Not a statistic. An 8-month-old girl is buried in the Democratic Republic of the Congo. Most deaths in the world aren't officially recorded.

How Do You Count the Dead?

Scientists agree they need better estimates for the death toll from the world's major killers. But they fiercely disagree on how to go about it

ONE OF THE BEST WAYS TO HELP THE living, says Prabhat Jha, is to count the dead. Understanding how many people die of which causes is invaluable for designing effective public health programs, says Jha, a global health expert at the University of Toronto in Canada. That's why he started an ambitious research project in India called the Million Death Study, which aims to record the causes of death for 1 million Indians between 1998 and 2014.

But counting the dead can be extremely difficult. The problem is that most of the world's deaths occur in places with few or no hospitals or doctors to record deaths and their causes. Last month, for example, an international research group published the latest statistics on global child mortality in *The Lancet*. They estimated that 7.6 million children under age 5 died in 2010, well over half from infectious diseases. But fewer than 3% of those deaths were medically certified—assigned a cause by a health worker and recorded in an official database. For the other 97%, the scientists are forced to make sophisticated guesses.

In doing so, they extrapolate from a patchwork of survey data, incomplete records, and research studies. Various groups use different statistical methods, however, sometimes resulting in very different numbers that are hotly debated. One study published in *The Lancet* in February, for example, found that 1.24 million people died from malaria in 2010; that's more than twice the estimate from the World Health Organization (WHO). Reactions from some in the malaria community were swift and harsh. "In terms of credibility I think public health science has been done a disservice by this paper," says Robert Snow, a veteran malaria epidemiologist at the University of Oxford in the United Kingdom and the Kenya Medical Research Institute in Nairobi.

Online
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Podcast interview with author Gretchen Vogel (http://scim.ag/pod_6087).

The paper was only a preview of a much larger project counting deaths and disease prevalence by the Institute for Health Metrics and Evaluation (IHME) at the University of Washington, Seattle. The Global Burden of Disease, Injuries, and Risk Factors 2010 (GBD 2010) study is the most massive study of deaths and disease ever undertaken. It involves more than 1000 researchers and aims to assemble the cause of 1 billion deaths worldwide going back to 1980. It will be published in a series of papers later this year and is likely to trigger new debates.

Some say that's necessary and healthy. "It's always worth looking at different approaches," says Ties Boerma, director of measurement and health information systems at WHO. "We're all trying to make the best of incomplete and inaccurate data." Others worry that the sharply diverging estimates and the bickering will erode policymakers' trust in science. "Can you imagine if I'm a minister of health in a country and am faced with new numbers every 2 years?" asks Zulfiqar Bhutta, an expert on maternal and child health at Aga Kahn University in Karachi, Pakistan. "At some stage we've got to stop confusing people."

Patchy data

In the case of IHME's malaria study, the large gap between its estimate and WHO's was mainly due to one category: deaths of youth and adults in Africa. WHO estimated that in 2010, malaria killed 55,000 Africans over the age of 5; the IHME team concluded that the number was 435,000. Snow says that although WHO's numbers are too low, IHME's estimates, especially for adult deaths in Africa, are far too high. He notes that in several countries that keep very good records for malaria, such as Swaziland and Djibouti, IHME's formulas count more deaths than

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documented malaria cases, a sign that they're fundamentally off.

The number of adult deaths surprised the IHME team as well, says epidemiologist and health economist Stephen Lim, the study's lead author. "There's lots of uncertainty," he concedes. "The data are patchy, particularly in the hardest-hit areas." However, after reexamining their data, the researchers remain convinced that their conclusions are on target. "Reasonable scientists will differ on a given point based on the evidence they have," says epidemiologist and global health expert Alan Lopez of the University of Queensland in Brisbane, Australia, another co-author. "We do not know who's right. We are simply following our evidence."

