Mailman School of Public Health
Case Consortium @ Columbia
Columbia University

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When BEST Intentions Go Awry: Arsenic Mitigation in Bangladesh

Public health research scientists spend their careers trying to prove or disprove hypotheses. Often, their laboratory research involves microbes or animals. When it comes to human subjects, however, researchers are expected not only to study the subject but, if possible, to alleviate (mitigate) existing harmful conditions. In 2000, a Columbia University multidisciplinary research team began a comprehensive study into the incidence of arsenicosis—or poisoning by arsenic—among residents of Bangladesh who were drinking contaminated water. Once the research component was in place, the scientists looked for ways to limit or prevent the poisoning, because health problems from chronic arsenic exposure were irreversible.

In spring 2006, the Columbia team launched the latest of its mitigation projects. It was called BEST, for Bangladesh Vitamin E and Selenium Trial. Scientists had unconfirmed evidence that the antioxidants in Vitamin E and selenium might at least stop the progress of arsenicosis—a painful and ultimately fatal disease. The BEST trial would not only measure the effectiveness of the vitamins, but also provide its participants with free filters to improve the quality of their water.

The trial was conducted in three locations. One was Araihazar, where the Columbia scientists had worked since 2000, and established credibility and trust. The second was neighboring Srinaga. The third was Laksam, 100 kilometers away. BEST added Laksam in March 2007 because the first two sites did not contain as many arsenicosis patients as the study required. Dr. Habibul Ahsan was BEST's principal investigator, Faruque Parvez was the US-based project coordinator, and Ahmed Talat Haider was the onsite project manager.

In Laksam, Haider retained Abdur Razzak, a local with broad experience working with non-governmental organizations (NGOs), to introduce the out-of-towners to villagers and help win their trust. Haider did not realize that Razzak also ran a small business selling water filters. Within months, Razzak was fired for apparent sabotage: removing key parts from the BEST-provided free filters to make them inoperable. Haider considered the matter closed.

This case was written by Ted Smalley Bowen and Kirsten Lundberg, Director, for the Case Consortium @ Columbia. (0412)

It was a considerable surprise, therefore, when on March 2, 2008, a local Laksam paper ran a story accusing BEST, among other charges, of poisoning study participants. Other papers picked up the story and, by early April, versions of it appeared in the national press. Several weeks after the articles appeared, an anonymous person sent an email to the presidents of the universities of Chicago (Ahsan joined Chicago in 2006) and Columbia and the dean of Columbia's public health graduate school complaining about the study.

Project Director Parvez was aware of the early local articles, but watched with dismay as the inaccurate story spread. Dismay turned to alarm as some participants threatened to withdraw from the study. In late spring 2008, Parvez and his senior colleague Dr. Joseph Graziano, director of Columbia's arsenic research programs in Bangladesh, called the Columbia University general counsel's office to let them know what was going on. Parvez and the rest of the BEST team were scientists, not public relations managers. But they knew they had to recover public and institutional trust. The question was: how?

Unnoticed geology, unanticipated consequences

The story of the Columbia project dated back to November 1998, when the *New York Times* ran a story that drew attention to a public health emergency in Bangladesh: arsenic in well water.[1] The *Times* story, "Death by Arsenic," chronicled a tale of unintended consequences. What the World Health Organization (WHO) dubbed the largest mass poisoning in history was largely the unanticipated legacy of a massive public health intervention that started in the 1960s. At that time, diarrhea contracted from contaminated surface water was a leading cause of death in Bangladesh, especially among children. The United Nations Children's Fund (UNICEF) led the way, followed by the government, in drilling millions of medium-depth "tube" wells that tapped into groundwater, protected by its depth from surface contaminants.[2] The well drilling also dovetailed with the green revolution, allowing farmers to grow a second annual rice harvest.

Sadly, an accident of geology and geography turned that intervention into a national health emergency. In the early 1990s, a growing incidence of arsenicosis led to the discovery that runoff from the Himalayas had left high concentrations of naturally occurring and carcinogenic arsenic in the groundwater of the Ganges River delta of Bangladesh. As a result, what was thought to be safe well water was often poisonous. Arsenic in high concentrations had been linked to cancers of the skin, liver, lung, kidney, and bladder.[3] It had also been found to cause diabetes,

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1 Barry Bearak, "DEATH BY ARSENIC: A special report; New Bangladesh Disaster: Wells That Pump Poison,"

2 Tube wells were narrow, typically less than a foot in diameter. The shafts were often fitted with retaining sleeves to prevent cave-ins. Pump mechanisms could be human- or machine-powered. Most wells used screens or slots in the lowermost sections of pipe to filter sediment. Depth varied according to water table, type of pump, etc.

