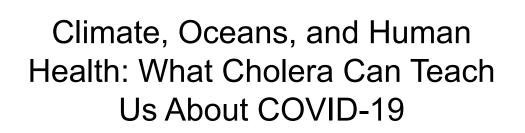
"...whoever wishes to pursue the science of medicine must first investigate the seasons of the year and what occurs in them."

Hippocrates, 4th Century B.C.



February 16, 2021

California State University, San Bernadino

Rita R. Colwell, Ph.D., D.Sc. Distinguished University Professor University of Maryland College Park



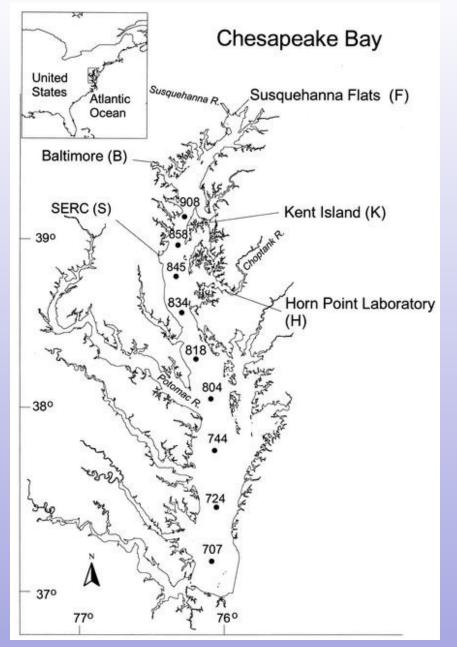
Water-related diseases

	Cases per year	Deaths per year			
Amoebiasis	48,000,000	110,000			
Arsenic	28-35m exposed to drinking water with elevated levels				
Diarrhoeal disease, Including cholera	1.5 billion	1,800,000			
Dracunuliasis (guinea worm)	> 5000	-			
Fluorosis	26 million (China)	-			
Giardiasis	500,000	Low			
Hepatitis A	1,500,00	-			
Intestinal helminths	133,000,000	9400			
Malaria	396,000,000	1,300,000			
Schistosomiasis	160,000,000	> 10,000			
Trachoma	500,000,000	-			
Typhoid	500,000	25,000			

Cholera: A Global Disease

- Acute water-related diarrheal disease
- Seventh pandemic started in 1960s
- Occurs in more than 50 countries affecting approximately 7 million people
- Bengal Delta is known as "native homeland" of cholera outbreaks
- Since cholera bacteria
 - exist naturally in aquatic habitats
 - evidence of new biotypes emerging, *it is highly unlikely that cholera will be eradicated but clearly can be controlled by provision of safe drinking water.*





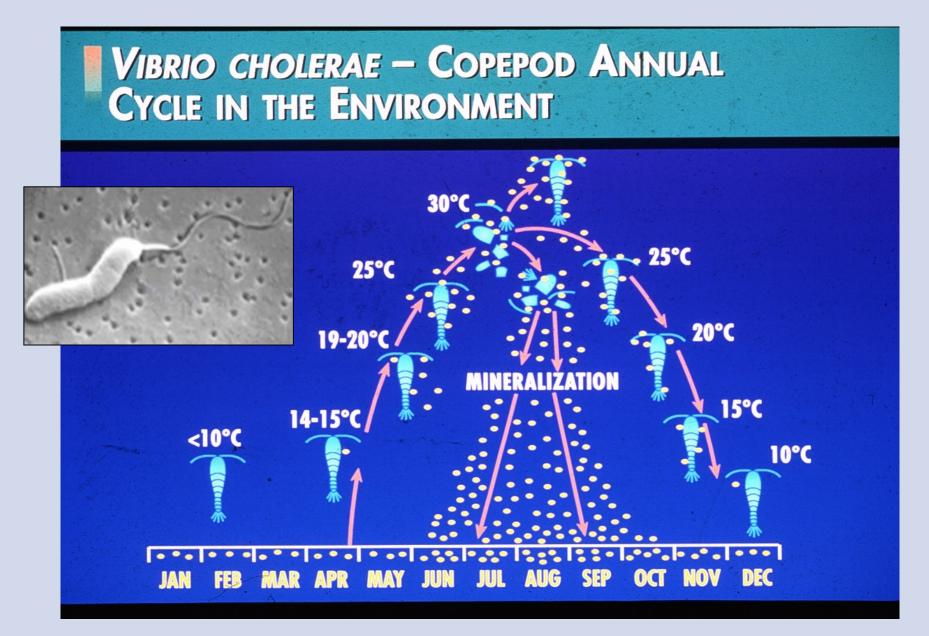








Map of Chesapeake Bay – beginning of the cholera chronicle 1965-1975 An early contribution of marine microbiology to human health: Determination of the *Vibrio cholerae* life cycle



The culprit – Calanus copepod host



MODEL FOR THE TRANSMISSION OF VIBRIO CHOLERAE FROM THE ENVIRONMENT TO HUMANS

PHYSICAL & CHEMICAL CHARACTERISTICS OF WATER

- temperature
- sunlight
- rainfall
- pH
- dissolved oxygen
- salinity & nutrients

FECAL SHEDDING returns V. cholerae to the water.

BIOLOGICAL CHARACTERISTICS

- algae bloom
- phytoplankton bloom

ZOOPLANKTON BLOOM (enters into non-culturable state)

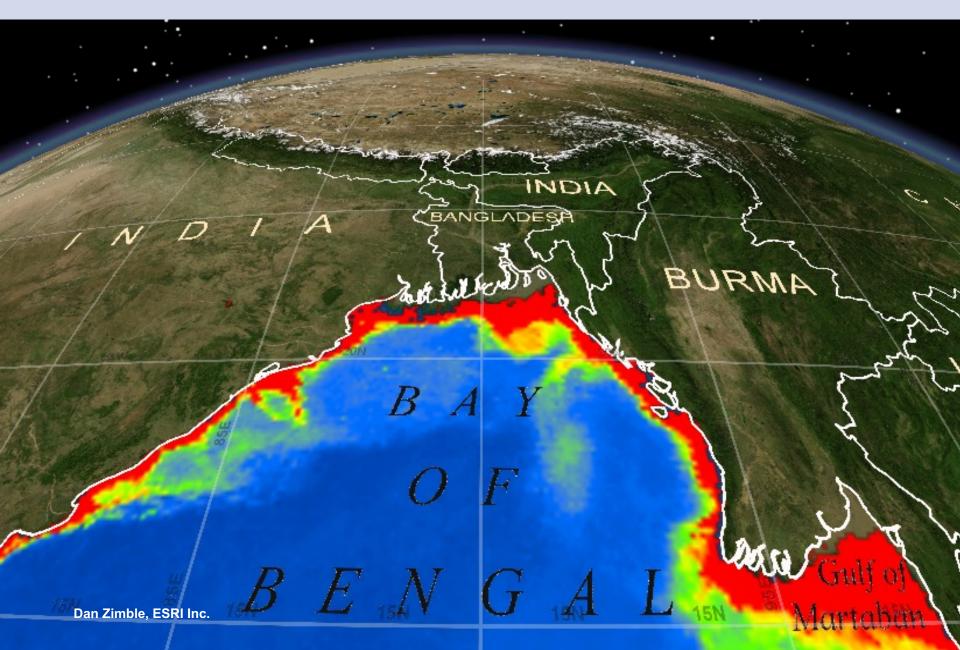
V. CHOLERAE viable but non-culturable state in the water column & attached to particulates. Commens

column & attached to particulates. Commensal or symbiotic relationships.