There is more at stake than academic reputations. Global health estimates help determine where billions of dollars in health funding goes. Campaigners use them to justify public health spending on certain causes, such as measles immunization campaigns or AIDS prevention. The numbers also help to measure whether a campaign has made any difference, and they are one of the ways policymakers determine whether they are spending their money wisely.

To understand how death-count studies can reach strikingly different results, consider one example. Suppose you're trying to find out how many people were sickened and killed by, say, pneumonia in Tanzania. The government's records of births and deaths are incomplete; only 17% of Tanzanian births are registered with officials, Boerma says. Hospitals have records, but they're not always accurate and up to date. Most important, most pneumonia patients never come to the hospital. They die at home without seeing a doctor who can make a diagnosis.

So health metrics experts gather the best data they can, first from government and hospital records, and then from surveys, clinical studies, or any other possible source. Birth history surveys, for example, ask women not only how many children they have but also how many times they have given birth, which helps identify children who were born and died without ever being noted in official records. In a technique called verbal autopsy, trained field workers ask relatives of a deceased person a standard series of questions and record a short narrative of events leading up to the death. Physicians—or sometimes computer programs—evaluate the information and assign a likely cause of death.

Researchers feed all the numbers into computer models that use sophisticated statistical techniques to fill in the gaps. Data on related circumstances such as rainfall, availability of clean water and health care, vaccine coverage, and mosquito densities—as well as data from nearby or comparable regions—all help the programs to churn out their estimates. The algorithms can fill in gaps in time as well as space. Data collected 5 years ago in one country can be combined with recent numbers from comparable sites to calculate current estimates.

Crunching the numbers

For their malaria estimates, Lim and his group generated thousands of models, which gave slightly different weights to various data sets. They then probed the models' accuracy by removing a subset of the data and testing each model's ability to predict the missing numbers. They used the same method to test so-called ensemble models, which combine individual models in different ways.

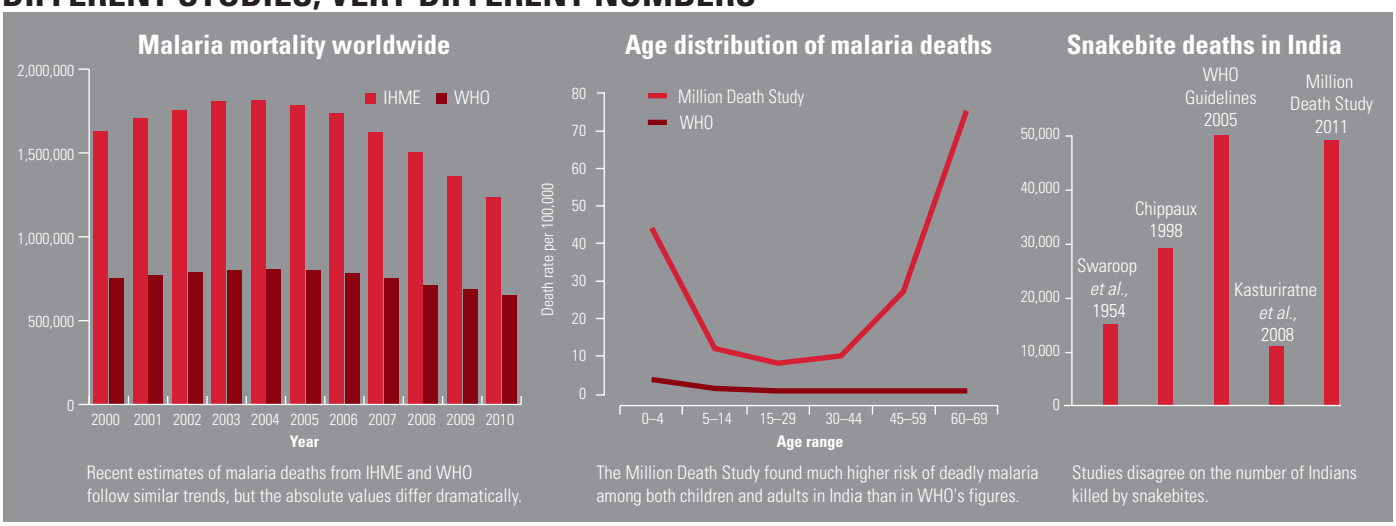
IHME's mathematical prowess is undisputed. "Their work has transformed the way we think about the metrics of disease," Snow says. Their approach "can be quite helpful: Gather all the data you can and see what they say," adds Ramanan Laxminarayan, director of the Center for Disease Dynamics, Economics & Policy in New Delhi and Washington, D.C. But powerful computers can't make up for data that are simply too sparse, Laxminarayan says. The result "has to fit with some sort of on-the-ground validation." For example, those who dispute IHME's malaria findings note that in the hardest-hit regions of Africa, most adults develop partial immunity to malaria, so a new infection is rarely deadly. If IHME's numbers are right, they would throw doubt on decades of malaria immunology and epidemiology, Snow says.