3 Smith et al., "Cancer risks from arsenic in drinking water," *Environ Health Perspect*. 1992 July; 97: 259–267. See: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1519547.

peripheral neuropathy, and cardiovascular diseases.[4] Symptoms ranged from skin lesions and blackened fingers and toes to scaly skin on palms and soles of the feet, white streaks on the fingernails, swollen limbs, numbness and tingling in the extremities, headaches, confusion and weakness.[5]

A 1998 study by the British Geological Survey (BGS) estimated that 35 million Bangladeshis were exposed to water exceeding the country's drinking water standard of 50 parts per billion (ppb) and 57 million people were exposed to water exceeding the World Health Organization's 10 ppb standard. One part per billion is equivalent to 0.01 milligrams of arsenic per liter of water. Though 61 of Bangladesh's 64 districts were affected, the greatest concentration of arsenic contamination was in the south and east.[6]

At Columbia University, the *New York Times* article caught the attention of several scientists, including those at the Mailman School of Public Health. As it happened, several had been following the Bangladesh situation for months and were looking for a way to help.

Interested parties

Bangladesh-born Dr. Habibul Ahsan was a young assistant professor of epidemiology at Mailman; he focused on environmental and genome factors in cancer and other diseases. Since childhood, Ahsan had been friends with Faruque Parvez, a pharmacist who worked for a US health maintenance organization and had a background in public health. Parvez knew how to design surveys, procure drugs, and improvise under challenging logistical and political conditions. He also had extensive experience conducting fieldwork in rural areas of Bangladesh. The two had often discussed the possibility of returning to their home country to conduct public health research.

In summer 1998, Parvez visited an uncle, a physician who ran a hospital in the Bangladeshi capital, Dhaka. During the visit, he learned about Bangladesh's arsenic problem, and that fall accompanied his relative on a tour of US East Coast public health institutions to discuss arsenic studies and potential mitigation programs. Parvez contacted Ahsan, and the two agreed to visit Bangladesh that winter to collaborate with the uncle on the arsenic problem.

Meanwhile, geochemist Dr. Alexander van Geen had learned about the Bangladesh arsenic problem from a visiting geologist from Calcutta. Van Geen was a research professor at Columbia's

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[4] Abernathy et al., "Arsenic: health effects, mechanisms of actions, and research issues," *Environ Health Perspect*. 1999 Jul;107(7):593-7. See: http://www.ncbi.nlm.nih.gov/pubmed/10379007.

[5] World Health Organization fact sheet. See: http://www.who.int/water_sanitation_health/dwq/arsenicun4.pdf

[6] For more on the British Geological Survey study, see: http://www.bgs.ac.uk/research/groundwater/health/arsenic/Bangladesh/reports.html

Lamont-Doherty Earth Observatory. The geologist "didn't have any scientific papers," recalls van Geen. "He had some pamphlets essentially written by NGOs and the like, saying that this was a serious issue."[7] Van Geen's specialty was the geochemical cycling of trace elements in natural and perturbed environments, such as mine tailings, coastal sediment, estuaries, and groundwater, as well as the reconstruction of past climate change in near-shore environments. He had pursued several interdisciplinary projects, teaming with health and social scientists to tackle complex environmental problems.

Finally, Dr. Joseph Graziano was a pharmacologist and environmental health specialist at the Mailman School. He studied genetic diseases of hemoglobin, such as sickle-cell anemia. In earlier years, he had been part of a team that discovered a drug to treat lead poisoning in children. His life's proudest work to date had been a 15-year project in the former Yugoslavia that studied the effects of environmental lead exposure. His Columbia lab specialized in analyzing metal in biological samples.

Superfund grant. Shortly after the *New York Times* article appeared, three earth scientists approached Graziano about working together on a project to study the naturally occurring arsenic—a phenomenon they found puzzling.[8] "We don't feel we would be credible without a public health partner," they told him. A week later Ahsan, who had recently joined the faculty, also approached Graziano. "He said, 'I'm a cancer epidemiologist. I'm a Bangladeshi-American. It's my country, and I want to work on it, but I don't have a lab. I know your lab can make measurements of arsenic in biological samples" remembers Graziano.

Graziano had recently headed the review of grant applications at the National Institute for Environmental Health Sciences (NIEHS)—a branch of the National Institutes of Health (NIH)—under its "Superfund" program to clean up hazardous waste sites. He wondered whether, because arsenic also occurred in groundwater in the US, the NIEHS might consider funding a multidisciplinary arsenic study based in Bangladesh.[9] "We could actually do something," he told his visitors. "The earth scientists got totally lit up by the fact that we could help people."[10]

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7 Bowen telephone interview with Alexander van Geen on March 7, 2012. All further quotes from van Geen, unless otherwise attributed, are from this interview.

8 The three were Martin Stute and James Simpson, geologists from Columbia's Lamont-Doherty Earth Observatory, and Yan Yheng, a geochemist from Queens College.

9 In the US, Western states had the largest concentration of water sources exceeding the EPA standard of 10 parts per billion (ppb). Groundwater in parts of the Midwest, Mid-Atlantic and New England also had arsenic levels higher than the EPA standard. For more information, see: http://water.epa.gov/lawsregs/rulesregs/sdwa/arsenic/Basic-Information.cfm

10 Authors' interview with Dr. Joseph Graziano on January 19, 2012, in New York City. All further quotes from Graziano, unless otherwise attributed, are from this interview.