TRANSMISSION OF V. CHOLERAE to humans via ingested water containing colonized copepods or other vectors.

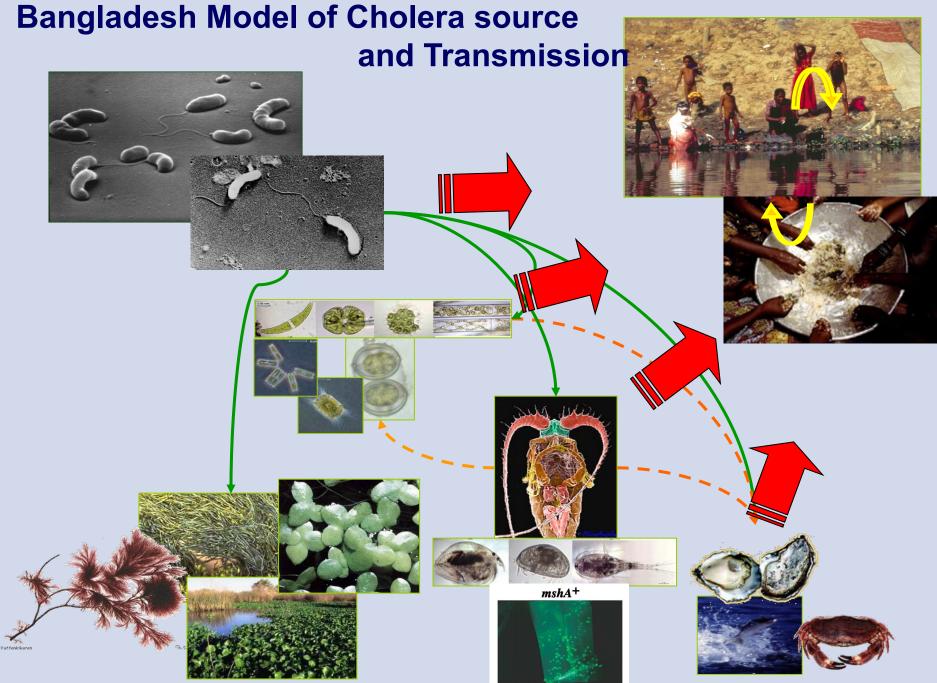


Work begins in Bangladesh in 1975

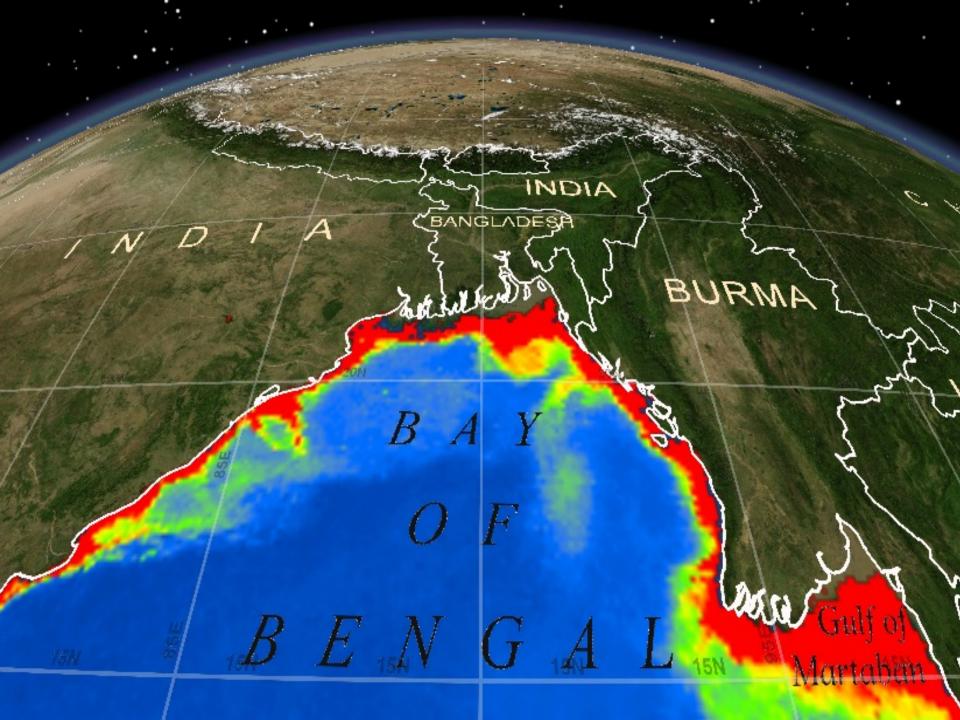




Villagers in Bangladesh collect filtered water in the same pond used for bathing

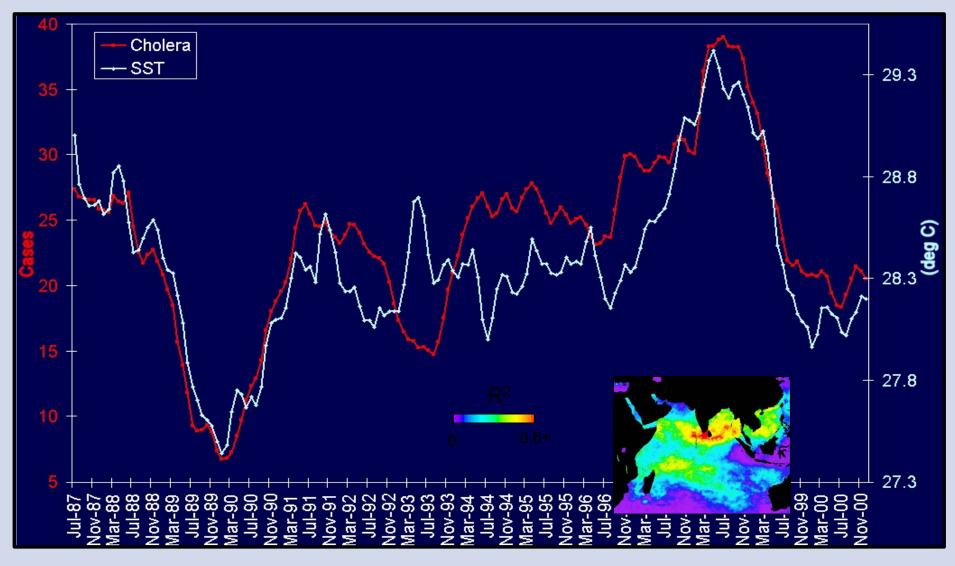


G. Constantin de Magny



Cholera and SST in the Indian Ocean 1985 - 2000

Six-month SST lead: R² = 0.72



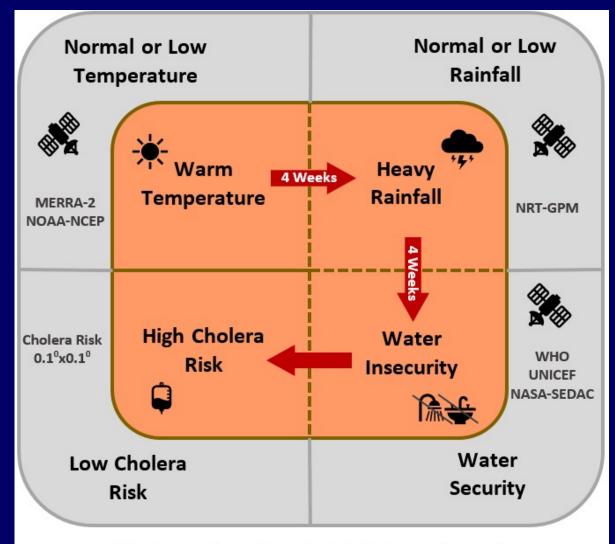
Lobitz et al., 2000, PNAS Vol. 97, No. 4 pp. 1438-1443

What is reported about cholera and macro-scale processes?

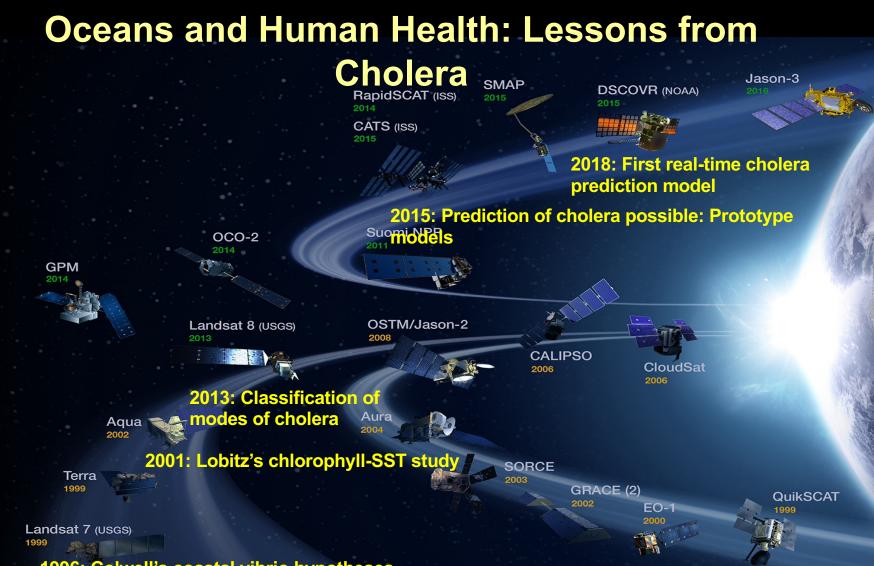
Cholera outbreaks have been linked to environmental and climate variables

