungunya pandemic (2014), a Zika pandemic (2015), and widespread pandemic-like extension of Ebola over five African countries, with cases exported globally (2014-2015). We have entered a new pandemic era, in which increasingly frequent emergence emergences of unfamiliar deadly diseases may well become the new normal.~~

Commented [PD3]: Just trying to reduce the use of the word "emergences" which is a bit grammatically awkward



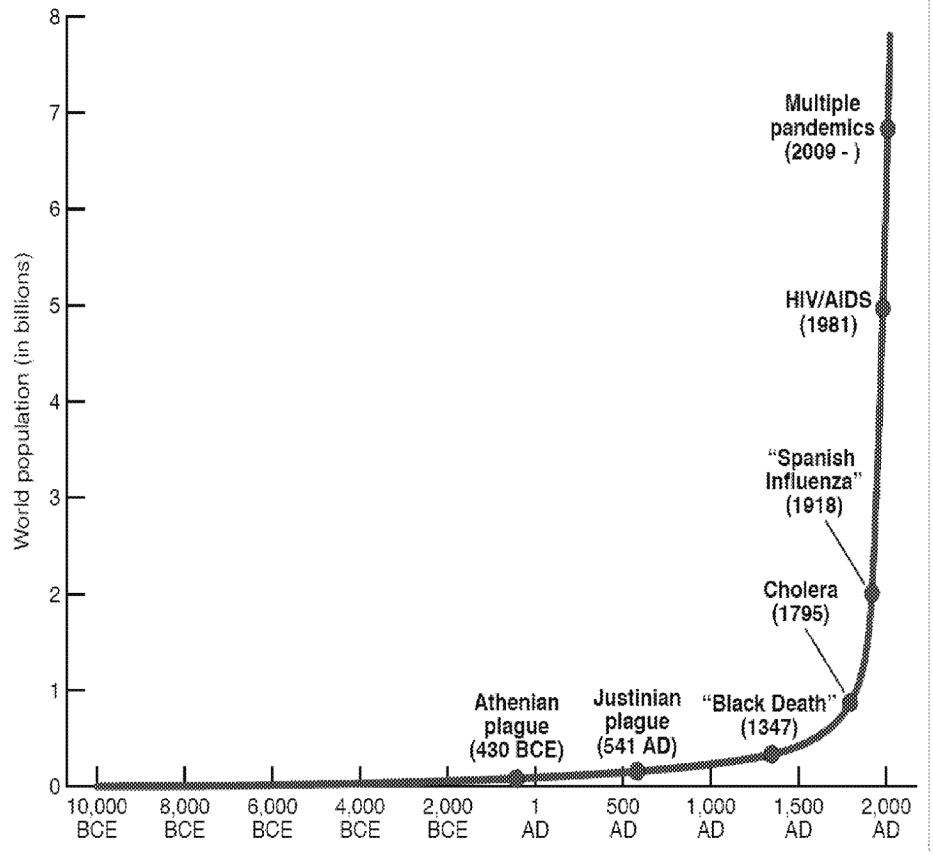


Figure 1. Estimated world population and selected known pandemics/widespread disease emergences, from 10,000 BCE – 2020 AD.

Early Pandemic History. Around 12,000 years ago, small family/clan groups of humans abandoned nomadic hunting-gathering to settle down in stable locations, cultivating crops and raising domestic animals for food, labor, and clothing (the neolithic revolution). For the first time, humans and newly domesticated animals were living together in complicated ecosystems of villages, towns and cities. Under conditions of intense human-animal proximity and environmental

alterations, enzootic and zoonotic diseases appeared. The agents of measles, smallpox, tuberculosis, gastric cancer-causing *Helicobacter pylori*, and many other future pandemic diseases evolved from animal pathogens that host-switched to become human infectious agents. As human populations continued to expand, these agents were able to initiate epidemics and pandemics (Figure 1). Some of the biblical plagues were probably emerging infectious diseases. The preserved mummy of Pharaoh Usermaatre Sekheperenre Ramesses V clearly shows smallpox lesions (Figure 2), indicating that fatal smallpox epidemics prevailed more than 3,000 years ago [2]. At some point ~~in the distant past~~, smallpox spread

Commented [PD4]: I'd insert a reference to a paper that goes into some detail on this: Dobson, A. P. & Carper, E. R. Infectious diseases and human population history. Biosci. 46: 115-126 (1996)