The group formed a team. The deadline for the next round of Superfund grants was May 1999—a ridiculously short time to assemble a standard scientific grant application. But the team decided to go for it. "We basically dropped everything. Five weeks later, we got on a plane and went" to Bangladesh, says Graziano.

Scoping the project

Ahsan and Parvez were the advance team. In December 1998, they flew to Bangladesh to arrange a visit by the larger group, which late that month arrived to meet with government officials and NGOs. They also scouted potential sites that would simultaneously serve the research goals of medical/biological, earth science, and geochemistry teams. They collected a few samples from wells to take back to the US.

In January 1999, Columbia sent a small group of faculty to map arsenic levels in well water and evaluate people showing signs of arsenic exposure. They were gratified to learn of the British Geological Society's recently completed nationwide wells survey. The goal was to identify the most promising area for research. It was important to identify a region where wells contained low, medium and high levels of arsenic so that study participants would reflect a range of exposure (creating de facto comparison groups). Geologist Martin Stute collected water samples from Sonargaon, a community about 25 km (15.5 miles) southeast of Dhaka known to have significant levels of arsenic contamination.[11]

They expected that areas with high concentrations of arsenic would also have a population with a significant incidence of arsenicosis. The health scientists planned to take urine and blood samples from study participants, while the geosciences researchers would focus on geology and the geochemistry of arsenic in the area and on potential strategies for mitigating arsenic exposure. That meant identifying safe and unsafe sources of water and figuring out how to get people to switch to the safe sources. Water from deep aquifers was generally safer than other sources, but as the researchers would discover, the depth of low-arsenic water varied considerably (from less than 30 meters/90 feet to more than 200 meters/600 feet), even within small areas.

By May 1999, the Columbia team had a grant application ready to go to NIEHS. Graziano was listed as Principal Investigator. "He knew the [NIEHS] system and that, I think, was critical to essentially attacking that problem together," says van Geen. They asked for $12 million over five years for a total of seven projects, three of them in Bangladesh.[12] The proposal included scientists

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[11] The team collected more samples on a subsequent trip, when Yan Yheng tested 113 wells in the vicinity, including the neighboring town of Araihazar.

[12] The group proposed to study the interaction of arsenic and lead in groundwater and the possible use of ferric chloride to remove arsenic. This study would use core samples and aquifer material from sites in Bangladesh, New Jersey and Maine. Also in the US, Columbia proposed Superfund projects on the absorption by humans of lead and

from Lamont-Doherty, Mailman, and Columbia's Earth Institute (itself an interdisciplinary unit examining issues from climate change to poverty and sustainability).

In November 1999, the team learned that they had been successful.[13] Nearly half the funding would go toward projects in Bangladesh: a $2.3 million long-term observational study of the effects of arsenic exposure; a separate $1.3 million study of arsenic's effects on pregnant women and child development; a $650,000 study of the geology and geochemistry of groundwater arsenic; and a $540,000 study of remediation. The grant money would run from 2000-2005.

The primary Bangladesh project was called Health Effects of Arsenic Longitudinal Study, and known as HEALS. It called for a cohort of 10,000 people.[14] Researchers would collect biological samples from each participant in order to observe the long-term effects of various levels of arsenic exposure. They would also gather demographic and behavioral information. As is common with such sustained, large-scale studies, the researchers also expected to spin off additional research projects.

Starting HEALS

The scientists were eager to get started even before the grant money was due to come through in April 2000. So in late 1999, they obtained $50,000 from the Mailman School and $100K from the Earth Institute. With this, in February 2000 van Geen and Ahsan flew to Bangladesh laden with 50 boxes of empty vials, a handheld GPS system, markers and tape to collect additional water samples.

Although the initial testing was concentrated in Sonargaon, a 25-square kilometer area in Araihazar emerged as the leading contender for the central research site. It had a fair number of contaminated wells and a population with symptoms of arsenicosis. It was also close to Dhaka with its international airport, which would make it easier to ship samples to the US.

Local partner. For any project in Bangladesh, the Columbia scientists needed a local partner. The public health researchers had originally planned to collaborate with Community Hospital in Dhaka. But the latter declined after failing to come to terms over logistics. So they turned instead to the National Institute of Preventive and Social Medicine (NIPSOM).

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arsenic from contaminated soil, the genetic-level effects of arsenic on mammalian cells, and an analysis of the spread of arsenic from Superfund sites in New Jersey and Maine.

[13] For more information on the Columbia University Superfund Basic Research Program, see: http://superfund.ciesin.columbia.edu/archive/home.html.

[14] The cohort eventually increased to 12,000 so that economists Alex Pfaff and Malgosia Madajewicz from Columbia's School of International and Public Affairs (SIPA) could simultaneously conduct economic and social science research projects.