precipitation (*Hashizume et al. 2008*) floods (*Koelle et al., 2005*) river level (*Emch et al., 2008*) sea surface temperature (*Colwell*, 1996; *Lobitz et al., 2000*) coastal salinity (*Miller et al., 1982*) dissolved organic material (*Worden et al., 2005*) fecal contamination (*Islam et al., 2006*) chlorophyll (*Lobitz et al., 2000, Magny et al., 2008*)

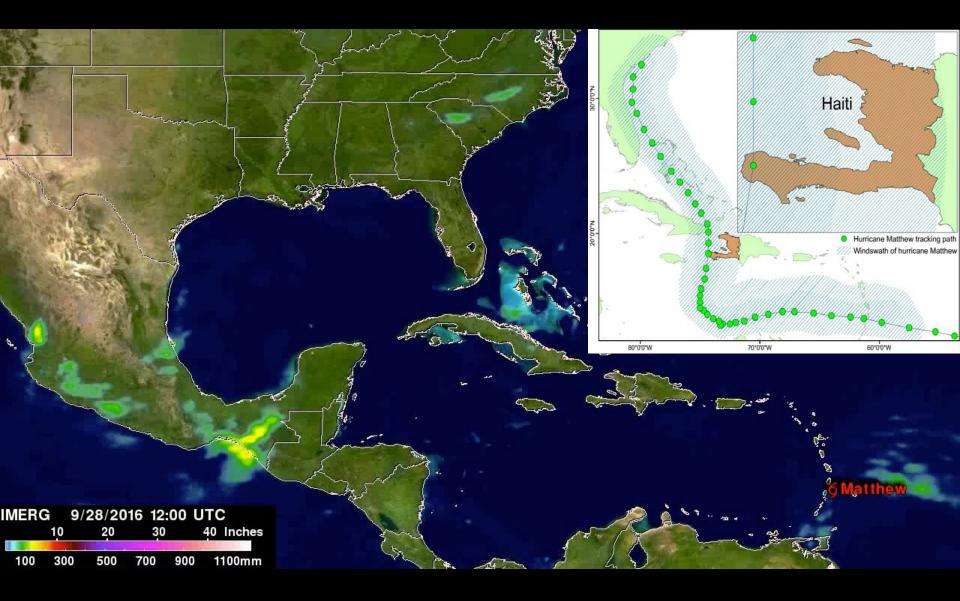
Theoretical framework for predicting cholera outbreaks in epidemic regions



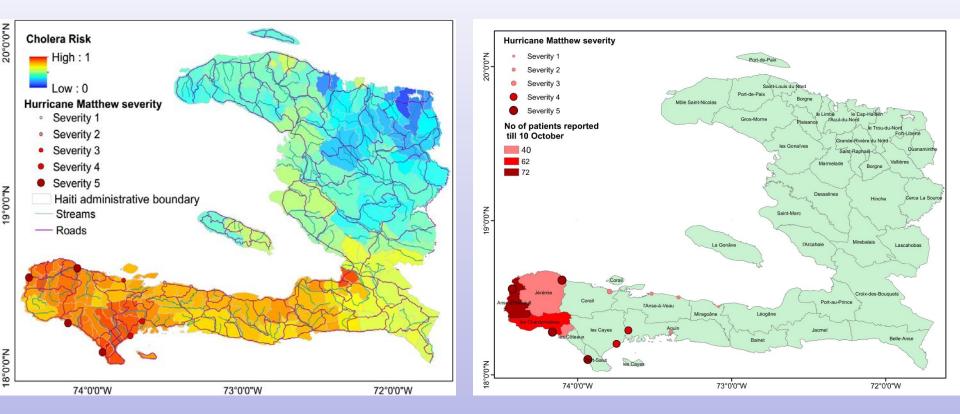
Warm temperature= above climatological average temperature Heavy rainfall= above climatological average precipitation Water insecurity=lack of access to water and sanitation access High cholera risk=probability of cholera greater than 50%