A BETTER SOURCE WOULD BE MCNEILL'S PLAGUES AND PEOPLE [HM]

Commented [TJ([5]: Replaced here with new version

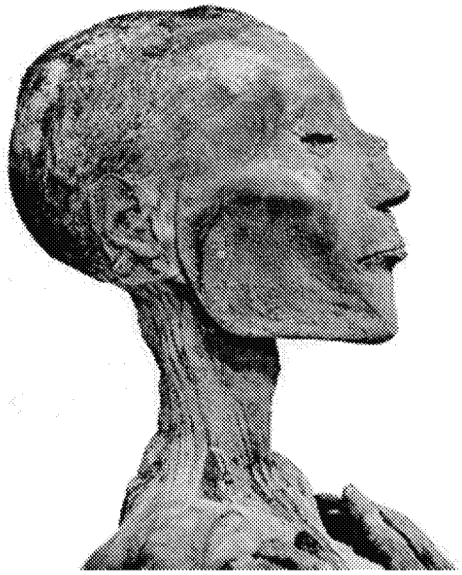


Figure 2. Mummy of Pharaoh Usermaatre Sekheperenre Ramesses V (c. 1196-1145 BCE), showing smallpox lesions, e.g., on the bridge of the nose.

pandemically over most of the world, sparing the Western Hemisphere for millennia, up to the 16th century ~~AD~~with the first known outbreak there in 1520. ~~[does this mean the first western hemisphere pandemic was in 16th c? if so give year!]~~

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Heralding the end of Greece's "Golden Age", the explosive "Plague of Athens" (430-425 BCE) was perhaps the first ~~scientifically~~ recorded pandemic: it spread over much of the world known to the Greeks, including the Mediterranean and Africa [3]. Although the cause of the Athenian plague has not been identified (anthrax, bubonic/ pneumonic plague, smallpox, and typhus are leading candidates), it was the first disease investigated and described using clinical and epidemiological approaches. It remains today a benchmark for pandemic comparisons.

S~~Over the millennia s~~ince the Athenian plague, there has been a steady stream of new pandemics of even greater ~~deadliness~~ mortality (Table; reference 1). Confronting them, only to quickly forget the lessons they left behind, has become a recurring theme in human existence. ~~We may imagine that today's pandemics are new and unprecedented, but~~ The repetitive nature of our struggles to combat these diseases is illustrated in countless history books and plague tractates ~~tell us that our forebears have been struggling against them for thousands of years~~with sometimes striking similarities in strategies across the centuries (Figure 3). ~~Undoubtedly, pandemics have been challenging the existence of the human species since long before there were written records that survived to today.~~

Commented [PD6]: may be semantics, but 'deadliness' could be interpreted by the reader to mean that pandemic pathogens have become more lethal over time, but what you're really saying is that pandemics have caused greater mortality over time.

Commented [PD7]: Added a comment in the first para to this effect

Commented [PD8]: Some phrases in section basically repeat the first couple of paras, so have suggested modifications.

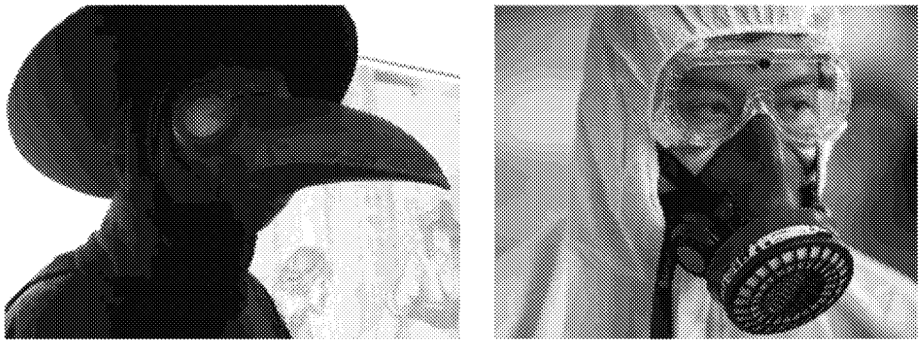

Figure 3. Fighting "plagues" in 1665 (caused by bubonic/pneumonic *Yersinia pestis*) and in 2020 (caused by SARS-CoV-2).