Dr. Iftikhar Hussain was a prominent member of NIPSOM, and in charge of the Ministry of Health and Family Welfare arsenic program. Dr. Hussain agreed to be the local director of the Superfund project. He had strong personal and professional connections to Araihazar, which reinforced the wisdom of basing the project there.

In February 2000, the project hired Parvez fulltime as HEALS project director, based in New York. His job was to design the surveys for the project, handle logistics, and act as liaison and general troubleshooter. In June, he flew to Bangladesh for what proved a six-month stay. He hired members of a 16-person team, which started preparatory fieldwork. The team gathered additional water samples, charted well depths and assembled demographic and household information in preparation for the study proper, which they hoped to start in the fall. By October, the researchers had identified and tested roughly 6,000 tube wells in the Araihazar study area; only then did they start demographic and behavioral surveys.[15]

Delays. Parvez had meanwhile to deal with a number of bureaucratic delays. In April, the team submitted an application for ethical approval to the Bangladesh Medical Research Council (BMRC). The BMRC's Central Ethics Review Committee monitored human experiments and was recognized as an institutional review board in the US. Approval finally came in July. The HEALS project celebrated its official launch days later.

In addition, the contract between Columbia and NIPSOM took months to finalize. In the fall, Graziano decided to make a personal visit to sort out the problems with the contract. Only in October was the final hurdle overcome and the contract signed.

Observational study launches

In October 2000, HEALS staff began the time-consuming and labor-intensive process of recruiting participants to the study. They began by addressing concerns about drawing blood, taking urine samples and interactions with women in the socially conservative Muslim community. In a country with an adult literacy rate only slightly above 50 percent, explanatory pamphlets were inadequate. Instead, they met potential participants face-to-face to explain what the researchers were doing, why they needed the biological samples, and how the results would help in the future prevention and treatment of arsenicosis.[16]

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[15] Ahsan et al, "Arsenic Exposure from Drinking Water and Risk of Premalignant Skin Lesions In Bangladesh: Baseline Results from the Health Effects of Arsenic Longitudinal Study," American Journal of Epidemiology, Vol. 163, No. 12. See: http://aje.oxfordjournals.org/content/163/12/1138.full.pdf+html

[16] UNICEF country statistics, Bangladesh; UNICEF statistics. See: http://www.unicef.org/infobycountry/bangladesh_bangladesh_statistics.html.

In 2001, Ahsan and Parvez realized that the daily commute for staff from Dhaka to Araihazar was too much. While the distance was short, traffic was chronically congested and the 25 km could take nearly two hours to travel. Project director Hussain introduced them to a local epidemiologist who owned land in Araihazar. The landowner made them an intriguing offer. If HEALS would help fund the construction of a three-story building housing a clinic, labs and pharmacy, he would then rent the building back to the researchers for the duration of the project. Ahsan and Parvez accepted.

By 2007, HEALS boasted a four-building campus in Araihazar, which included a health clinic for study participants and their families. The clinic, which provided basic health services, went a long way toward cementing villagers' trust in the HEALS project.

Leadership change. But by 2003, to Ahsan and Parvez's disappointment, relations with onsite project director Hussain, as well as with NIPSOM, had deteriorated. Hussain had done a fine job of hiring and managing staff, but the Columbia directors suspected him of unethical conduct. He was fired in February. In September, Ahsan prevailed upon veteran public health administrator Dr. Tariqul Islam to replace Hussain. Islam, who in addition to his medical degree held a masters in public health, had spent 13 years with Bangladesh NGO Gonoshasthaya Kendra and another three years at CARE International working on reproductive health projects. Ahsan was convinced that Islam was the type of reliable, charismatic, confidence-inspiring leader the program needed. Islam was hesitant, but agreed—on certain conditions. He recalls:

> I told them I am a public health program implementer. If you [want me to conduct] science and research, I cannot help you. If you agree to teach me research, then I can.[17]

Mitigation

But observation was only one part of a public health study. Another crucial element was mitigation or remediation—trying to make matters better for the study participants. When engaged on human-subject research, scientists observed a variety of ethical and behavioral codes; each institution, professional organization and funder had its own guidelines. But they shared a few principles: such experiments required the approval of a research ethics committee and the informed consent of subjects; and studies should minimize risks and keep them proportionate to the potential benefits.[18] Apart from this, however, there were no clearly defined obligations for researchers. The guidelines did not address such questions as when or how to provide benefits like

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[17] Lundberg interview with Tariqul Islam on February 4, 2012, in Araihazar, Narayongonj, Bangladesh. All further quotes from Islam, unless otherwise attributed, are from this interview.

[18] For more on ethics guidelines for research funded by the National Institutes of Health, see: http://ohsr.od.nih.gov/guidelines/index.html

healthcare and education to test subjects.[19] In practice, each research project devised its own response. Sometimes scientists argued that the research itself would benefit subjects through the discovery of new treatments, or improvements in understanding a given illness.

