AUTHOR COMMENTARIES - From Special Topics

Tuberculosis - January 2009
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Mario Raviglione
From the Special Topic of Tuberculosis

According to our Special Topics analysis on tuberculosis (TB) research over the past decade, the work of Dr. Mario Raviglione ranks at #9 by total citations and #7 by citations per paper, based on 49 papers cited a total of 3,593 times. Three of these papers are also on the list of the most-cited papers in this topic. In Essential Science Indicators℠ *from Thomson Reuters, Dr. Raviglione's work can be found in the field of Clinical Medicine.*

Dr. Raviglione is the Director of the Stop TB Department of the World Health Organization, a position he has held since 2003. He is also the recipient of the Princess Chichibu TB Global Award from the Japan Anti-TB Association.

In the interview below, ScienceWatch.com *correspondent Gary Taubes talks with Dr. Raviglione about his highly cited work on TB.*

SW: Your most-cited article in our analysis is a 1999 *JAMA* paper on the global burden of TB (Dye C, *et al*., "Global burden of tuberculosis—estimated incidence, prevalence, and mortality by country," *JAMA* 282[7]: 677-86, 18 August 1999). Do you consider this to be your most significant contribution to TB research?

Actually, a *JAMA* paper I wrote in 1995 may be in its way more important. I wrote this earlier paper with Dixie Snider, who was at the CDC at the time, and Arata Kochi, who was director of the TB program at WHO. The 1995 paper was called "Global epidemiology of tuberculosis—morbidity and mortality of a worldwide epidemic," (Raviglione MC, Snider DE, Kochi A, *JAMA* 273[3]: 220-6, 18 January 1995) and it was actually what turned our knowledge of TB around. It is the one that, more than any other paper before, announced to the world the global problem of TB and that of multidrug-resistant TB and it did so by being in a highly visible journal like *JAMA.* That paper was among the most-cited papers I have—it's still cited today—and it ended up in the *New York Times,* making the global TB situation better known to the wide public

You have to realize that at that time the management was really not keen about the idea of having WHO staff publishing peer-reviewed papers. This paper actually changed the environment. The debate at the time in WHO was whether we should write peer-reviewed papers for scientific journals as though we were academic experts, or should we merely be officers who do administration and simply convene other experts who write the papers. Even in the TB program this debate was going on. Is it cost effective for WHO staff to work as though they're academicians writing peer-reviewed articles?

When that *JAMA* paper came out in 1995, it made people understand the importance of scientific communication. We all realized that by

writing a scientific paper like that and getting it published in a journal like *JAMA* we could get to the front page of the *New York Times* and people would suddenly pay attention to the problem we were discussing. It was far more effective than, for instance, paying hundreds of thousands of dollars to do advocacy and communications based on anything rather than science. The realization was quite clear that if we publish in highly visible journals like *JAMA,* we get the advocacy and communication free of charge, in a way, by getting directly to the front page of major newspapers. That was a very important understanding. At that point we really started targeting more and more visible journals any time we had an important paper or an important topic to discuss and disseminate.

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A field visit in Swaziland, at the tent of a MDR-TB patient living in the bush and attended by a Faith-based organization.

SW: What prompted you to start calculating the global burden of TB as you did in the 1999 *JAMA* paper?

This was actually a repeat of an exercise we also did a few years earlier, which we also published. The earlier one had a less complex methodology, but it was the first to use a simple mathematical model to assess the global burden of TB, in the sense of global estimates of TB morbidity and mortality, the association between TB and HIV/AIDS, and so forth. Our intention was to communicate widely about the burden of TB in the world.

We repeated this exercise again in the 1999 *JAMA* paper, and then again every two to three years. On those papers I worked primarily with our team previously headed by Chris Dye, who is a mathematical modeler and epidemiologist. That team has done a huge amount of work on the TB epidemic, using the statistics and data we receive and putting them into a mathematical model that can derive quite important conclusions about how we might handle the TB problem.

SW: Can you tell us how the model and its conclusions influence your actions at WHO?

Before making policies about intervention we often, if not always, study the potential implication and impact on the TB burden. Let's say we have two or three interventions we could use. These models tell us which is likely to be the most cost effective. If we do this particular prophylaxis or treatment, for example, how much TB is it going to be cut in the next, say, 10 or 20 years? Then we can apply cost-effective analysis and economic analysis to these epidemiological exercises and projections. Now we can say not only will this intervention cut the number of deaths by x percent, but it will eventually cut costs by y percent. This kind of analysis is now done regularly in our program.

SW: How has the state of our knowledge about TB evolved in the last decade?

First of all we have better understanding of the disease epidemiology. The more we improve surveillance methods in countries, the more data we collect, the more countries themselves improve and report on TB, the better we get in terms of estimating the global burden. So now we're more confident about the quality of what we're saying.