What is a pandemic? "Pandemic" has never been a scientific term, but rather a subjective popular term. In usage since the mid-1600s, the word "pandemic" (or "pandemick") was at first so imprecise that it could mean different, even contradictory things in different contexts [4]. At its most specific, it conveyed the vague notion of an impressively large epidemic and its Greek roots, "pan"—all—and "demos"—people, reflect their widespread nature. "Epidemic" is often translated from the Greek as "that which is upon the people", i.e., a highly incident or widely prevalent ~~condition~~condition, and usually one that has a rapid temporal and geographical spread. Following the sudden emergence of global influenza in 1889, the term "pandemic" acquired, and as of today retains, the narrower meaning of a disease "…occurring widely throughout a region, country, continent, or globally" [4]. "Pandemic" has also been sub-categorized into trans-regional (widespread within a continent or other large region), inter-regional (involving two or more regions), and global [5]. In practice, "pandemic" and "epidemic" are most often applied to infectious diseases, largely replacing such historical terms for emerging infections as *loimos*, *peste*, pestilence, and plague (in situations where "plague" is used generically, rather than in specific reference to bubonic/pneumonic plague caused by *Yersinia pestis*). [CITE Hippocrates, Epidemics, I, II, III]

Commented [PD9]: Isn't there a notion of the rapid temporal nature of the rise in cases – i.e. the percentage of people infected increases rapidly so that it becomes widely prevalent.

What lessons have we learned from this long history of pandemics, and how do they relate to the current situation with COVID-19? ~~Several important aspects should be emphasized.~~

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1. **Human beings are the ultimate causes of pandemics**. Pandemics are caused by specific organisms, but these same organisms, or their ancestors, have almost always been around us for millennia without causing pandemic harm. As noted above, it was the historical congregation of humans and domestic animals in villages and cities that provided the opportunity for ancestral organisms to host-switch to humans and cause human smallpox, measles, and other diseases. While these originated in wild animals that we then domesticated, our growing ecological footprint is currently leading to an exponential rise in the spillover of other microbes directly from wildlife to people. ~~But it is not just human/animal proximity, crowding, and movement that creates fertile soil for pandemics, it is also human-initiated environmental stresses and changes to the balance of ecosystems in which~~

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Commented [PD10]: I inserted 'almost' because some are truly novel and caused directly by our influence, e.g. some drug-resistant microbes (even though many already circulate in wildlife and other animals).

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Commented [PD11]: Best ref probably Jones, K. E., Patel, N., Levy, M., Storeygard, A., Balk, D., Gittleman, J. L. & Daszak, P. Global trends in emerging infectious diseases. Nature 451: 990-993 (2008)

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~~they live.~~ Deforestation, ~~building~~agricultural intensification, urbanization and ~~, and land management~~ ecosystem disruption bring people into contact with wildlife and their potentially zoonotic pathogens. These activities have led to emerging diseases as diverse as hemorrhagic fevers, Nipah infection, and Zika [6-8]. Since 1999, China's numerous live animal markets have led to three important epidemics and now one pandemic: ~~emergences~~ the emergence of deadly "bird flu" associated with ~~the~~ poultry-adapted influenza A viruses known as H5N1 and H7N9 have killed over a thousand people; SARS killed 774, and came close to causing a global pandemic in 2003; and now in 2019-2020 the SARS-like SARS-CoV-2 is causing our newest pandemic, COVID-19. One seemingly simple human behavior – establishment of multiple large live animal markets in ~~one~~ a populous ~~country~~ region – has within two decades caused the emergence of four fatal zoonotic diseases ~~emergences~~, including one barely-prevented near-pandemic, and one we have clearly failed to prevent~~nt, and which is now spreading globally~~.

2. **When people travel, germs travel [9]; when germs travel pandemics become possible.** Beginning around 1320, the "Black Death" followed trade routes from what is now Mongolia and China, across Asia, and into Europe (1347-1348). Likewise, cholera spread along travel routes from India to Europe in 1831-33, 1845, 1866 and 1892; its approach was reported in the media in "real time", forcing the realization, even without a concept of microbial infection, that cholera advanced exactly as fast as human travel. HIV is believed to have emerged at some time between 1880 and ~~-~~1920, but it only became pandemic in 1981 when population size had expanded, human movement had become more geographically extensive, and complex facilitative human behaviors had been more fully developed, e.g., trans-national road building and truck routes, leading to travel-related prostitution, and affordable international air travel. The 1889-1893 influenza pandemic was the first to have its progression 'tracked' in real time, spreading east to west from Asia and quickly reaching almost every region of the globe. The 1918-1919 influenza pandemic, which stands as the most fatal single event in human history, killed an estimated 50 million. The place of origin of the 1918 virus is obscure and

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Commented [PD12]: I think that sounds a bit too focused on China, when the truth is the wildlife trade is just as intense and diverse in countries like Laos, Vietnam, Cambodia, and others.