1996: Colwell's coastal vibrio hypotheses

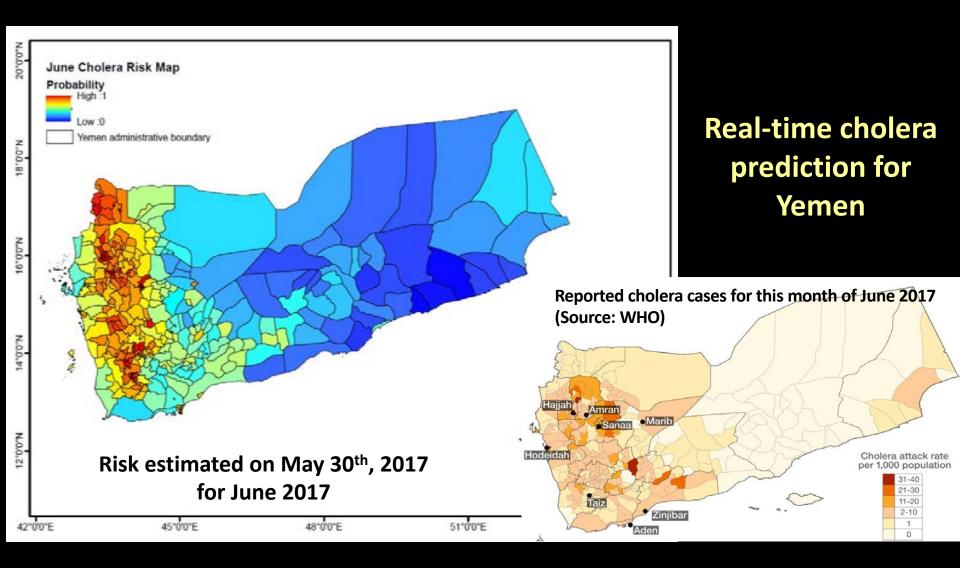


Cholera in Haiti



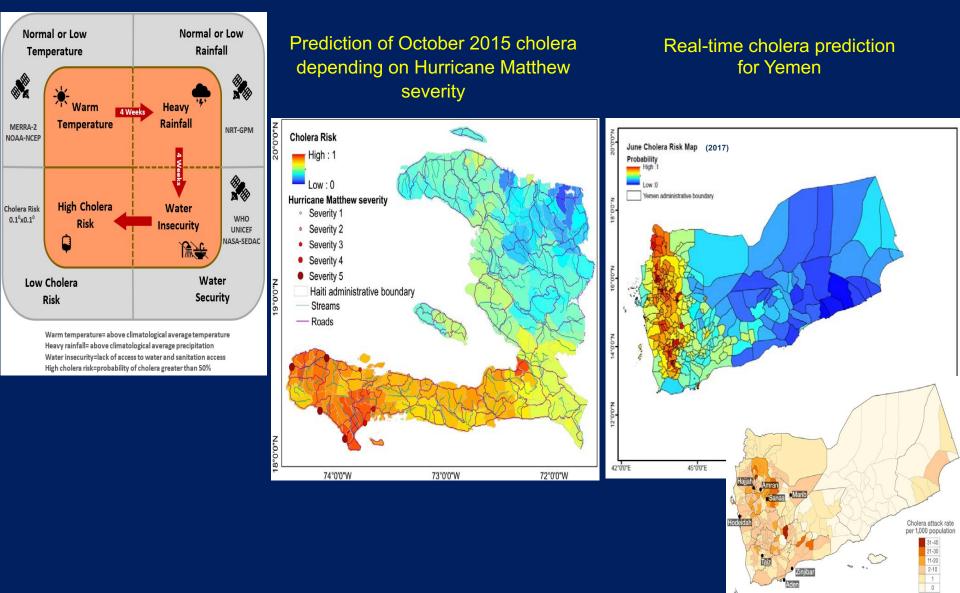
Prediction of October 2015 cholera depending on Hurricane Matthew severity

Actual cholera in October 2015 following Hurricane Matthew



Epidemic Cholera

- Sporadic outbreak
- Usually occurs following floods or inundation of large landscapes
- Warm temperatures may increase growth of bacteria in aquatic bodies.





NEXT GEN SEQUENCING AND METAGENOMICS IDENTIFICATION



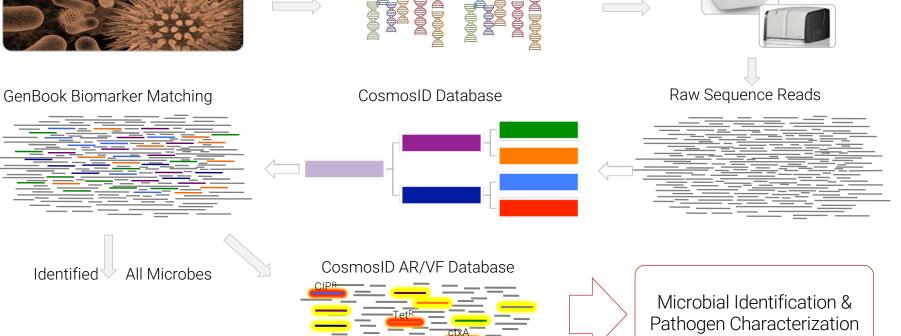
Shotgun whole (meta)genome sequencing

Biological specimen



Community DNA

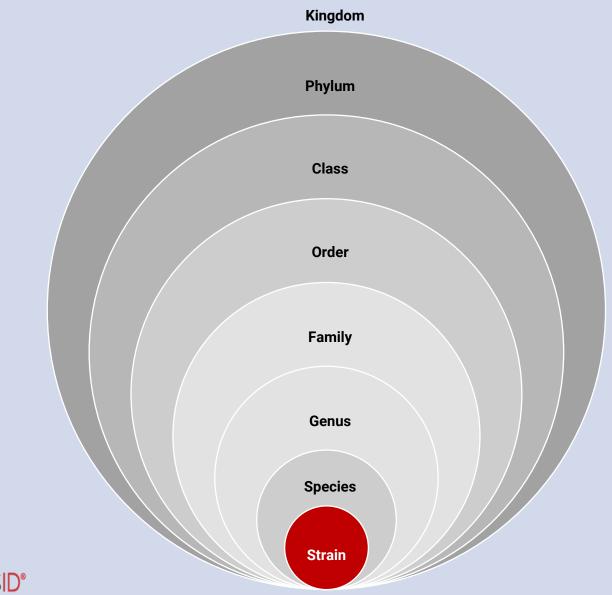
DNA Sequencing







Strain is the Clinically Informative and Actionable Unit





Microbiome Analysis of Acute Diarrheal Patients Compared with Healthy Individuals