In Bangladesh, the Columbia team wanted to help those it proposed to study. In addition, the Columbia University institutional review board (IRB) and the BMRC (acting as IRB in Bangladesh) insisted that remediation efforts accompany any observational study of human subjects. Notes Graziano:

> After all, we're in public health. We want to intervene. [Plus] the institutional review boards, both here and in Bangladesh, [insisted on it]. They said you may do this [observational research], but you have to do everything possible to mitigate.

One difficulty was that none of the NIEHS funds could be used for mitigation alone. Says Graziano: " We get federal funding to do the science. [But] then when you realize what the solution is, you're on your own." Intervention was permitted as part of a study of mitigation strategies or if a test protocol called for it. In this way, they could drill some wells, hand out water filters, provide arsenic education. But for the most part, it meant looking for money anywhere and everywhere. Van Geen was in charge of mitigation strategies. "On every trip you say OK, how could we lower exposure? What can we do in the practical setting?" he says.

Early efforts were relatively low-cost. For example, HEALS helped label wellheads safe or unsafe so that villagers could easily tell the difference. Working with Columbia economists and NIPSOM researchers, van Geen and Graziano also organized a public awareness campaign involving parades and posters.[20] Dr. Hussain orchestrated an arsenic education program incorporating music and dance. Separately, with funding from an anonymous donor, the researchers drilled 50 deep wells to replace the medium depth wells that were contaminated in the Araihazar study area.

Results. As early as 2003, the Superfund projects in Bangladesh were yielding results in areas as diverse as geochemistry, hydrology, genetics, epidemiology, and children's health. For example, cohort studies like HEALS were intended to spark other ideas for ways to analyze the masses of data they produced. So in 2002, Ahsan had spun off a project looking for genetic and other biomarkers as well as susceptibility factors for arsenicosis. The small-scale study turned up some likely genetic suspects and led to a three million dollar grant from the National Cancer

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[19] London, Alex John, "Responsiveness to Host Community Health Needs" (2008). Department of Philosophy. Paper 402. See: http://repository.cmu.edu/philosophy/402.

[20] Malgosia Madajewicz et al., "Can information alone change behavior? Response to arsenic contamination of groundwater in Bangladesh," *Journal of Development Economics* 84 (2007), pp.731-754. The Columbia economists were Pfaff and Madajewicz (ref footnote 14).

Institute (NCI) for a larger study in 2004.[21] As part of the geology and geochemistry group's work on mitigation strategies, van Geen orchestrated the publication in 2006 of a Policy Forum in the journal *Science* demonstrating that the most effective way to stop people from drinking arsenic-contaminated water was to test existing water sources, label contaminated wells, and provide water from safe deep wells. They encouraged the drilling of deep community wells.[22]

Looking for BEST treatment options

By 2003, satisfied that the HEALS study was running smoothly and wouldn't require as much of their attention, Ahsan and Parvez began to look for opportunities to help study participants, "not only answering scientific questions, but also helping in resolving the potential public health impact of the problem in Bangladesh," recalls Ahsan. "We were looking at ways of countering the effects of arsenic poisoning in people with [pre-cancerous] skin lesions... who had already accumulated a critical amount of exposure."[23]

Ahsan and Parvez were aware of the common practice in Bangladesh of treating patients with antioxidants for various ailments. (Antioxidants are chemical compounds thought to protect cells from damage by unstable molecules, known as free radicals, which are released by oxidation.) The researchers also knew of several promising studies that suggested antioxidants might stop the progress of some arsenic-induced illnesses. But there had been no large-scale randomized trial of antioxidants' effectiveness in combating arsenic poisoning. They decided to try a small-scale pilot project to see whether administration of two antioxidants, selenium and Vitamin E, might arrest or slow the progress of arsenicosis.

Pilot study. The researchers decided on a six-month, 121-person study, a "two-by-two" randomized, double-blind trial. In a "two-by-two" trial, a quarter of participants are given substance A, a quarter substance B, another quarter substances A plus B, and the final quarter a placebo. Participants are unaware of what they're taking.

The pilot study showed that the antioxidants slightly lessened the severity of skin lesions.[24] It also demonstrated a suitable methodology for a larger trial. In 2004, Ahsan decided to apply to the National Cancer Institute for a grant to conduct a much larger cohort study. The NCI

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21 Habibul Ahsan et al., "Oxidative stress genes myeloperoxidase and catalase and susceptibility to arsenic-induced hyperkeratosis," *Cancer Letters* 2003; 201(1): 57-65.

22 M.F. Ahmed et al, "Ensuring safe drinking water in Bangladesh," *Science* 314, 1687-1688, December 15, 2006. See: http://www.ldeo.columbia.edu/~avangeen/publications/documents/Ahmed_Science_06.pdf

23 Authors' phone interview with Habibul Ahsan on January 23, 2012. All further quotes from Ahsan, unless otherwise attributed, are from this interview.