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Commented [PD13]: That's redundant because pandemics by nature has spread 'globally'

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there is little evidence of directionality of spread other than chaotic global multi-directionality. The 1957-1958 and 1968-1969 influenza pandemics followed the pattern of appearance in Southeast Asia with subsequent global spread, while the 2009 influenza pandemic originated in Mexico before spreading globally. The 1957, 1968, and 2009 pandemics were all genetic descendants of the 1918 influenza, such that we are still in the 1918 'pandemic era' today.

~~ADD 1-2 LINES ABOUT 1899 AND 1918, 1957, 1968 FLU PANDEMICS?~~The *Aedes aegypti*-borne diseases (yellow fever, dengue, chikungunya and Zika) are all associated with human crowding/imperfect sanitation, peri-domestic water storage, exportation of vector mosquitoes, and human development of novel mosquito breeding sites such as discarded rubber tires. These four arboviral diseases have all exploded in recent decades, the delayed result of emergence and adaptation of a single mosquito species in response to water storage behaviors of humans beginning more than 5,000 years ago, and which are being greatly amplified today [10]. The unwitting spread of microbes by humans, a process termed "pathogen pollution", accelerates the geographic spread of emerging diseases and their impact on morbidity and mortality. In a world now dominated by a globalized economy that depends on international travel and trade, it has led to significant economic losses, e.g., $30-50 billion for SARS, and multiple hundreds of billions of dollars for COVID-19.

The reality that humans are the ultimate cause of pandemics is demonstrated most tragically by what historian Alfred Crosby has referred to as the "Columbian Exchange" [11]. After the first voyage of Columbus to the Americas in 1492, syphilis was apparently brought back to Europe; far more devastating consequences quickly followed. Europeans soon brought smallpox, measles, and other unknown diseases to the New World, wiping out millions of native peoples, e.g., the infamous *hueyzahuatl* pandemic of 1520, which killed 3.5 million. During the next several hundred years, all over the Americas, countless millions of native people died from these and other imported diseases. Beginning in the 1700s, the tragedy was extended to the Pacific islands and nations. The near-extinction of native peoples over half of the globe occurred on a scale so massive that it could not be adequately measured. The age of exploration might more appropriately be called the age of global microbial devastation.

Commented [TJ([14]: Refs:
Pandemic influenza--including a risk assessment of **H5N1**.
Taubenberger JK, **Morens** DM.
Rev Sci Tech. 2009 Apr;28(1):187-202.

The persistent legacy of the 1918 influenza virus.
Morens DM, **Taubenberger** JK, **Fauci** AS.
N Engl J Med. 2009 Jul 16;361(3):225-9. doi: 10.1056/NEJMp0904819. Epub 2009 Jun 29. No abstract available. Erratum in: N Engl J Med. 2009 Sep 10;361(11):1123.

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Commented [PD15]: I've got refs if you need them.

Commented [PD16]: Ref. to Jones et al. 2008 (above)

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3. **Expect the unexpected.** ~~No~~ The exact time and place of the origin of a pandemic has never been anticipated; each appears unexpectedly with respect to time, place, and clinical-epidemiologic features. No explosive sexually-transmitted disease had ever been seen in Europe when the syphilis pandemic appeared suddenly in the late 15th century. The horrifying gummatous deformities (Figure 4) and tragic deaths characteristic of the first decades of the pandemic were likewise unprecedented [12]. Four centuries later, the HIV/AIDS pandemic was just as shocking in its ability to cause high fatality and tragic deaths, but this time in association with multiple modes of transmission (e.g., sexual, needle sharing, blood product transfusion, maternal transmission) significantly complicating control efforts. More than a millennium of at least 20 pandemic influenza recurrences (at least one every 57 years, and since 1700 AD,

Figure 4. 1665 Portrait of renowned painter, poet, and public intellectual Gérard de Lairesse (1641-1711), by Rembrandt Harmenszoon van Rijn (1606-1669). Lairesse's facial deformities, causing him to be shunned be some contemporaries, are now thought to have resulted from congenital syphilis.

