

## Chinese research register joins WHO network, raising hopes for improved clinical trials

China's acceptance, along with India, into the new WHO International Clinical Trials Registry Platform will help spur greater transparency and registration of research involving human's in the world's most populous country. But much work is needed to bring China's trial standards up to standard.

Chinese scientists for years have conducted unregistered clinical trials on humans that have raised concerns about the level of controls and transparency in place, as well as the kinds of safety standards available to trial subjects.

But the World Health Organization's July 2007 addition of recently launched Chinese and Indian registers into its new global clinical trial network has raised hopes that medical research standards would start benefiting from greater scrutiny.

The WHO International Clinical Trials Registry Platform was launched in May 2006 to bring different clinical trials registers from around the world into one network. It aims to increase the transparency and accountability of clinical research conducted by companies and institutions, and thus boosts public trust and confidence in that research. The initiative follows a number of high-profile cases in developed countries, where negative research results were withheld from the public.

China's new state-backed registry, known as the Chinese Clinical Trial Register, was launched in 2005 in response to calls for greater transparency of the clinical trial process in the world's most populous country. It is run by the Chinese Evidence-Based Medicine Centre, sponsored by institutions such as the state-run Sichuan University and Chinese Ministry of Health, and was designated by the government to join the WHO platform.

Associate Professor Taixiang Wu, administrator of the register, estimated at least 30 000 clinical trials

were performed annually in China, but information on them is limited. Since 2006, some Chinese researchers have been registering their trials at <http://www.ClinicalTrials.gov>, a web

site run by the United States of America National Institutes of Health, or at the International Standard Randomised Controlled Trial Number scheme sponsored by the Medical Research Council in England, which aims to simplify trial identification and improve reporting traceability. But despite this recent trend, most trials in China remain unregistered,

Wu said. Fewer than 300 current Chinese trials have been recorded in international registers that contributed research to WHO.

The new Chinese register "aims to help trialists (i.e. researchers) correctly report their trials to let the public know how the trial was planned and detail its results", Wu told the *Bulletin*.

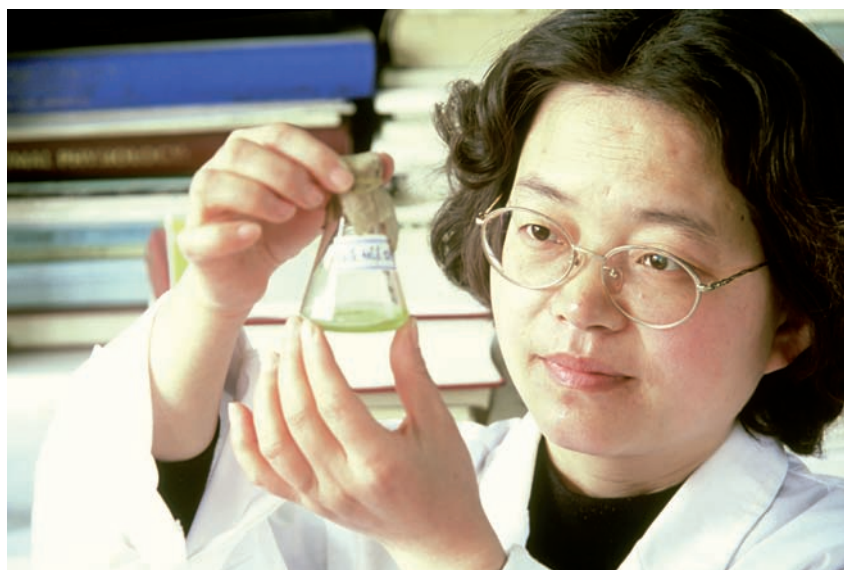
Its aim is to encourage widespread trial registration within China, a country where millions live in far-flung regions and where close scrutiny and consumer activism for improving medical procedures are weak. The Chinese register faced a "very big challenge", Wu acknowledged.

Dr Davina Ghera, WHO platform coordinator, said bringing China and India into the network was "extremely important because of the vast populations in those two countries, the amount of research that is being done there, and the need to meet the needs of the populations of the two countries".

"The sketchiness of information relating to trials in China deprives both the public and scientific community of potentially valuable information", Ghera said.

“ [The Chinese Clinical Trial Register] aims to help trialists correctly report their trials to let the public know how the trial was planned and detail its results. ”

Taixiang Wu, administrator of the register.



Keystone

The WHO International Clinical Trials Registry Platform has welcomed China's new state-backed registry, the Chinese Clinical Trial Register, into its network in a move to enhance transparency and strengthen standards surrounding clinical research in the world's most populous nation.