pre-publication results

Study Cohort

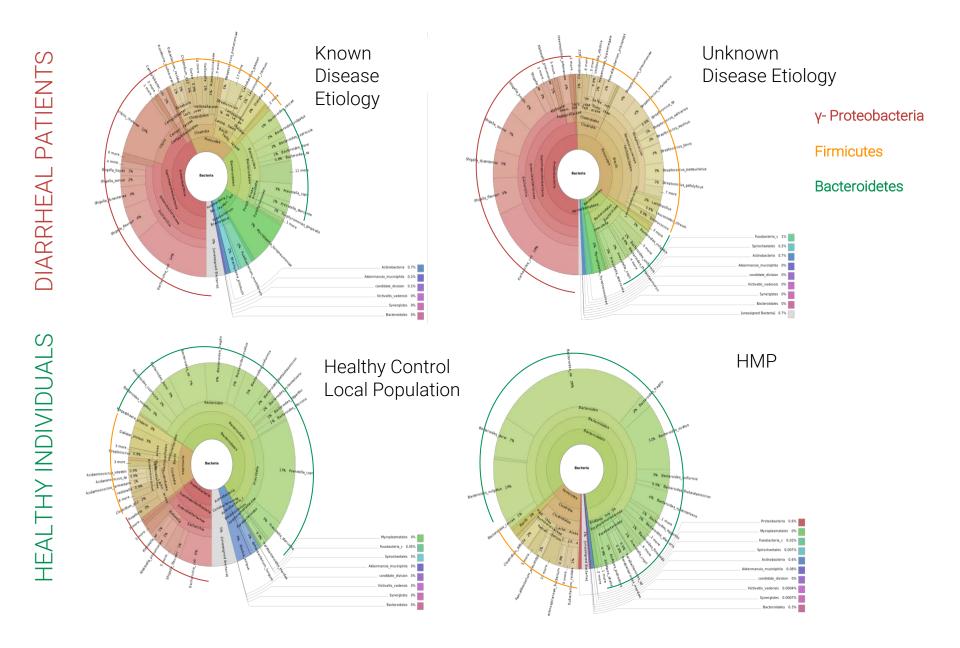
@ 2% Surveillance (every 50th patient) at the National Institute of Cholera and Enteric Diseases (NICED), Calcutta, India

PHASE I 9 9 0 0 PHASE II 28 0 18 10 PHASE III 37 17 10 10 Enteric Pathogens monitored Virus Parasites V cholerae O1 and O139 Rotavirus Giardia lamblia V cholerae O1 and O139 Virus Parasites V cholerae O1 and O139 Norovirus GI Giardia lamblia V cholerae O1 and O139 Norovirus GI Enternoeba V cholerae O1 and O139 Norovirus GI Enternoeba V cholerae O1 and O139 Sapovirus Enternoeba V cholerae O1 and O139 Norovirus GI Enternoeba V cholerae O1 and O139 Sapovirus Biastocystis	Study Phases Samples		Known Etiology	Unknown Etiology	Healthy Control	
PHASE III 37 17 10 10 Enteric Pathogens monitored Enteric Pathogens monitored Bacteria Virus Parasites V. cholerae O1 and 0139 Rotavirus Giardia lamblia V. cholerae Non 01 and Non 0139 Rotavirus Giardia lamblia V. parahaemolyticus Norovirus GI Cryptosporidium V. fluvialis Norovirus GI Entamoeba Shigella dysenteriae S. flex.neri Blastocystis	PHASE I	9	9	0	0	
Enteric Pathogens monitored Bacteria Virus Parasites V. cholerae O1 and O139 Virus Parasites V. cholerae Non O1 and Non O139 Rotavirus Giardia lamblia V. parahaemolyticus Adenovirus Giardia lamblia V. fluvialis Adenovirus Cryptosporidium parvum Aeromonas spp. Norovirus GI Entamoeba histolytica Shigella dysenteriae S. flexneri Blastocystis	PHASE II	28	0	18	10	
Bacteria Virus Parasites V. cholerae 01 and 0139 Rotavirus Giardia lamblia V. cholerae Non 01 and Non 0139 Adenovirus Giardia lamblia V. parahaemolyticus Adenovirus Cryptosporidium parvum Aeromonas spp. Norovirus GI Entamoeba histolytica Shigella dysenteriae S flexneri Blastocystis	PHASE III	37	17	10	10	
S. boydii Astrovirus hominis	V. chole V. chole V. parah V. fluvia Ca Ca	eteria rae 01 and 0139 rae Non 01 and Non 0139 aemolyticus lis Aeromonas spp. mpylobacter jejuni ampylobacter coli igella dysenteriae S. flexneri S. sonnei	Virus Rotavirus Adenovirus Norovirus GI		iardia lamblia vptosporidium parvum Entamoeba histolytica	

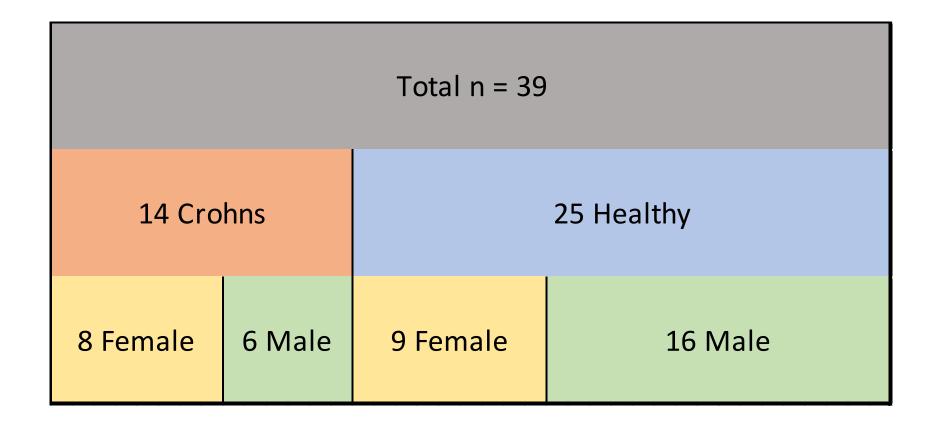
ETEC group (LT, ST, LT+ST) EAEC EIEC STEC