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Commented [PD17]: I don't think that's completely correct – many of us repeatedly stated that Clade 2b bat-origin SARS-related coronaviruses in China are a likely source of the next pandemic, for example (exactly the nature of SARS-CoV-2)

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Commented [PD18]: But we've shown that pandemics emerge largely from distinct geographic hotspots.

Commented [PD19]: Suggest this sentence instead: "It has not, so far, been possible to predict the exact timing, place of origin, or clinical-epidemiologic features of any of the recent pandemics." This sentence says what you intended, but leaves room for the section I've added on new strategies to predict the geography, host origin, and microbial nature of future pandemics.

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one every 32 years [5]) has surprised us in each instance, in some cases, e.g., 1918, with extraordinary mortality and inexplicable epidemiologic features. Such reactions to the unexpected and frightening have characterized almost all pandemics, including reactions to highly fatal Ebola and the tragic deformities of babies during the Zika pandemic, and our fear and shock at the overwhelming of hospitals by COVID-19. However, science is beginning to provide hope that we can predict some aspects of pandemic emergence, and begin to lower the risk. Tracking past pandemic origins allows us to identify the underlying causes of emerging diseases, and the hotspots where they are most likely to originate, albeit that these are large regions. Analyzing host-virus relationships allows us to identify the wildlife species that carry the highest risk of as-yet undiscovered viruses, and to estimate how many of these there are in wildlife. Analyses of air travel pathways provide real-time data to anticipate the likely spread of novel diseases once they have gained a foothold in the human population. Much remains to be done, but these efforts provide the first approaches to what may become a preventative approach to pandemic emergence. If land use change and agricultural intensification drive their emergence, future programs to reduce human-wildlife contact around these activities may reduce the risk of future pandemics.

Commented [PD20]: Ref to Jones et al. 2008

Commented [PD21]: Ref: Olival, K. J., Hosseini, P. R., Zambrana-Torrelio, C., Ross, N., Bogich, T. L. & Daszak, P. Host and viral traits predict zoonotic spillover from mammals. Nature 546: 646-650 (2017)

Commented [PD22]: Ref: Carroll, D., Daszak, P., Wolfe, N. D., Gao, G. F., Morel, C. M., Morzaria, S., Pablos-Méndez, A., Tomori, O. & Mazet, J. A. The global virome project. Science 359: 872-874 (2018)

Public health and civil organizational management ~~are the most critical first steps~~**are critical to pandemic control**. Even in our modern era of drugs and vaccines, the most important first steps in pandemic control are preventive and educational. Infection-specific drugs and vaccines are rarely available at the outset and may not be available for years. When they become available, stockpiles may be insufficient, especially in the developing world. Moreover, diagnostics may be unavailable or non-specific, and there may be too few medical providers and facilities. An influenza or a COVID-19 pandemic as fatal as the 1918 influenza pandemic, even before adjustment for the significantly older US population age structure [DMM: make this calculation], might require, over a period of 2-3 months, as many as 2-4 million fully staffed ICUs with ventilators, drugs, and supplies. The current US surge capacity is estimated to be about 45,000. Public health efforts — including ~~both organized public health provided by~~those organized by local and State health departments, and ~~public health~~

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Commented [PD23]: To distinguish from the earlier para about prevention.

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Commented [TJ([24]: Perhaps qualify this a bit as estimated at the low end as 45000 ventilators.

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~~actions~~those provided by government, industry, and NGOs [13] — are by far the most critical components of early pandemic responses. These must be greatly strengthened.

4. **What does pandemic history tell us about confronting COVID-19?** Every pandemic is different ~~from every other~~. Roughly 140 weeks into the COVID-19 pandemic (192 March 2020) we remain unsure of what lies ahead. Controlling a pandemic can be compared to dancing with an unpredictable leading partner. Neither where the dance is going, nor the direction of the next leading step, can be known. The trick is to remain alert, flexible, and capable of changing strategy at any moment as the situation itself changes. To complicate matters, the changing situation requires not only good management of uncertainty, but good communication about uncertainty to a confused public.