24 Verret et al, "A Randomized, Double-Blind Placebo-Controlled Trial Evaluating the Effects of Vitamin E and Selenium on Arsenic-Induced Skin Lesions in Bangladesh," *Journal of Occupational & Environmental Medicine*, October 2005 - Volume 47 - Issue 10 - pp 1026-1035

had recently funded an ongoing 35,000-person, North American trial of antioxidants' ability to lower the risk of prostate cancer, and it made sense to try the same treatment on arsenic-related skin cancer. In 2005, Ahsan and his collaborators won $10 million for the first five years of a planned 10-year study—the Bangladesh Vitamin E and Selenium Trial (BEST). The local partner was the International Centre for Diarrheal Disease Research, Bangladesh (ICDDR,B), whose ability to recruit allowed the researchers to expand the trial to 7,000 subjects from an original 4,444. Each partner would enroll 3,500 participants.

Testing an intervention. If mitigation was important in HEALS, an observational study, it was much more so in a clinical trial like BEST, and the researchers felt an extra obligation. Recalls Ahsan: "Because we are making them take vitamin E or selenium, which they would otherwise not have been taking, for 10 years, we must provide these participants arsenic free water." The design of the trial required that test subjects have access to drinking water with safe levels of arsenic, both for the sake of the scientific results and as a mitigation strategy. Drilling wells would be relatively expensive. The team looked for another route to safe water.

Filters. In the summer of 2006, another possibility opened up. Ahsan had just recruited epidemiologist Dr. Mahfuz Rahman, who had worked for the ICDDR,B, to join the BEST project. Through a friend who worked for UNICEF, Rahman learned that the UN agency would be distributing free water filters in the region. Parvez recalls that, with surprising ease, the agency agreed to distribute its filters to BEST study participants:

> It worked out well. We wanted to provide arsenic free water and they wanted a credible partner. We could also provide them with follow-up and feedback on the filters.

But winning funding and lining up the filters were only the first steps. The next was to recruit participants. That proved more time-consuming than anticipated. The criteria were: men and women between 25 and 65, not pregnant, with pre-malignant skin lesions. Importantly, they had to be willing to provide blood and urine samples. Field workers had believed that there were some 5,000 individuals afflicted with arsenicosis-related skin lesions among the HEALS cohort in Araihazar. As it turned out, there were only some 1,200. Apparently, villagers had been keen to enroll in BEST for the benefits, which included access to the health clinic, and may have overstated the incidence of symptoms.

The Columbia partner in BEST needed to find a total 3,500 participants. By 2006, they had lined up 870 in Araihazar, plus another 1,060 in neighboring Sonargaon. They needed another 1,500-plus. For advice on where to expand, the BEST team turned to its partner, ICDDR,B. BEST researchers also consulted with area non-governmental organizations (NGOs) and culled government health rolls. In early 2007, they added Laksam, a town of 60,000 (within an

eponymous sub-district of half a million) some 60 miles southeast of Dhaka. Laksam had a significant incidence of arsenicosis.

In March 2007, Dr. Talat Haider—who had already worked on BEST for a year in Araihazar—was made project director in Laksam. Together with two field supervisors and a research assistant, he moved to Laksam to begin recruitment.[25]

BEST intentions

Unlike Araihazar, Laksam was unfamiliar to the BEST researchers and their Bangladeshi staff. They had no local connections: the Bangladesh Medical Research Council, which had granted permission for BEST, had no local presence, and the local office of the Ministry of Health and Family Welfare wasn't much help. Nor did the government agencies work together effectively. Recalls Parvez: "The ministry is huge. It is more focused on running the national health system than [coordinating with] this small office of medical and ethical clearance" [BMRC]. Nonetheless, Haider and Parvez made the rounds of local officialdom, touching base with the health authority and the Department of Public Health Engineering (DPHE). The DPHE oversaw the public drinking water supply and had a natural interest in arsenic-related research projects. Parvez explains:

> By law you should contact your local medical authority or local governmental facility when you are doing a study, especially if you do something on a large scale in relation to arsenic.

Haider and the three field workers he had hired went first to the local hospital to put together a list of study candidates. They then plunged into the exhausting task of educating potential participants about the trial and trying to persuade them to take part. Several aspects of the trial protocol made it difficult to recruit subjects. For one, the area was culturally conservative. Women, for example, rarely left the house. That had implications for the study: it might be difficult to persuade women to contribute blood and urine samples. Another problem was what might be called research fatigue. Over the years, villagers in high-arsenic areas like Laksam had experienced drive-by visits from international research teams more interested in collecting samples and moving on than engaging with the community and addressing its need for safe water.[26]

For all these reasons, a priority was to find a local liaison—someone known and trusted by the community who could introduce the researchers and give the project credibility. Says Parvez: "In these situations, if you are an outsider and you don't know a lot of people, that will make you very nervous."[27] The researchers felt fortunate when Abdur Razzak contacted them in April 2007

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[25] The two supervisors were Binoy Datta and Sanowar Hassen; the assistant was Tarun Kanti Barman.

[26] Islam.