The controversy stems primarily from IHME's choice of data sets. The team made a systematic effort to find as many verbal autopsy studies as possible, turning up thousands of studies. They then used computer programs to adjust for misclassified or unclear causes of death. But many researchers question whether verbal autopsies are a reliable way to measure malaria deaths, especially in adults.

Even when a patient is alive, lab tests are often the only way to tell whether a sudden fever is caused by malaria, dengue, meningitis, or Japanese encephalitis. Some scientists contend that an accurate diagnosis based on a family's description of symptoms weeks or months after a death is impossible. "The tool is blunt," Snow says. For determining whether an adult fever death was due to malaria, "it is probably as good as flipping a coin."

Jha counters that even if diagnosing an individual fever death as malaria is unreliable, researchers can check the population-level

DIFFERENT STUDIES, VERY DIFFERENT NUMBERS



Recent estimates of malaria deaths from IHME and WHO follow similar trends, but the absolute values differ dramatically.

The Million Death Study found much higher risk of deadly malaria among both children and adults in India than in WHO's figures.

Studies disagree on the number of Indians killed by snakebites.

SOURCE CREDITS (LEFT TO RIGHT): IHME AND WHO *WORLD MALARIA REPORT 2011*; CENTER FOR GLOBAL HEALTH RESEARCH, UNIVERSITY OF TORONTO; SWAROOP *ET AL.*, BULL WORLD HEALTH ORGAN.; CHIPPAUX, BULL WORLD HEALTH ORGAN.; *GUIDELINES FOR THE CLINICAL MANAGEMENT OF SNAKE BITES IN THE SOUTH-EAST ASIA REGION*; WHO REG OFFICE FOR S.E. ASIA.; KASTURIRATNE *ET AL.*, *PLOS MED.*; MOHAPATRA *ET AL.*, *PLOS NEGL. TROP. DIS.*

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results by looking at the proportion of fever deaths that were caused by various diseases, taking into account other factors such as parasite prevalence or viral transmission patterns. Lim's IHME colleagues have conducted several studies to find out how accurate verbal autopsies are. In those analyses, Lim says, verbal autopsy actually seems to underestimate malaria deaths.

WHO, in contrast, uses verbal autopsy data primarily for malaria deaths in children younger than 5 and in areas of low malaria transmission. (Most researchers agree that among common childhood diseases, malaria is distinct enough that verbal autopsy data are reliable.) WHO's main source of data are national registration and hospital records, which most experts say vastly undercount malaria deaths. For adult deaths in regions with heavy malaria burdens, WHO estimates the number of people living in areas with high, low, or no risk of malaria and uses mathematical models to extrapolate death rates based on the childhood numbers.

Filling the gaps. A field worker in Bangladesh trained to conduct verbal autopsies asks a relative of a deceased person about the circumstances that led to the death.

