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EDITORIAL

Shorter drug regimens for tuberculosis: the multiple applications of decision models

FOR MANY READERS of this *Journal*, a shorter treatment regimen for active tuberculosis is a perennial Holy Grail. Originally eighteen months or more in duration (and requiring injectable agents),[1,2] curative regimens are now down to six months and are relatively well-tolerated.[3] Now, after a lapse of over two decades, a novel drug pipeline has ignited a new series of clinical trials designed to reduce treatment to four or even two months. Given that hundreds of trials over many decades were required to establish current standard therapy,[4] it is reasonable to ask whether or not the pursuit of further treatment shortening is worth the resources it will take to realize.

In this issue of the *Journal*, Owens and colleagues demonstrate some of the reasons why we should still invest in shorter regimens. In their article, they describe the results of a decision analysis comparing standard therapy with a hypothetical shorter (two or four month) regimen.[5] Not surprisingly, their model suggests that a shorter regimen with equal efficacy would improve treatment completion and therefore prevent tuberculosis-related deaths. More importantly, they demonstrate scenarios under which a shorter regimen could be cost-saving over the long run even if it is more expensive up front. By performing analyses considering low, medium, and high delivery costs, they found threshold drug costs under which such a regimen would be expected to save money.

None of these findings are particularly surprising; one would expect any shorter regimen ultimately to be cost-saving, especially if program costs are high. Furthermore, because they used a hypothetical drug regimen, there is no immediate applicability of this particular model to any tuberculosis control program. Why, then, does this article warrant an editorial?

The importance of their approach is the use of decision analysis in the advanced stages of clinical trial design. First, they demonstrate that a shorter regimen will be cost-saving under reasonable programmatic assumptions, even when programmatic costs are low, supporting the hypothesis that a new regimen would be useful in almost any setting. Second, they provide threshold drug costs that could be used by both drug companies and tuberculosis programs when setting prices, thus helping to maximize profitability for the company (and providing an incentive to invest) while maximizing drug availability.

However, one of the most important applications of such a model is in guiding research expenditures. It is an unfortunate reality that in many cases, research funds and program funds come from the same budget. Therefore, not only are research expenditures sharply limited, they necessarily take money away from standard program activities such as case finding, contact tracing, and treatment of latent infection. It is therefore possible to directly compare the potential gain achieved by an investment in research with that achieved by using these same funds elsewhere. By giving us these data *in advance of any clinical trials*, not only does Owens et al.'s model suggest that an investment in research is worthwhile, it could also be used to determine roughly what that investment should be.

Decision analysis has been used by pharmaceutical companies for decades to analyze their drug development pipelines and project revenue over multiple-year periods. This same strategy could be utilized by public health researchers, where the analysis of the economic impact of different interventions is of paramount importance. In that regard, the article by Owens and colleagues is a step in the right direction.

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References

1 Blake D H. The treatment of chronic cavitating pulmonary tuberculosis by long-term chemotherapy. Tubercle 1961; 42: 438–443.
2 Mitchell R S. Control of tuberculosis. N Engl J Med 1967; 276: 905–911.
3 Combs D L, O'Brien R J, Geiter L J. USPHS Tuberculosis Short-Course Chemotherapy Trial 21: effectiveness, toxicity, and acceptability. The report of final results. Ann Intern Med 1990; 112: 397–406.
4 Fox W, Ellard G A, Mitchison D A. Studies on the treatment of tuberculosis undertaken by the British Medical Research Council Tuberculosis Units, 1946–1986, with relevant subsequent publications. Int J Tuberc Lung Dis 1999; 3 (Suppl 2): S231–S279.
5 Owens J P, Fofana M O, Dowdy D W. Cost-effectiveness of novel first-line treatment regimens for tuberculosis. Int J Tuberc Lung Dis 2013; 17: 590–596.