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That China has been able to achieve at least short-term regional control reminds us of the often-unused potential of public health police power. Yet other countries with sophisticated public health capacity, e.g., Italy, have not had early success at controlling viral spread, and there is growing realization that, as is true for many other respiratory viral diseases, "silent spreading" of SARS-CoV-2 by people who are either pre-symptomatic (incubating), asymptomatic, or with mild or atypical symptoms, may be driving the COVID-19 pandemic [14]. Confronting these dynamics will be of critical importance. Ever since the late 19th century ~~Typhoid Mary scandals of a century ago [15]~~, U.S. and most Western public health experts have recognized that there is usually far more to be gained by fostering public trust than by threatening public health police power, e.g., by forcibly isolating, quarantining, or preventing travel and movement. [CITE: Markel H, Lipman HB, Navarro JA, et al. Nonpharmaceutical Interventions Implemented by US Cities During the 1918-1919 Influenza Pandemic. *JAMA*. 2007;298(6):644–654 AND Markel, H. Quarantine! East European Jewish Immigrants and the New York City Epidemics of 1892 (Baltimore: Johns Hopkins University Press, 1997) Even so, public health control options lie on a continuum from informative/suggestive to coercive; the right balance must always be sought, and can be expected to change as the pandemic progresses. Already, in addition to formal public health efforts, businesses, schools, cultural entities, and

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government agencies are taking public health actions against COVID-19, including temporary or indefinite closures. So far, the US public seems to be moving in step with recommendations of public health, civic, and industry leaders. Personal, private and non-governmental efforts may be definitive. It is critical that such efforts be sustained as the pandemic worsens.

5. **"We must all hang together, or we will all hang separately".** How well we will succeed in mitigating the pandemic of COVID-19 cannot be predicted. But going forward, we must keep an eye on the abundant lessons left us by past pandemics. We must also take note of what is going on in nature all around us. Other species have not been as lucky as we have been so far. Species of bats, bees, and frogs are now being threatened with extinction by pan- and epizootic diseases; we should not imagine that humans will be exempt from natural laws of microbial evolution [16]. The Justinian plague is said to have killed half of humanity. What assurance do we have that something as deadly will not soon appear?

When the COVID-19 pandemic has run its course, whatever the level of devastation it has left in its wake, it will be time to take stock and rethink how we can fix inadequate pandemic defenses. This must be a cooperative global undertaking, because we can expect to be facing pandemic challenges again and again, and global pandemic threats cannot be managed by national responses. In a densely interconnected world of nearly 8 billion humans, we have no choice but to follow Benjamin Franklin's revolutionary advice and hang together for the good of all.

Pandemics are nature's loud wake-up call that we humans are mismanaging our own existence in the complex ecosystem we have recklessly shaped, within which we live, and upon which our survival depends – planet earth. We must not only wake-up, we must now get up with energy and start building a safer future on a healthier planet.

2,293 words

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Commented [PD28]: Two potential references that may be better:

Daszak, P. & Cunningham, A. Extinction by infection. Trends in Ecology & Evolution 14: 279 (1999).

Schloegel, L. M., Hero, J. M., Berger, L., Speare, R., McDonald, K. & Daszak, P. The decline of the sharp-snouted day frog (Taudactylus acutirostris): The first documented case of extinction by infection in a free-ranging wildlife species? Ecohealth 3: 35-40 (2006)

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Commented [PD29]: This alludes to the growing 'Planetary Health' movement, which has some legs (e.g. the new Lancet Planetary Health journal.)

REFERENCES

1. Morens DM, Folkers GK, Fauci AS. Emerging infections: a perpetual challenge. *Lancet Infect Dis* 2008;8:710-719.

2. Hopkins DR. *Princes and Peasants: Smallpox in History*. Chicago: University of Chicago Press, 1983.

3. Morens DM, Littman RL. "Thucydides Syndrome" reconsidered: new thoughts on the Plague of Athens". *Am J Epidemiol* 1994;140:621-628.

4. Morens DM, Folkers GK, Fauci AS. What is a pandemic? *J Infect Dis* 2009;200:1018-1021.

5. Morens DM, Taubenberger JK. Pandemic influenza: certain uncertainties. *Rev Med Virol* 2011;21:262-284.

6. Morens DM, Folkers GK, Fauci AS. The challenge of emerging and re-emerging infectious diseases. N*ature* 2004;430:242-249. [Erratum: 2010;463:122].

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