Microbial Community in Healthy vs Diarrheal Patients



Crohn's Disease and the Microbiome

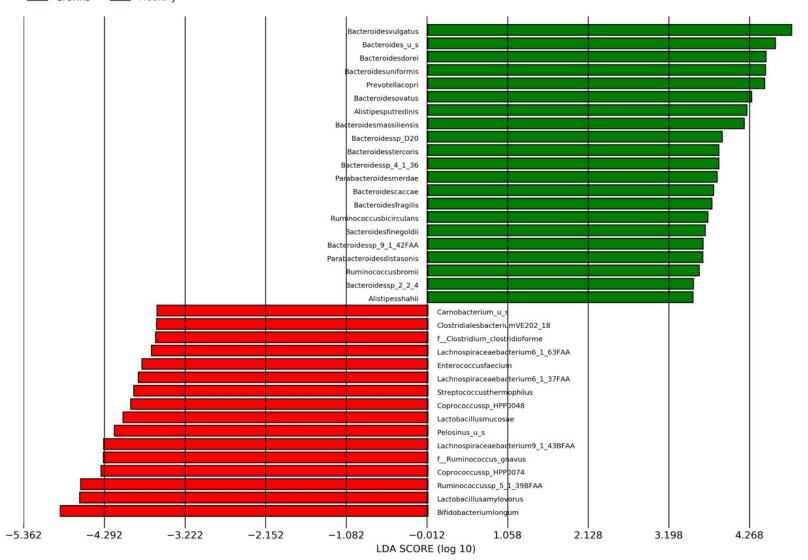


- 1: Crohn's data come from SRA Bioproject PRJNA46321 " Metagenomic Analysis of the Structure and Function of the Human Gut Microbiota in Crohn's Disease"
- 2: Healthy data come from SRA Bioproject PRJNA48479 "Human Microbiome Project (HMP) Metagenomic WGS Projects, deeper sequencing of the human microbiome samples: Production Phase"



Species Enrichment in Healthy vs Crohn's

Crohns Mealthy





Analysis provided by CosmosID

Water Safety







SINCE 1933

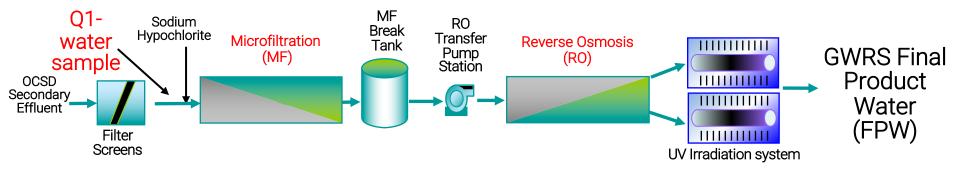
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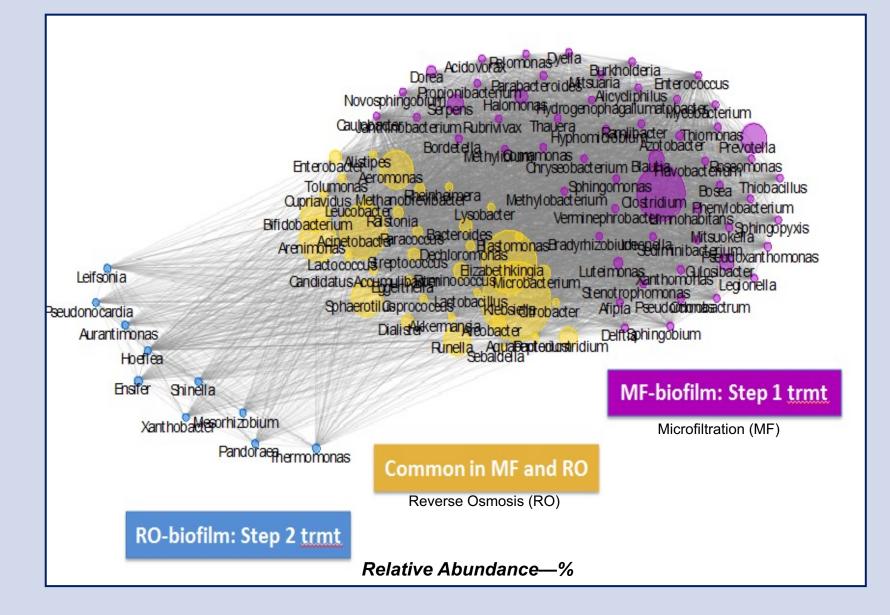
Characterization of Microbial Signatures From Advanced Treated Wastewater Biofilms

Author(s): Leddy, Menu B.; Hasan, Nur A.; Subramanian, Poorani; Heberling, Colin; Cotruvo, Joseph; Colwell, Rita R. Publications: Journal - American Water Works Association Issue Date: November 2017 Volume / Number: 109, Number 11 Page(s): E503-E512

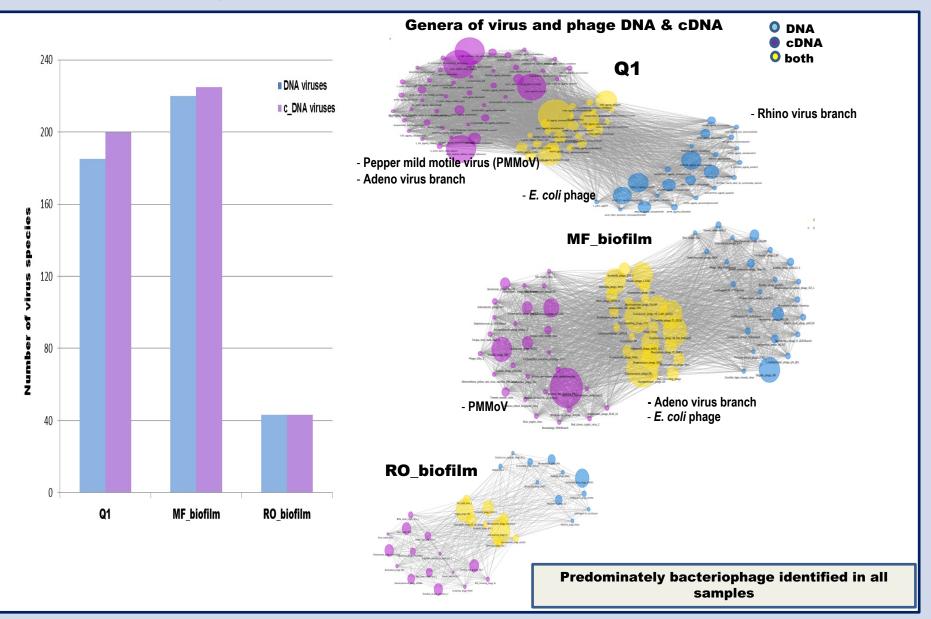




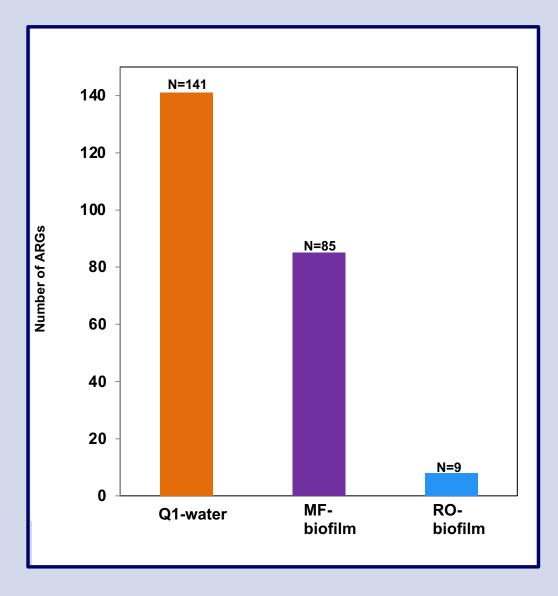
Stepwise reduction of bacterial genera from MF to RO



Viral Diversity



Distribution of antibiotic resistance genes (ARGs) and stepwise reduction of ARG's in MF and RO-biofilms

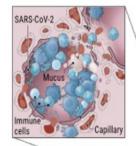


Is COVID-19 polymicrobial and systemic?