In some developed countries, editors of peer-reviewed medical journals have pressured researchers to publicly register their protocols and results. The International Committee of Medical Journal Editors, a group that represents the world's leading general medical journals, announced in 2004 that it would only publish results of clinical trials registered before the first patient's enrolment.

The new Chinese register wants to build consensus for such a move by enrolling the editors of 52 key Chinese journals in the Chinese Clinical Trial Registration and Publication Collaboration, which was formed in 2006.

The collaboration was established by the Chinese Evidence-based Medicine Centre, the Ministry of Health, the Chinese Cochrane Centre and the

International Clinical Epidemiology Network Resource and Training Centre of the West China Hospital. It aims to build an effective trial registration system by fostering agreement among key journals that only research relating to registered trials will be published. China has some 1100 medical journals.

Ghersi said China's government has supported involvement in the WHO platform to improve clinical trials. "Having a register in China supported by the Ministry of Health will give it the support

needed to successfully identify all the clinical research being done in China," she said.

In many developed countries, consumer activism has led to transparency, registration of clinical trials and improved standards governing them.

But this has not happened in China. Wu said that public consumer scrutiny of clinical trials helps promote these goals.

"Although consumer action in China is very young, I believe it will become stronger in the future", Wu said. "Joining the WHO (clinical trials) network will be very helpful in promoting such action to become a movement, and will feed back into promoting the rate of trial registration."

A Chinese advocate for patient involvement in improved clinical trials, Professor Mingming Zhang, said major obstacles, including large populations and poorly distributed health services, hindered public participation in efforts to raise research standards.

"The establishment of the Chinese Clinical Trials Register is a big step for those of us who understand why it is important", said Mingming, a member of the Cochrane Consumer Network Committee. "But Chinese patients know nothing about it at the moment, so raising awareness among the public is the first step." ■

Martin Adams, *Beijing*

“The sketchiness of information relating to trials in China deprives both the public and scientific community of potentially valuable information.”

*Davina Ghersi, coordinator of the WHO International Clinical Trials Registry Platform.*

## Marburg fever outbreak leads scientists to suspected disease reservoir

Uganda's rapid response to the recent fatal Marburg haemorrhagic fever outbreak not only stopped the spread in its tracks, but also raised hopes the discovery of the disease's reservoir, possibly in a bat-infested jungle mine.

The news reached Dr Sam Okware via a text message from the United States Centers for Disease Control and Prevention (CDC). "Marburg virus isolation confirmed by CDC lab in Atlanta. More later", read Okware, a senior epidemiologist and commissioner of health services at the Ugandan Ministry of Health.

The 30 July confirmation was, at that time, the latest in a chain of actions initiated by Ugandan authorities to contain what investigators suspected was a rare outbreak of Marburg haemorrhagic fever.

The disease emerged in two labourers who worked at a gold and lead mine in the western Ugandan jungle. One miner died on 14 July, while the other remains in quarantine. The two are the outbreak's only confirmed cases.

Within hours of the CDC message, Ugandan Minister of Health Dr

Stephen Mallinga issued a statement to Parliament. Uganda's health services director-general, Dr Sam Zaramba, issued another to the public through the media. On 9 August, Mallinga announced that the outbreak had been contained, but added that disease control activities would continue until the end of the month.

The World Health Organization (WHO) helped in the control effort through its Global Outbreak Alert and Response Network (GOARN) and the recently updated International Health Regulations (IHR), which led to neighbouring countries being alerted

of the outbreak's threat. WHO also dispatched a team of experts to Uganda to help in the control and detection of the disease reservoir.

"There is acceptability of WHO's capacity to respond (to outbreaks) in compliance with the International Health Regulations", said Dr Melville O George, WHO country representative for Uganda. "So there was no need for panic."

Besides quickly containing the outbreak, WHO investigators believed they were close to discovering the outbreak's reservoir, a first in the history of Marburg fever. "We believe the chances are very good, but we need to undertake more studies to be sure", Dr Pierre Formenty of WHO's Epidemic and Pandemic Alert and Response (EPR) told the *Bulletin* during an interview in Kampala.

The hunt for the fever's host shone suspicion on 5 million bats, plus rats, ticks and other wildlife, living in and

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WHO/Pierre Formenty

WHO scientists remove a bat captured in a net erected in a mine in western Uganda where the two miners, including one who died, infected in the recent Marburg fever outbreak had worked.

around the mine in the Kamwenge district of western Uganda's Kikasi Forest Reserve. One of the two miners was known to have skinned a colobus monkey. An infected monkey sparked the fever's first-recorded outbreak in a laboratory in the German town of Marburg in 1967. One line of investigation is to assess what link, if any, exists between the host creatures and primates, who do not survive exposure to the virus, and infected humans. Monkeys are often used as a source of food by humans in the Ugandan jungle.