Epidemiological terrorism

WHO's methods receive plenty of criticism as well, and IHME's malaria numbers are not the first to diverge from WHO's estimates. Jha's Million Death Study, carried out with Indian colleagues, has also come up with significantly higher death totals, especially among adults. The researchers are monitoring 14 million people in 2.4 million Indian households that constitute a statistically representative sample of the population. Surveyors visit regularly to record births and deaths; if they hear of a recent death, a second field worker conducts a verbal autopsy. Two independent physicians evaluate the information and assign a cause of death. If they disagree, a third physician decides.

Local support for the project "was phenomenal," Jha says. "We throw these mortality numbers around. But for the families, [each death] is a tragedy"—and in many cases, the survey is the first time someone with authority is paying attention. "These invisible deaths become visible."

Jha likes to refer to his work as "epidemiological terrorism," because it tends to explode public health experts' assumptions. For malaria, the team put India's annual death toll at 200,000 in a 2010 publication—more than 13 times WHO's estimate—with most deaths occurring among people aged 15 and older. Those numbers were controversial, but many experts said they could be plausible; malaria rates are lower in India than in sub-Saharan Africa, so adults have less natural immunity and are at greater risk of dying.

Disputes about numbers aside, the study is revealing important patterns that can help policymakers, Jha says. In April 2011, the group reported that an estimated 50,000 people per year in India are dying of snakebites. (Other estimates had suggested it was 50,000 worldwide.) The country's snakebite deaths were concentrated in certain areas, the study found—an estimated 8700 occurred in the state of Uttar Pradesh alone. That suggests directing antivenom supplies to high-risk areas could save lives.

The study has also found dramatic regional differences in death rates from cervical cancer, the leading cause of cancer deaths among Indian women. Rates in Muslim-majority areas are significantly lower than in Hindu-majority regions, perhaps because male circumcision reduces the risk of sexual transmission of the human papillomavirus (HPV), which causes cervical cancer. It also suggests, Jha says, that focusing HPV vaccination campaigns in high-prevalence regions might have the most effect. "None of these questions were hypothesized when we started the Million Death Study," he says.

More feuds expected

The global health community is bracing for more explosions when the GBD 2010 results are published later this year. IHME plans to release complete and comparable estimates for the global death and disability caused by more than 200 conditions in 1990, 2005, and 2010. Observers from many fields "will see patterns and results that are surprising," Lopez promises. New feuds are sure to result.

Everyone agrees that the way to resolve those fights is to collect more complete information on the ground. "There is much more expenditure on places like IHME that are taking the data and churning them through black box models" than on strengthening reporting systems, Laxminarayan says.

But so far, several attempts to improve the developing world's health record-keeping have come up short. In 2005, the Bill and Melinda Gates Foundation and WHO established the Health Metrics Network (HMN) to strengthen national health information systems. That's the right goal, says Kenneth Hill, a demographer at Harvard School of Public Health in Boston; improving civil registration systems is "where the world needs to go." It's not there yet, however. "It's safe to say HMN has been a complete failure," Hill says. "We really don't know how to improve registration systems. There hasn't been enough systematic research."

In countries without strong central registration systems, families and community officials have few incentives to register births or deaths, he says. "In most developing countries, bureaucracy is awful. Digging a hole is a hell of a lot simpler" than registering a loved one's death with local authorities.

There are some positive signals, however. New technologies—cell phones and Internet access—are starting to have an impact, Snow says. "People are beginning to send real-time information to health authorities," he says, and the supply of commodities to manage malaria, such as drugs and diagnostic tests, are now tied to providing reliable stock and disease information.

Such information could help researchers come closer to a set of numbers they all can agree on. In the meantime, Jha hopes policymakers will see good news in a few things all studies agree on: for instance, that malaria deaths, especially among children, have fallen thanks to control programs. Similar success is possible if authorities take adult malaria seriously, as well, he says: "That message was a bit lost in the shouting about the numbers." **–GRETCHEN VOGEL**

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