How does coronavirus kill? Clinicians trace a ferocious rampage through the body, from brain to toes

By Meredith Wadman, Jennifer Couzin-Frankel, Jocelyn Kaiser, Catherine Matacic. Science, Apr. 17, 2020, 6:45 PM

https://www.sciencemag.org/news/2020/04/how-doescoronavirus-kill-clinicians-trace-ferocious-rampagethrough-body-brain-toes



1 Lungs

A cross section shows immune cells crowding an inflamed alveolus, whose walls break down during attack by the virus, diminishing oxygen uptake. Patients cough, fevers rise, and it takes more and more effort to breathe.

2 Liver

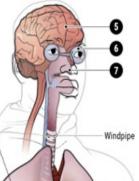
Up to half of hospitalized patients have enzyme levels that signal a struggling liver An immune system in overdrive and drugs given to fight the virus may be causing the damage.

3 Kidneys

Kidney damage is common in severe cases and makes death more likely. The virus may attack the kidneys directly, or kidney failure may be part of whole-body events like plummeting blood pressure.

4 Intestines

Patient reports and biopsy data suggest the virus can infect the lower gastrointestinal tract, which is rich in ACE2 receptors. Some 20% or more of patients have diarrhea.



O

are directly caused by the virus. 6 Eyes Conjunctivitis, inflammation of the membrane that lines the front of the eye and inner eyelid, is more common in

5 Brain

Some COVID-19 patients have strokes, seizures, mental confusion, and brain inflammation. Doctors are trying to understand which

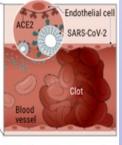
7 Nose

Bronchii

Bile duct

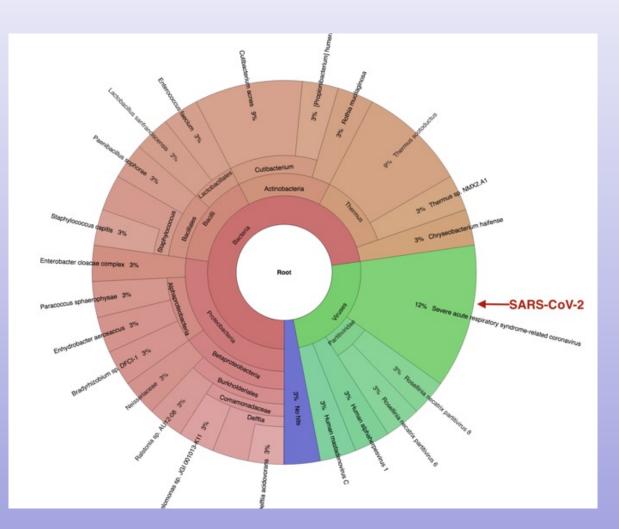
the sickest patients.

Some patients lose their sense of smell. Scientists speculate that the virus may move up the nose's nerve endings and damage cells.



8 Heart and blood vessels The virus (green) enters cells,

likely including those lining blood vessels, by binding to ACE2 receptors on the cell surface. Infection can also promote blood clots, heart attacks, and cardiac inflammation. Identification of Bacteria and Viruses Present in Respiratory Samples in which SARS-CoV-2 has been Detected



SARS Cov-2 viral RNA has been detected in 48.1% of stool samples

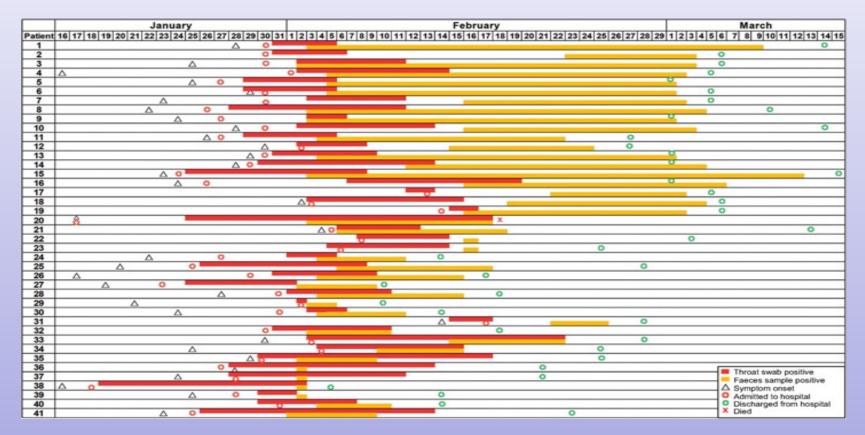
Stool viral RNA positivity rate

							P	revalen	ce		Weight	Weight
Study	Events	Total						(%)		95%-CI	(fixed)	(random)
Xiao F	39	73			-			53.42	[41.37	; 65.20]	55.8%	45.2%
Zhang W	4	15			-			26.67	[7.79	; 55.10]	9.0%	10.9%
Zhang J	5	14		-				35.71	[12.76	; 64.86]	9.9%	11.9%
Wang W	5	13	-	* 1		s		38.46	[13.86	; 68.42]	9.4%	11.4%
Young BE	4	8			-			50.00	[15.70	; 84.30]	6.1%	7.7%
Kim JY	0	2 ⊷			_			0.00	[0.00]	; 84.19]	1.3%	1.7%
Yang Z	3	3			-		-	100.00	[29.24;	100.00]	1.3%	1.8%
Cheng SC	0	1 ⊷					_	0.00		; 97.50]		1.5%
Holshue	1	1 -						100.00	[2.50;	100.00]	1.2%	1.5%
Cai J	5	6						83.33	[35.88	; 99.58]	2.6%	3.3%
Zeng L	1	1 -					-	100.00	[2.50;	100.00]	1.2%	1.5%
Zhang Y	1	1 -					-	100.00	[2.50;	100.00]	1.2%	1.5%
Fixed effect model		138		V	>			48.88	[40.41	; 57.41]	100.0%	-
Random effects model				\leq	>			48.06	[38.33	57.94]		100.0%
Heterogeneity: $I^2 = 7\%$, τ^2	= 0.0361,	p = 0.38	1	1	1	1			-			
		0	20	40	60	80	10	D				