[27] Bowen telephone interview with Faruque Parvez, January 31, 2012.

about work. He was well connected locally, an experienced administrator who had worked on both government and NGO arsenic projects. He had heard of the BEST project and offered his services. Haider and Parvez hired him as local coordinator, helping to screen and recruit participants for the trial.

With Razzak to introduce them, the group began to approach village elders one by one. The elders in turn called meetings of the villagers, at which the BEST team explained the project. They then scheduled meetings one-on-one to go over details. Razzak was invaluable. Although barred from recruiting in his home village because another NGO was already conducting research there, Razzak knew many people in neighboring communities.[28] By the end of May, BEST had enrolled an additional 1,099 participants in Laksam. That brought the number near the required cohort of 3,500 from BEST, with another 3,500 supplied by ICDDR,B. BEST was fully launched.

At the urging of Bangladesh-Superfund Director Islam, the research team created a standard operating procedure for implementing the research protocol, and trained all project workers including field research officers, non-medical workers, and lab technicians. They also circulated the standard international Good Clinical Practice (GCP) guidelines among the medical staff and made sure that staff involved in every aspect of the trial understood and practiced them.

In June 2007, Haider appointed Razzak a village health worker, responsible for 40 or 50 study participants. Razzak was one of 233 field workers BEST hired to check on participants in other villages. Recalls Haider:

> We wanted our village health workers to visit each of the participants five or six days a week to know whether the participants were taking their pills regularly or not. And whether they had any health problems, whether they were visiting hospital, or anybody died. All that information was collected, almost each and every day of the week.[29]

Unfortunately, Razzak seemed to have some unacceptable ideas about his autonomy as a health worker. Haider had reports that Razzak was trying to divert and sell pills intended for BEST participants. The attempt was unsuccessful, because the supply was carefully tracked. Moreover, he may have been stymied by the fact that the pills were intentionally unmarked, so neither Razzak nor anyone else could tell a placebo from a functional pill. When confronted, Razzak pleaded a misunderstanding. Haider kept him on, but watched him more carefully.

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[28] The NGO conducting other research was Dhaka Community Hospitals.

[29] Kirsten Lundberg interview with Ahmed Talat Haider February 4, 2012, in Araihazar, Narayongonj, Bangladesh. All further quotes from Haider, unless otherwise attributed, are from this interview.

Meanwhile, under the agreement Parvez and Rahman had secured, UNICEF and the Dhaka-based consulting firm Participatory Management Initiative for Development (PMID), in August began to distribute for free the Sono water filters to BEST participants in Laksam who lacked access to safe water. PMID employees trained villagers how to use and clean the drip filters, which slowly and percussively yielded five liters a night. The distinctive filters included a red bucket for arsenic- contaminated water, which then filtered into a green bucket for safe water.

Razzak, however, again ran afoul of his BEST supervisors. In August, he sabotaged some of the filters, disabling them by removing some of the parts and claiming they were defective. Haider felt he had no option but to dismiss him, and by September Razzak was no longer with BEST. Haider thought no more about it.

Blindsided

After delays in setting up the BEST trial, by the fall of 2007 and winter of 2008 the fieldwork was generating a steady flow of data. Evidence of the antioxidant treatment's effectiveness would not be available for a number of years. But Parvez was glad to learn that both the US and Bangladesh data safety and monitoring boards (DSMBs), which kept tabs on the study as protocol required, found the trial was doing its subjects no harm. The filters, provided they were properly maintained and performed as designed, largely eliminated arsenic from water.

Thus in early March 2008, Haider was surprised when he read a story about BEST in a local paper which cast the clinical trial in a very unfavorable light The English-language *People's Daily View* in Chittagong on March 2 published an article titled "Not Drugs, but Arsenic-free Water Imperative." In it, the journalist accused BEST of poisoning subjects with capsules of arsenic-contaminated water.

The article invented several points, including a meeting—which had never occurred—of BEST researchers, a UNICEF representative and engineering and public health officials from Laksam. The story also referred to a press release by "the foreigners"—a press release BEST had never issued.[30] In another newspaper, study participants posed for photographs that ran next to stories claiming the villagers had been poisoned. The villagers later told Haider that reporters and photographers had promised the village new facilities if they would pose for pictures. Haider forwarded the articles to Ahsan and Parvez in the US.

At first, Ahsan and Parvez shrugged it off. It wasn't practical to respond to every misunderstanding, and they thought local staff should be able to handle any fallout. But some of the local journalists also wrote for national publications, which within a month picked up the story.

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[30] "Not Drugs But Arsenic-Free Water Imperative," *The Daily People's View, Chittagong*, March 02, 2008.

Locally, it was covered by papers like *Somoyer Dorpon, Laksam Barta,* and *Dainik Comilla* and nationally by *Jai Jai Din*, and *Dainik Dinkal*. The hostile articles included one on March 31 airing charges that BEST participants weren't getting promised medical care and were demanding an investigation into Columbia's actions. The articles also claimed that trial subjects had not been given contact information for Columbia officials.

