

► unscientific,” says meteorologist Madhavan Nair Rajeevan, secretary of India’s ministry of Earth sciences, which oversees the country’s meteorological institutes. Computer models and meteorological forecasts are used in Europe and the United States to predict the rate at which water flows into reservoirs and how much water needs to be stored — but few authorities in India use such systems, says Rajeevan. He suggests that prediction systems should be introduced across India.

An increase in development over the past two decades in the Western Ghats — a large mountain range that runs parallel to India’s west coast and across several states — might also have exacerbated the flooding, say several Indian scientists. “The land and soil disturbances have triggered landslides and blocked streams, contributing to the floods,” says Madhav Gadgil, an ecologist at Goa University in Taleigão.

In 2011, Gadgil headed a committee that investigated environmental damage from unsustainable development and illegal mining in the Western Ghats. The committee recommended that the entire mountain range be declared “ecologically sensitive” — it contains 30% of India’s plant, fish, bird and mammalian species — and that mining and the construction of dams and coal-fired power plants be banned to conserve biodiversity.

But the government ignored the report’s recommendations. Instead, in 2013, it accepted the advice of another committee, which suggested that only 37% of the Western Ghats be made off-limits to mining and construction.

Gadgil says that the state governments have continued to approve infrastructure projects across the Ghats, including dams, power plants and buildings, many without reliable environmental-impact assessment reports. “There has been a proliferation of building and road construction,” he says. He adds that there’s also been an increase in illegal mining.

Jason von Meding, who studies disaster risk-reduction at the University of Newcastle in Australia, says the government should explain why it rejected the Gadgil-committee report, which emphasized the need to curb development excesses and focus on conservation. “Uncontrolled mining, dam construction, deforestation and poorly planned construction have multiplied the risk of flooding and landslides in recent years,” he says.

Earth scientist Rajiv Sinha at the Indian Institute of Technology Kanpur also points to an increase in the numbers of canals and bridges, which can reduce the width of rivers, leading to a build-up of sediment that slows water flow. After a sudden downpour, there is not enough space for the water, so it floods the surrounding area, “leading to disasters like the one we are witnessing in Kerala,” says Sinha. India’s poor infrastructure planning will be exacerbated by its vulnerability to extreme rainfall events, which are projected to happen more frequently as a result of global warming, he says. ■

## PUBLIC HEALTH

# Experimental Ebola drugs face tough test

*Researchers are devising a clinical-trial protocol to test three medicines in Africa’s latest outbreak.*

BY AMY MAXMEN

Health workers fighting the ongoing Ebola outbreak in the Democratic Republic of the Congo (DRC) have given nearly 20 people experimental drugs to treat the virus since mid-August. But because the drugs have been dispensed on a case-by-case, ‘compassionate use’ basis, it is hard to know whether any are effective. Now, desperate to determine which therapy works best, researchers from the DRC and US governments, the World Health Organization (WHO) and other groups are meeting to plan a clinical trial that will compare multiple drugs as the outbreak continues.

For ethical reasons, the trial scientists do not intend to give any study participants a placebo. Instead, they hope to compare the two experimental medicines already in use to ZMapp, an antibody therapy that showed promise three years ago during a major Ebola epidemic in West Africa (The PREVAIL II Writing Group. *N. Engl. J. Med.* 375, 1448–1456; 2016). Patients in the coming trial would receive one of these three drugs at random. The study design draws on a flexible clinical-trial framework that the WHO expects to unveil this week. The framework is intended for use in multiple Ebola outbreaks, to produce data that can be pooled over time.

The scientists working on the DRC trial hope to launch the effort in the coming weeks. “A clinical trial will give us the scientific evidence we need,” says Jean-Jacques Muyembe-Tamfum, director-general of the National Institute for Biomedical Research in Kinshasa, which will lead the study.

But planning for the trial is complicated by the realities of working in the DRC’s North Kivu and Ituri provinces, where fighting has killed more than 5 million people over the past two decades. Instability in the region could prevent clinicians from carrying out their work. “Armed groups can do what they want,” Muyembe-Tamfum says.

The current outbreak began on 1 August, and has grown to include 115 confirmed and probable cases of Ebola — including 77 people who have died, the DRC health

ministry said on 28 August. Public-health workers have vaccinated 4,645 people, and doctors have given 3 people the antiviral drug remdesivir, made by Gilead Sciences of Foster City, California. Another 13 patients have received mAb114, an experimental treatment derived from antibodies found in the blood of a person who contracted Ebola in 1995 and survived.

That swift response is a major shift from the handling of the Ebola epidemic that struck West Africa in 2014. Experimental drugs were not used widely in West Africa then because there was no proof of their safety or efficacy — clinical trials did not begin until the outbreak was near its end. That delay helped to drive the death rate among Africans infected with Ebola to 63%. But several Westerners infected with Ebola received the nascent therapies at top hospitals; the fatality rate for this group of patients was just 18%. This disparity eventually prompted the WHO to develop guidelines aimed at ensuring wider access to experimental treatments during future Ebola outbreaks.

But the only way to determine how well a drug works is through a randomized, controlled clinical trial. Thus far, researchers have not managed to complete a trial of any experimental Ebola drug, because outbreaks of the disease have ended before enough patients enrolled. So the WHO has been working with international experts to create a basic trial design that can be adapted as data accumulate and logistical challenges change.

Muyembe-Tamfum says that the trial being planned now will use that framework, and is likely to test mAb114, remdesivir and ZMapp, made by Mapp Biopharmaceutical in San Diego, California.

Stationing a large number of medical professionals in an Ebola unit now is particularly fraught because there are more than 100 militias roving the eastern DRC. If armed groups show up at a treatment centre, workers might flee rather than risk their lives — and any trial could stop. But Ana Maria Henao Restrepo, who helps to lead the WHO’s Ebola Research and Development team, is unfazed. “Every trial has its own challenges,” she says. “That’s why we are coming out with an approach that’s flexible.” ■