Over the rainbow: the pot of gold for neglected diseases

Book Review for "Strong Medicine: Creating Incentives for Pharmaceutical Research on Neglected Diseases", Michael Kremer and Rachel Glennerster, Princeton University Press, November 2004.

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Over a hundred people in developing countries will have died of infectious or parasitic diseases by the time you have finished reading this article. Many could have been saved by access to viable vaccines and drugs, and much pain and suffering could have been avoided. Yet, barely 1% of global expenditure on pharmaceuticals goes into the research and development of products for diseases affecting 90% of the world's population. It is a sign of hope, of frustration, and of the craving for human dignity that the best way to redress this imbalance is currently under wide-ranging – and sometimes argumentative and painful – debate.

Michael Kremer and Rachel Glennerster's *Strong Medicine: Creating Incentives for Pharmaceutical Research on Neglected Diseases*, part of a larger body of work by the Washington-based Center for Global Development, is an important contribution. They begin with a succinct summary of the problem—the pity is that it needs repeating. But it does. Of the dramatic improvements in health and life expectancy in developing countries consequent on relatively cheap medical advances, the extreme cost-effectiveness of vaccines stands out. Vaccines (in particular for HIV, tuberculosis, and malaria) are thus the focus of this book.

British readers of a certain age will be familiar with the notion of "strong medicine" as a drastic root-and-branch operation on the body economic. The spin here is much less radical: the body pharmaceutic is deemed to be in robust health, just in need of a little nip and tuck, as it were, in the shape of "advance purchase commitments", which are sort of blockbuster end-of-the-rainbow pots of money to be divided between vaccine developers, paid for later by taxpayers. "Strong" refers to the alleged superior strength, dollar for dollar, of this mechanism compared with current approaches; up to four-and-a-half times "stronger" than publicly funded research and joint ventures. But, after a 6-year campaign to get this policy proposal to the top of the heap, it is disturbing to find

so little of the underlying mechanism laid bare, and no evidence to support the assertion that the mechanism is indeed "strong" for these vaccines. In fact, the authors promote advance purchase commitments in much the same way that some pharmaceutical companies promote wonder drugs: emphasising the positives, burying the negatives, and ending up suggesting that we now have all the answers—or rather just the one answer—that we need. This is a shame, because the underlying idea has potential as part of something greater.

Kremer and Glennerster expend most of their firepower on early-stage vaccines (where there are no viable vaccines on the horizon and many scientific problems have not been resolved) and this is the main source of *Strong Medicine's* weakness. To strengthen their case, they simplify the state of difficult and unpredictable science to one that it is fixed at basic and applied levels with, among other artifacts, no benefits from information sharing, no patents on anything except end products, no coordination problems across public and private sectors in research or vaccine purchase decisions, and an idealised set of financial markets. Once these simplifications are thrown out—and we enter the real world—we face an elaborate trade-off between, on the one hand, inflexible rules based on expectations of future vaccine science, and on the other, layers of discretionary committees, treaties, and centralised control of the global public research process.

The authors' core justification for their approach is that it massively improves the choice of research leads. They deliberately favour large pharmaceutical firms over small and new biotechs and not-for-profit, university-based, and developing country-based research. Yet, they present no empirical evidence that such firms are the most efficient at vaccine research. As the only evidence of the "plague" of failure of current programmes, we get the USAID Malaria Vaccine Program debacle of the early 1980s (which wasted a couple of ten-thousandths of 1% of the total US National Institutes of Health budget of the past 25 years). This is sad. And ungenerous to the many who, often at great personal sacrifice, give their lives to research into these difficult areas.

In its cloak of strong patents and secrecy, *Strong Medicine* also sets up an unnecessarily confrontational stand-off with those who argue for more open, collaborative approaches. The Gates Foundation and the G8 have been exploring these alternatives, following the recent proposal of a "Global Vaccine Enterprise" (Science 2003 300: 2036–39) along the lines of the successful human genome project. The strongest setting for a purchase commitment for a complicated vaccine like HIV is likely to be as a fairly late, and small, part of a much larger

package of measures, with the information revealed by earlier collaborative mechanisms used to set the terms of "contingent" purchase commitments. This would allow for more guidance on the quality of vaccines, fewer institutions and rules, more control over the eventual intellectual property, products priced pretty close to production costs, and quicker release to competitive generic producers. The real challenge is to work out how each part of this larger mechanism creates and handles information and risk, and how different parts fit together to reduce overall costs, speed up discovery, and ensure high-quality vaccines.

That Strong Medicine has "growing political support" is a testament to the persuasiveness of drastically simplified ideas, the lack of desire to think through tough issues, and the political appeal of programmes for which the payment can be pushed way off into the future. One of Kremer and Glennerster's main criticisms of the current system is that if publicly funded researchers don't have to prove the worth of what they're doing by results, vested interests will lead them to overstate the chance of success. Their book is an excellent demonstration of this principle in action. We will never truly know whether early-stage advance purchase commitments will work for HIV, tuberculosis, and malaria until after they have been tried. Given the authors' assertion that public-sector failure is at the heart of the current system's inadequacies, it would be ironic indeed if such failure happens when choosing the mechanism itself. Kremer and Glennerster should refuse to tolerate political support that comes without awkward questions or demands for solid empirical evidence.

All sides in the debate over the funding for neglected diseases exaggerate to get noticed; it is always nice to think that one's ideas are those chosen by policymakers. Disagreement is part of the discovery process. When, at the end of Hans Christian Andersen's tale, a small child squeals that the emperor has in fact got no clothes on, the emperor cringes but carries on the procession to its bitter end, while his chamberlains continue to hold up the train of his cloak, even though they know that it is not actually there. Let's hope that, after reflection, policymakers do not uncritically swallow all of "Strong Medicine". It will make them feel better for a while, but the effect would be short-lived. Sooner or later, we will need to develop something stronger.

Andrew Farlow
andrew.farlow@economics.ox.ac.uk
More information and further reading at:
http://www.economics.ox.ac.uk/members/andrew.farlow