Marburg virus, from the same family as Ebola, produces symptoms such as severe haemorrhaging, diarrhoea, nausea, vomiting, and chest and abdominal pains. Contact with bodily fluids of infected people during health care or burial procedures increases the risk of transmission. The disease is confined to a few African countries and the deadliest known Marburg outbreak killed nearly 250 people in Angola in 2005.

The latest outbreak emerged on 28 June near the Kitaka mine site

in Kamwenge. A 29-year-old miner rushed a workmate to a clinic who had been displaying fever and bleeding from all orifices of the body.

The sick miner, aged in his early 20s, was referred the next day to an area hospital and on 1 July was sent to Mulago National Referral Hospital in the Ugandan capital, Kampala. About a week later, the man was discharged from hospital after recovering.

But his friend was not so lucky. After his workmate was discharged, the 29-year-old miner visited a Kampala clinic suffering from similar symptoms and died days later. Ugandan authorities sent blood samples from the dead man to CDC, and acting on the suspicion

that they had a disease outbreak on their hands, began searching for the miner who had recovered.

During the search, investigators learned that two weeks before the younger miner had fallen sick; he had skinned a colobus monkey. The monkey's hide was traced to a Kampala suburb and sent to CDC Atlanta for analysis. The miner was eventually found heading back to his village, some 200 kilometres from Kampala, before being isolated and placed under observation. Investigators started identifying all people the two miners

had come into contact with and placed them in isolation for 21 days, the length of Marburg fever's incubation period.

“The Ugandan response was very transparent and what struck me was the openness of the Ministry of Health and how it worked with WHO, the international community and the media to deal with the outbreak.”

*Pierre Formenty of WHO's Epidemic and Pandemic Alert and Response.*

An outbreak taskforce was established, comprising experts from both the Ugandan Ministry of Health and Wildlife Authority, as well as WHO. Police officers joined with village council and district leaders to ensure compliance with quarantine orders. Experts are conducting tests at the mine and on the bats, rats and other creatures living there. The link, if any, between the wildlife at the mine and the outbreak has not yet been determined, but investigators are sending samples of the bats and other creatures to CDC for testing.

WHO's George said 55 suspected contacts had been isolated in Kampala together with another 58 miners in Kamwenge. The mine's owner said the site had been closed for decades before reopening earlier this year, George added.

The mine owner also told investigators that there had been past cases of people falling ill and dying from fever and haemorrhaging, according to Okware. The "strange" undiagnosed disease would kill up to four people before burning out on its own.

Formenty, of the EPR team, praised the response to the outbreak, saying it demonstrated the heightened



WHO/Pierre Formenty

A WHO scientist performs an autopsy on a bat captured inside a mine in western Uganda amid efforts to find the reservoir for the recent Marburg fever outbreak.

vigilance in controlling the spread of diseases in Uganda, which has witnessed outbreaks of Ebola and Marburg fevers in the past.

"The Ugandan response was very transparent and what struck me was the openness of the Ministry of Health and how it worked with WHO, the

international community and the media to deal with the outbreak", Formenty said. "We have been working with Uganda for a long time and it is clearly one of the most advanced countries for IHR implementation." ■

Carolyne Nakazibwe, *Kampala*

## War-scarred Iraqis face health burdens in foreign lands

More than 2 million Iraqis have fled their war-ravaged country since 2003, with most taking refuge in neighbouring Jordan and the Syrian Arab Republic. A recent WHO-hosted regional consultation highlighted the new troubles faced by many of those displaced, including limited access to health care in their host countries.

Adel Abdel Jabar found the chilling message on his car windscreen one morning. "You're a dead man." That was enough for him to leave his job as a translator with the coalition military in the southern Iraqi city of Basra, and flee with his wife and two sons into neighbouring Jordan.

But the 45-year-old's problems didn't stop once he arrived in the Jordanian capital of Amman in December 2006. "We sold the family car and we've been living off of that money, but it is running out", Abdel Jabar told the *Bulletin*. "I have another problem though, a huge problem. I was diagnosed with bladder cancer in Jordan and although I have undergone several operations the doctor says it is not completely removed."

Like many other Iraqis who have sought refuge in Jordan, Abdel Jabar is unemployed and cannot pay for needed health care.