Gastroenterology

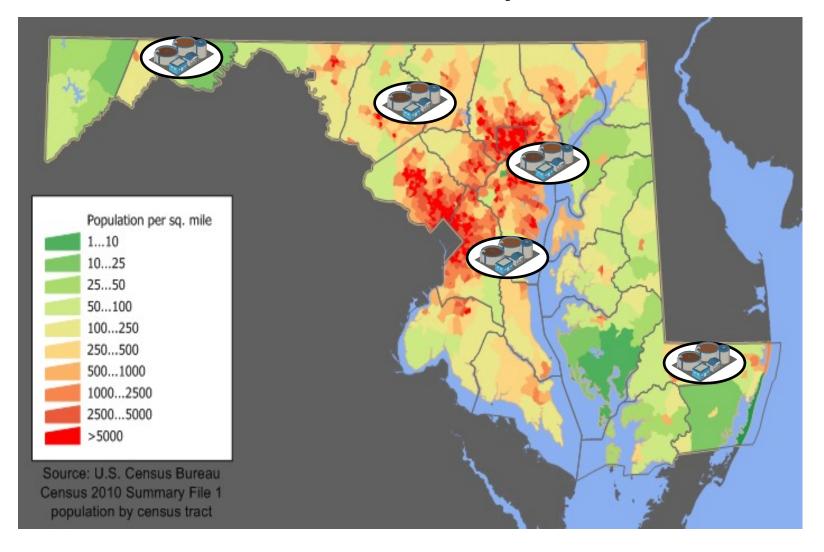
Cheung et al., (2020). Gastrointestinal Manifestations of SARS-CoV-2 Infection and Virus Load in Fecal Samples from the Hong Kong Cohort and Systematic Review and Meta-analysis. Gastroenterology. Pre-Proof

Positive Stool Samples Detected After Respiratory Sample Tested Negative During Recovery

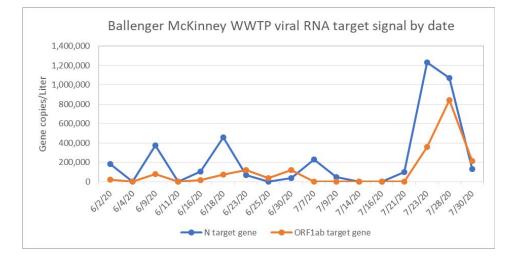


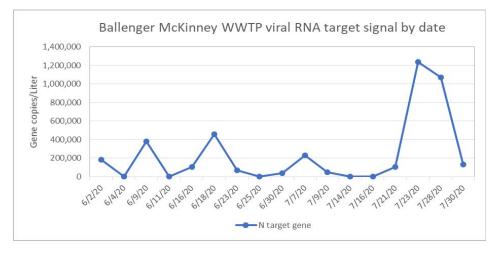
Wu Y, Guo C, Tang L, et al. Prolonged presence of SARS-CoV-2 viral RNA in faecal samples. 2020 The lancet Gastroenterology – hepatology. Volume 5, Issue 5, 434 - 435

COVID-19 tracking in wastewater underway



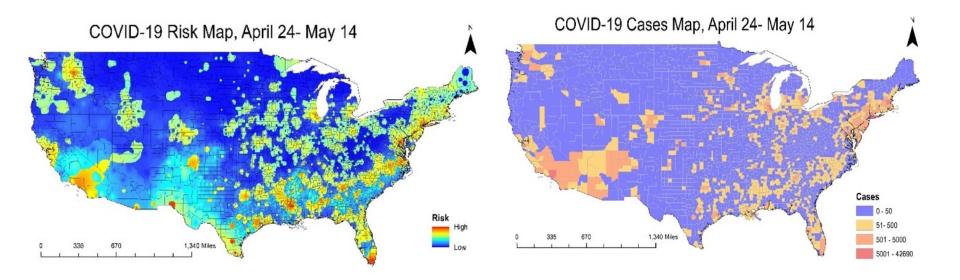
Results from Frederick, Maryland sites







Prediction of coronavirus risk



Left panel: **Prediction** made on April 24th 2020 and valid until May 14th, 2020. Right panel: **Actual number** of COVID19 cases during those three weeks: a heuristic prediction model developed in GeoHLab

A Simple, Sustainable Method for Reducing Cholera



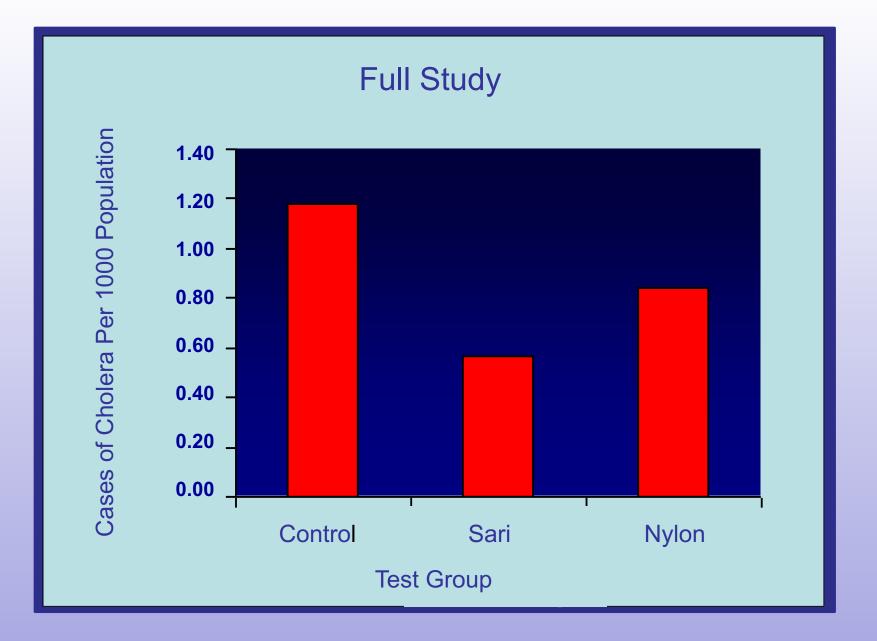
Vibrio cholerae





(3-1)





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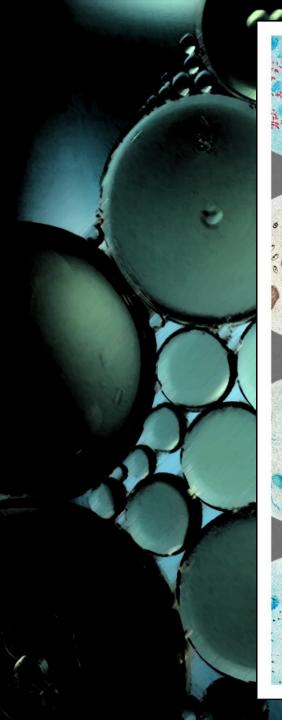


Dr. Seon Young Choi, Visiting Scientist, University of MD, College Park, MD

Safe water is a global challenge



Courtesy of GB Nair, NICED, Kolkata, India



A Lab of One's Own

One Woman's Personal Journey Through Sexism in Science

Former Director of the National Science Foundation
RITA COLWELL, PHD
and
SHARON BERTSCH McGRAYNE