What we can conclude now, from a number of different exercises, is a consistent number—about 9 million cases of TB a year, and 1.7 million deaths. We've also seen that the TB epidemic may have actually peaked in 2004. The absolute numbers might give the impression that it is still growing or is being stagnant, but that's because population growth is more rapid than the decline in rate per capita. What we think today is that rate per capita may be coming down all over the world, even if the absolute number of cases keeps growing, although very slowly.

By mid-January 2009, we finished our latest assessment, and this is still the feeling we have, as we said in our latest Global Report published in March 2009. That's a big difference from earlier in the decade, and we think it's due to the expansion worldwide of TB prevention practices. As a consequence we may now actually be seeing some impact in the actual burden of disease.

SW: What is the most challenging aspect of doing this kind of global TB epidemiology that you've been doing at WHO?

In a way, as the person responsible for the global TB program, the most important and challenging thing is to be constantly up to speed with the literature and where the science is moving. In other words, as director of the WHO program, I'm not just a manager; I'm directing a huge operation and must study the technical and strategic directions. The direction itself is what we announced in a *Lancet* paper in 2006 when we presented the new Stop TB Strategy, but I still have to keep up with the literature to allow us to

adjust, innovate, and change direction appropriately as new challenges emerge.

The latest challenge, for example, is XDR-TB—extensively drug-resistant tuberculosis, which is just what it sounds like. The first description of XDR-TB was in March 2006. Since then, there has been a mushrooming of papers about XDR-TB all over the world. This is the latest challenge, and we have to be on top of it—we have to be at the forefront when it comes to global policies, surveillance, data analysis, and so on.

"In the global village that we now live in, we can't stop TB at the border."

It's also critical for us here to maintain a certain level of credibility in our research, because we're not in academia but we want our work to be taken seriously and have the necessary impact. If you look at your list of the top 20 authors in TB, you'll find that Chris Dye, myself, and maybe one more are the only ones not formally involved in academia and basic research. Most of the most highly cited papers are on very basic research, and most of the authors do basic research. So in WHO, getting back to this point, we have to maintain the credibility of our program and the people working here, and one way to do that is to be active in the scientific literature.

SW: What would you like to convey to the general public about your work?

Well, the big issue is that TB is a major disease, second only to HIV/AIDS in terms of the number of deaths a year from a single infectious agent. TB kills over 5,000 people a day; 1.77 million a year. That's an enormous number of people. Now consider how much press is given to avian flu, for instance, which might have killed 200 people so far. Or even SARS, which killed a bit more than 1,000 people altogether—or less than a fourth of what TB kills on a single day. The problem of TB is not often seen from this perspective. There are people who say that if SARS struck again today and killed 4,000 people, you'd have a public health revolution in the world with all leaders in the forefront to mobilize money and resources. For TB, only very few care. Humanity has been living with TB for a millennia. It's not a story. Why bother? That's exactly the attitude we're facing all the time. Let alone the sense that TB is a disease of the past and that is extinct in this world. This is a constant question by media when they discover that it kills in the South as in the North, today, we all our advances in medicine and the availability of a curative treatment.

You can call this neglect, denial, whatever you like. The reality is that TB mortality comes in just after that for HIV/AIDS, but the threat of HIV/AIDS receives much more prominence in decision-making environments than TB does. This is something we cannot accept. That's why in the last two years, we've been pushing the agenda, trying to involve personalities and celebrities, so we can make a better case for paying attention to TB. Thus, the big message is be aware that TB is around, and it's still killing everywhere. Not a single country in the world has eliminated it, and it kills 5,000 people a day. Now we're facing the challenge of these extremely drug-resistant forms that do not respond to conventional anti-TB drugs or even the anti-TB drugs we have in reserve. If we don't act, if countries don't move now, we will let the epidemic continue, there will be more resistant forms spread, and TB will continue to kill.

The last point is that TB is not just a disease of Africa, Latin America, or Asia. It's a disease of the whole world. In the global village that we now live in, we can't stop TB at the border. The disease is transmitted by a cough and a breath. The point is that no one should feel safe; it can come to our door anytime. Thus, we need to act assertively and invest what is necessary to fight it back, while supporting more research to get better tools than we have today.

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Mario Raviglione's current most-cited paper in *Essential Science Indicators*, with 1,246 cites:

Dye C, *et al.*, "Global burden of tuberculosis—Estimated incidence, prevalence, and mortality by country," *JAMA* 282(7): 677-86, 18 August 1999. Source: *Essential Science Indicators* from Thomson Reuters.

Additional Information

Interview with coauthor Christopher Dye.

KEYWORDS: TUBERCULOSIS, GLOBAL BURDEN, EPIDEMIOLOGY, MORBIDITY, MORTALITY, HIV/AIDS, SURVEILLANCE METHODS, TB PREVENTION PRACTICES, XDR-TB.