Many Iraqis in Jordan and the Syrian Arab Republic suffer from chronic diseases such as high blood pressure, cardiovascular disease and diabetes, said Dr Ala Alwan, World Health Organization (WHO) Assistant Director-General.

Iraqis receive no special discount or consideration at state-run Jordanian health facilities, paying the

same as any Jordanian or other foreigner in the kingdom. "Iraqis in Jordan are provided with the same medical care as Jordanians who do not have insurance", said chief Jordanian government spokesman Nasser Judeh.

Demands for health care and other services needed by displaced Iraqis in neighbouring countries are placing huge strains on their host states. A WHO-organized conference held 29–30 July in the Syrian capital, Damascus, discussed these issues and sought ways to improve access to services. The meeting was attended by health and foreign affairs officials from Iraq, Egypt, Jordan and the Syrian Arab Republic, the latter three countries hosting the bulk of more than 2 million Iraqis who have fled their homeland since the war began in 2003.

“We live in tension from the ordeal we experienced. All Iraqis have psychological illnesses stemming from the stressful circumstances we faced and the life we now live.”

Displaced Iraqi woman Fawzi Hussein Yassin, 64.

Representatives of UN agencies, and the Red Crescent Societies of Jordan and the Syrian Arab Republic also attended.

The host nations agreed that displaced Iraqis should have the same access to health services as their own populations. Alwan said this was a major commitment that required extra resources for the health sector. Participants agreed to seek additional funding from the international community and the Iraqi government, which has already promised its support.

Alwan said the most urgent priority is to ensure access to primary health care, including preventive and curative treatment; maternal and childhood medical services; emergency care; and provision of essential drugs and medical supplies.

“All displaced Iraqis living outside Iraq should be able to freely and safely return to Iraq in due course, so the strategy for meeting their health-care needs in host countries should be seen as a temporary one”, Alwan, a former Iraqi minister of health, told the *Bulletin*. “Meanwhile, the international humanitarian community and Iraqi government must support countries like Jordan and the Syrian Arab Republic to enable their health systems to address the increasing burden of providing health services for displaced Iraqis.”

The Iraqi Red Crescent office in Amman said the governments of Jordan and other host countries are waiting for Baghdad to pay the US\$ 25 million pledge it promised to assist displaced Iraqi civilians, particularly in the health sector.

Jordanian spokesman Judeh said the presence of some 750 000 displaced Iraqis was straining the kingdom's infrastructure. Another 1.4 million



Nader Daoud

A family of displaced Iraqis at a makeshift camp on the Jordanian side of the desert frontier with Iraq. More than 2 million displaced Iraqis are requiring health care from host countries, placing increased burdens on strained health sectors in nations like Jordan and the Syrian Arab Republic.

Iraqis have moved to the Syrian Arab Republic since 2003, with substantial numbers arriving in Egypt, Islamic Republic of Iran, Lebanon and Turkey. More than 50 000 Iraqis continue to leave their homeland monthly, mainly to Jordan and the Syrian Arab Republic, according to the United Nations High Commissioner for Refugees (UNHCR).

“This has put an incredible burden on the Jordanian economy in terms of health, food, medicine, education, infrastructure and resources”, Judeh said.

Abdel Jabar has spent most of his money on chemotherapy and needs additional treatment, including complicated surgery. International Catholic relief agency Caritas provided financial support for his initial treatment, but the Iraqi said he needed 6000 to 8000 Jordanian dinars (US\$ 8470 to US\$ 11 290) for further treatment. “This is beyond my capability and Caritas

cannot fund it”, he said. “I am praying that the UNHCR can help.”

Caritas worker Hania Bisharat said her agency only helps Iraqis living on under US\$ 80 per month. Last year, Caritas provided some 3000 displaced Iraqis with medical treatment and has helped a similar number so far this year.

Other governmental and nongovernmental aid agencies, such as the Iraqi and Jordanian Red Crescent Societies, Medicines Sans Frontières and Care International, provide additional medical services and other assistance to Iraq's displaced.

At a Caritas clinic in Amman, Iraqi woman Fawzi Hussein Yassin waited with her husband, Ahmed, 64, who still receives treatment for bullet wounds suffered after being shot by militants in Baghdad, an attack that prompted them to flee to Jordan in February.

“The situation is drastic in Iraq and it's worsening”, the wife, wearing a black headscarf, said. “We live in tension from the ordeal we experienced. All Iraqis have psychological illnesses stemming from the stressful circumstances we faced and the life we now live.” ■

Dale Gavlak, *Amman*

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