



## Maintaining Public Trust in Medical Advice—Could Less Be More?

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The truth of the assertion that “drugs don’t work in patients who don’t take them,” attributed to the former US Surgeon General C. Everett Coop, may be self-evident, but of course the drug must be effective in the first place. Implementation science investigates methods to help realize the benefits of advances in clinical care. Luepker et al<sup>1</sup> are to be congratulated on conceiving and testing a comprehensive educational and interventional campaign designed to increase the uptake of aspirin for the primary prevention of cardiovascular disease in Minnesota between 2015 and 2019, using surrounding states, where the program was not implemented, as comparators. The campaign failed to increase aspirin uptake. Only 1 in every 20 people surveyed recalled promotional aspirin messaging and the use of aspirin decreased, both in Minnesota and in the surrounding states. We should learn as much or more from failure than we do from success.

The program had an integrated, well-crafted, multipronged approach with educational messages conveyed by advertising on billboards and radio, newspaper articles, an Ask About Aspirin website that received more than 1 million visits, and engagement of more than 1000 primary care physicians and other health care professionals in educational programs. The authors believe that the population was exposed to the aspirin promotional message approximately 24 million times per year. Moreover, a health system quality improvement program sought to identify and contact people who were thought to be appropriate candidates for use of aspirin through participating primary care centers. Despite this enormous effort, a survey suggested that less than 6% of the population of Minnesota ever became aware of the campaign.

In 2015, only 49% of the people in Minnesota who had an indication for use of primary prevention aspirin, according to US Preventive Service Task Force (USPSTF) 2009 guidelines, were receiving it, which was slightly higher than in surrounding states (40%). By 2020, use of aspirin had decreased both in Minnesota and, to a lesser extent, in the surrounding states. The decrease was temporally associated with the publication of 3 large randomized clinical trials showing either no benefit or harm from use of primary prevention aspirin and was consistent with national guidance,<sup>2,3</sup> suggesting that many clinicians and patients had acted responsibly in the face of new evidence. Prescribing inertia will have prevented a more profound decrease because people who have taken aspirin for years without obvious problems may be reluctant to change their routine; neither will physicians press them to do so. However, the outcome of the campaign probably would not have been substantially different even in the absence of changes in evidence and guidance, because few of the target audience became aware of the message.

What lessons can we learn from this? First, there is so much supposedly good advice these days on so many health issues that many people probably just ignore all but the most trusted sources of information. In that sense, the results of this implementation study are encouraging. People appear to follow the evidence rather than the media when it comes to health. Being British, I cringe every time I see a US television advertisement for a medical product. I cannot help feeling that many of my US cousins feel the same way. A hard-sell may have negative results, especially when it turns out that the product for sale does not work. The opioid crisis has undermined trust in both regulators and physicians.<sup>4</sup> Many popular films and television series now highlight recent medical misdemeanors. We cannot afford to make more mistakes based on shaky evidence.

Second, the public may be smart enough to do the math. For instance, in the US Physicians Health Study on use of primary prevention aspirin (325 mg on alternate days) in more than 20 000 men followed up for an average of 5 years, there were only 2 fewer cardiovascular deaths and 84

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fewer nonfatal myocardial infarctions but 10 more sudden deaths and 18 more nonfatal strokes during more than 100 000 person-years of follow-up.<sup>5</sup> Furthermore, aspirin reduced neither the development of angina nor the number of coronary revascularizations.<sup>6</sup> Accordingly, for every 1000 people treated with aspirin for a year, it is unlikely that there was any discernible net benefit. The public might ask, if a heart attack is so deadly, why was there no reduction in mortality? Did aspirin just change the presentation of disease from nonfatal myocardial infarction to sudden death?<sup>3,7,8</sup> Many individuals will be impressed by neither the strength of evidence nor the magnitude of benefit.<sup>7</sup>

Third, is the evidence for long-term aspirin use for secondary prevention of cardiovascular disease any better than for primary prevention? Most physicians probably imagine that there are a lot of well-designed placebo-controlled trials demonstrating the benefits of life-time administration of aspirin for individuals with atherosclerosis. This is simply not true.<sup>3,7,8</sup> I encourage my colleagues to read the original trial evidence. Enlightened readers will quickly learn that the evidence of benefit for aspirin rapidly dwindles within 4 to 6 weeks after a vascular event.<sup>3,7,8</sup>

Finally, we should be very cautious about making strong recommendations based on inconclusive evidence.<sup>9</sup> We will lose public trust if we continue to reverse guidelines. Meta-analysis of inconclusive trials should not be the basis for guideline recommendations but rather for determining what size of trial is required to deliver conclusive evidence. If the answer is a trial with very large numbers of participants, then maybe the clinicians, payers, and public are just not interested in the answer. We should be looking for substantial benefits for the individual, which may require longer-term trials rather than more participants. We should be as patient as the patients are, proffer advice based on the balance of evidence but avoid aggressive campaigns based on flimsy evidence that we may eventually regret. Physicians have enough to do without the distraction of prescribing ineffective medicines and managing their adverse effects. Even if aspirin is benign, this might not be true for long-term use of proton pump inhibitors, which are often prescribed to manage dyspepsia, and because of the fear of gastrointestinal bleeding. Polypharmacy almost certainly reduces adherence. Deprescribing of useless or harmful medicines is a beneficial health intervention.<sup>10</sup> Prescribing a useless drug, even if it is safe, can also be considered harmful if it is a displacement activity that prevents a useful treatment being prescribed and consumed.

Hopefully, others will not be discouraged by the failure of this excellent piece of implementation research. More emphasis on the science of implementation to realize the benefits of better-proven therapies than aspirin is certainly required.

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## ARTICLE INFORMATION

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