A Virtuous Cycle to Improve Hypertension Outcomes at a National Level

Linking Public Health and Individualized Medicine

Robert M. Califf

Compared with the seemingly orderly approach to science associated with controlled laboratory environments, the assessment of broad changes in clinical practices and their impact on society is maddeningly complex and difficult to ascertain with confidence. Yet, in the end, the favorable regard of most societies toward public funding of biomedical science hinges on the belief that the end product of such research will benefit human health. This critical societal trust has been eroded by a growing skepticism directed toward the biomedical research enterprise and its associated industries, particularly the pharmaceutical industry.

In this issue of Hypertension, Campbell et al report on their analysis of the impact of a program to improve the treatment of hypertension across Canada, one that has corresponded with increased use of antihypertensive medications and reduced incidence of death, stroke, myocardial infarction, and heart failure. The authors took advantage of the confluence of a major change in guideline recommendations, concerted national efforts linking professional societies and public health to control hypertension, and excellent sources of public data. These data allowed them to track prescriptions written by Canadian physicians and to correlate them with rates of key events (death and major cardiovascular and neurologic events) in the overall population. Using the powerful statistical technique of time series analysis, they demonstrated that rates of these critical events declined in direct proportion to the increase in prescription of antihypertensive medications, beginning in 1999. Taken at face value, this study provides compelling evidence that broad changes in medical care, when supported by convincing evidence from clinical trials, can result in improvements in death and disability for populations at the national level.

Skeptics will point to the obvious weaknesses in this study. This is not a randomized clinical trial, and all of the epidemiological studies, even those using sophisticated methods such as time series analysis, are subject to unpredictable biases and confounding. There is no way to prove that the strong correlations observed are separate from other changes, such as prescription of other risk-altering medications or improved lifestyle. Although the time series analysis provides strong epidemiological evidence, it cannot be considered definitive. It is worth noting, however, that performing a randomized clinical trial to address such a question would be horrendously expensive and run a major risk of contamination, because patients randomly allocated to the control group would know about the practices being applied to the interventional group and would be likely to make use of them. In addition, the ethical problems inherent in withholding proven antihypertensive medications would make a randomized trial a “nonstarter.”

Despite these caveats, this analysis demonstrates that large-scale changes in the use of medications can have a significant effect on disease burden for an entire country. Conceptually, this “cycle of quality” (Figure) is proving to be a robust societal approach to the prevention and treatment of disease and has already been seen to work in hospitals, clinics, and health systems. This report, as well as a recent publication regarding acute coronary syndromes, shows that the cycle can be effective at much broader levels.

Massive investments have been made in basic biological sciences and engineering to develop targets for intervention, investments that have come mostly from the National Institutes of Health and the medical products industry (pharmaceuticals and devices). In the case of hypertension, numerous drugs composing several major classes have emerged from research into these targets. These compounds are developed by means of risky, complex, and expensive early phase evaluations, after which promising therapies are tested in definitive clinical outcome trials. The complex array of results from clinical trials is then assembled into clinical practice guidelines to assist the individual healthcare provider in helping patients to make informed decisions about appropriate diagnosis and risk stratification, which treatments to use, and how to monitor the effect of treatment. The most definitive results from clinical trials with the clearest pathway to guideline recommendations can then be used to make reimbursement decisions or to devise pay-for-performance programs. Ultimately, through assessment of outcomes in registries and population studies, gaps in practice can be filled in by the generation of new evidence. This system may work best when continuous feedback about individual adherence is available, along with aggregate results of the practice, bolstered by reimbursement schemes that support effective practices.

The opinions expressed in this editorial are not necessarily those of the editors or of the American Heart Association.

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Hypertension is available at http://hyper.ahajournals.org
DOI: 10.1161/HYPERTENSIONAHA.108.121608

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The development of drugs for hypertension, the demonstration of their clinical benefit in large clinical outcomes studies, and application of those results in practice with the support of guidelines provide a great story, one now solidified by the present analysis. The Canadian time series data are consistent with recent clinical trials, all of which show a direct and rapid reduction in events, particularly stroke, when a randomized intervention creates a difference in blood pressure. They validate the use of clinical trials data, despite all of the well-publicized problems of generalizability, to construct broadly applicable practice guidelines. Another notable effect of the manner in which hypertension drugs are developed, clinical trials are conducted, and practice guidelines are constructed is that compared with many other classes of pharmaceuticals, there is little public doubt about the value of treatment.

These results also provide validation for the notion that at their core, public policies of investment in basic biomedical research and the development of medical products through competitive private industry make good sense. However, when we consider the new “flat world” of the integrated global economy and the fact that diseases such as hypertension know no national boundaries, a careful examination of the inefficiencies in our global systems for translating scientific findings into effective medical treatments is clearly needed. There is a difficult balance to be struck between requiring high-quality evidence that new therapies add something useful and enabling investment in the risky business of developing better medical products, particularly when investors can choose among other industries. It is ironic that, as this report is being published, we learn that major pharmaceutical companies such as Pfizer are abandoning cardiovascular drug development, because barriers to entry are too high. We can certainly reduce the cost of definitive clinical trials by streamlining efforts, enacting more effective regulatory strategies, and developing a more effective national infrastructure for conducting clinical trials. An ideal system would require first-rate evidence of the comparative risk and benefit of new products but would generate that evidence in an efficient, low-cost manner and would reward companies that successfully develop innovative therapies.

Despite this positive news, we must not fall prey to complacency, because rates of death and disability from hypertension will continue to escalate despite successes, such as the ones described in this article. The aging of populations in economically developed regions and the reduction of premature deaths from infectious diseases in the young, coupled with epidemics of diabetes mellitus and obesity, will continue to expose enormous numbers of people to the risk of death and disability because of hypertension. The greatest benefit will come from balanced strategies that continue our investment in discovery science, reward industry for producing innovative therapies, insist on efficient comparative effectiveness trials to understand which treatments are most useful, and use evidence-based guidelines and performance measures to increase the use of effective treatments. We now know that we can extend these systems of quality from local clinical environments to encompass entire countries.

Disclosures
R.M.C. receives significant salary support from grants from Novartis Pharmaceutical and Schering Plough (all payments are made to Duke University). R.M.C. also receives significant funding (more than $10 000) from Heart.org (Conceptis) and Kowa Research Institute (activities create revenue for Duke University). R.M.C. receives nonsignificant consulting funding (less than $10 000) from Amylin, Bayer, Boehringer Ingelheim, Boston Scientific, Glaxo SmithKline, Heart.org (Conceptis), Medtronic, Novartis, Roche, Sanofi-Aventis, Scius, Targacept, University of Florida, and Virus, as well as significant consulting funding (more than $10 000) from Kowa Research Institute, Nitrox LLC, and Schering Plough. All of the consulting income is donated to nonprofit organizations, with the majority being designated for the Duke Clinical Research Institute’s clinical fellowship fund. R.M.C. holds equity in excess of $10 000 in Nitrox LLC.

References


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Hypertension. 2009;53:105-107; originally published online December 29, 2008;
doi: 10.1161/HYPERTENSIONAHA.108.121608
Hypertension is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0194-911X. Online ISSN: 1524-4563

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://hyper.ahajournals.org/content/53/2/105

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