Much of the coverage was negative and sensationalized. Some journalists pointed to the double-blind aspect of the trial as evidence that the researchers "don't know what they're providing," recalls Haider. Not all media took a negative view, however; a number of articles endorsed the project or provided neutral accounts of it. In April and May of 2008, local and national publications carried stories that detailed the extent of arsenicosis in the area and highlighted the project's mitigation efforts. One of these, an article in the May 8 edition of *The Daily Dinkal* titled "Hundreds Affected by Arsenic Exposure; Foreign Organizations Provide Help," informed readers that the researchers were working in 14 local villages, providing participants with free filters and medical screenings.[31] Haider says sympathetic reporters let the BEST team know what was going on behind the scenes in the local media.

Source. That information helped Haider track down the source of the stories: the disaffected village health worker, Razzak. Unbeknownst to BEST, Razzak had long been a distributor of water filters in Laksam. When BEST began to distribute the free UNICEF filters, Razzak saw his business dry up. He hadn't expected the researchers to be able to distribute filters for free. Recalls Haider: "It was beyond his thinking, because he sold the filters for 3,500 taka to 5,000 taka, a lot of money in Bangladesh." But at the time, Razzak didn't complain about the dent in his business. "Rather, he said that we were doing a great job," Haider says. "He said the fact that people are getting filters free of cost is great. We could not predict what he was thinking." Haider also learned belatedly that Razzak in previous jobs had allegedly stolen drugs and sold them on the black market, and charged previous study participants for drugs.

In fact, Razzak was resentful—especially after his dismissal. He had tipped off the press to his perverted version of BEST's activities. He also found other water filter merchants willing to line up behind him. With his strong family and business connections in the area, he began to turn community sentiment against the BEST project. Says Haider:

> He had a plan to bring down the program. He also went to local political and religious leaders. He persuaded two of the local religious leaders to speak against the program during Friday prayers, warning listeners they would not go to heaven if they participated in the study.

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[31] "Hundreds Affected by Arsenic Exposure; Foreign Organizations Provide Help," *Daily Dinkal*, May 8, 2008.

By mid-April, Razzak's campaign began to yield results. Bangladesh at the time was under an army-backed caretaker government. BEST opponents sent copies of the negative press to the local army base. That was troubling, but the worst was the effect on participants: a number of them expressed loudly their intention to withdraw from the study. "Our participants said they would withdraw. That would have been devastating," Haider says. "It was a very crucial moment. We were under very big pressure."

While relatively few of the 1,200 BEST subjects in Laksam actually threatened to withdraw, the publicity was highly damaging. As the situation escalated, recalls Parvez, "we really became nervous because we didn't want to stop this important trial, and we also thought of the safety of our staff," some of whom had received threats.[32] Nor was there much support from local authorities, he adds.

> Even if the local health authority wanted to help us, they really could not go against the will of the local political elite. Their position was very neutral. But at the same time we had a feeling they were much more siding towards [the local elites] because if you think of the power struggle, those guys were more powerful than us.

Superfund-Bangladesh Project Director Islam says the situation became even more confused when local reporters, who had started the controversy, made it clear that positive coverage could be bought. "They wanted cash, because many other NGOs, when they have any problems, they just pay something under the table to the journalist," he recalls. BEST, however, was not willing to do that.

Matters came to a head for Ahsan and Parvez when an anonymous correspondent in Bangladesh emailed complaints about BEST to the presidents of the University of Chicago and Columbia and the dean of the Mailman School of Public Health at Columbia, as well as the senior researchers.[33] The researchers found it disconcerting to see the campaign to discredit them brought to their institutional backyards. This prompted Graziano and Parvez to contact Columbia Associate General Counsel Edward Silver. With Silver on speakerphone in Graziano's office, the two explained the situation in Laksam and fielded the lawyer's questions. Parvez recalls:

> He wanted to know about BEST, how it was run. He said the university would get involved if there was a liability issue, if anyone was planning to sue. It was nerve-wracking at the time.

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[32] Authors' interview with Faruque Parvez on January 19, 2012, in New York City. All further quotes from Parvez, unless otherwise attributed, are from this interview.

[33] No one involved had retained a copy of the email.

On the ground in Bangladesh, Islam decided it was time to confront the criticism head on. He called a press conference for May 8, 2008. The BEST team had to decide who should speak for the researchers and explain the study. They also considered whom to invite onto a panel—which local officials with credibility could vouch for BEST? The public health researchers were not trained in managing a public relations crisis, and yet there was no one else to handle it. As Parvez puts it:

> I was not ready for this. You have to be very careful and ready for unexpected things to happen. It's hard to really draw a boundary. How many outside people do you involve into your projects? A lot of times, that can damage what you're trying to do. So you have to [introduce yourself and explain your activities], but at the same time, you have to have some sort of boundary. You have to maintain a working relationship, but at the same time, you don't get them involved in your project. These things aren't covered in any manual. It cost us sleep.