The "direct" dilemma

Oral anticoagulants and the parameters of public prescribing

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While sitting opposite your 78-year-old male patient, you craft an explanation that will make sense to him: "Your heart is beating irregularly: that means your blood could clot, and increases your chance of having a stroke." The atrial fibrillation was identified incidentally, an irregular pulse found during a physical examination for a noncardiac complaint. His CHA_2DS_2-VASc* score is 3, and his HAS-BLED† score is 1: the balance clearly falls on the side of anticoagulation. He had a comprehensive private drug plan available during his working years, but could not afford the premiums after retirement. He now depends on provincial formulary coverage.

When it comes to issuing the anticoagulant prescription, you know that a number of national and international guidelines (Canadian Cardiology Society,[1] American Heart Association,[2] European Society of Cardiology[3]) recommend use of a direct oral anticoagulant (DOAC) as first-line therapy in preference to a vitamin K antagonist (eg, warfarin). At the same time, if you are practising medicine in any Canadian province or territory other than Quebec, you also know that public formulary coverage of DOACs is contingent on meeting a number of clearly defined criteria, including adequate renal function, absence of severe mitral stenosis or a mechanical heart valve, and failure of an initial trial of warfarin, or the inability to monitor the patient's international normalized ratio.

You now have the following 2 choices.

- Option 1: Inform the patient that the recommended preference for treatment is a DOAC, and further explain that the government will not cover the medication, but it will pay for warfarin.
- Option 2: Write a prescription for a DOAC, attaching a limited-use code (substitute *special authorization* in Alberta, or *exception status* in Nova Scotia) that you know is fraudulent.

Is this a realistic synopsis of the decision Canadian physicians are making? Although it is impossible to establish the frequency with which physicians are choosing option 2, it is undeniable that prescribing rates for DOACs are increasing rapidly.[4] A 2017 report by the Canadian Institute for Health Information notes that direct factor Xa inhibitors were fourth in their contribution to the growth in public drug spending in 2016, with costs increasing more than 50-fold from 2011 to 2016.[5]

Competing priorities

The prescribing scenario above is similar to the "Heinz dilemma," a hypothetical situation used most famously by Lawrence Kohlberg in his work on moral reasoning.[6] Subjects were presented with a story about a man who was unable to afford medication to save his dying wife, and were asked whether the man was justified in stealing the medication. Kohlberg's primary interest lay not in the specific answers that people selected, but in the nature of the arguments marshaled to support those conclusions. Analogous to the arguments in favour of theft in Kohlberg's experiments, a physician might reason that, given the evidence that DOACs are at least noninferior to warfarin in stroke prevention in atrial fibrillation, and that drugs in this class show a statistically significantly lower risk of intracranial bleeding compared with warfarin,[7] provincial governments are being negligent in failing to allow unfettered access to the newer medications.

One problem with this line of reasoning is that it minimizes a provincial or territorial government's prerogative to determine how money is spent. Warfarin is pennies a dose; the daily cost for a patient with atrial fibrillation taking DOACs is about $3 a day. The earliest assessment of DOACs by the Canadian Agency for Drugs and Technologies in Health (CADTH) confirms that warfarin therapy is substantially cheaper, even factoring in the cost of monitoring international normalized ratio values.[8] Consequently, it is not surprising that governments responded to the introduction of DOACs by publishing restrictions for their prescription; much of the language in provincial formularies adopts the 2012 CADTH recommendation that warfarin be the first-line treatment for most patients with nonvalvular atrial fibrillation.[8]

Clearly, the demonstration of clinical superiority alone does not provide a sufficient argument for those who fund health care services in Canada: we need a convincing analysis of cost-effectiveness. We know that warfarin is cheaper but that DOACs reduce the risk of intracranial hemorrhage.[9] So, how do we balance these (and many other) factors in determining what we are prepared to pay?

As the existing complement of cost-effectiveness studies demonstrates, this area of research is complex: it requires that numerous assumptions be made (regarding compliance, cost, characteristics of treated patients, etc) that can

*Congestive heart failure, hypertension, age ≥ 75 years, diabetes mellitus, stroke or transient ischemic attack, vascular disease (previous myocardial infarction, peripheral artery disease, or aortic plaque), age 65 to 74 years, sex category (ie, female).

†Hypertension with a systolic blood pressure > 160 mm Hg, abnormal renal or liver function, stroke (caused by bleeding), bleeding, labile international normalized ratio, elderly (age > 65 y), drugs (acetylsalicylic acid or nonsteroidal anti-inflammatory drugs) or alcohol (≥ 8 drinks/wk).

alter the outcome. However, there is a growing opinion that some DOACs (in some situations) meet our generally accepted criterion of what we are prepared to pay to extend our lives in better health.[10] In support of this position, the National Health Service in England (based on guidance from the National Institute for Health and Care Excellence[11]) and the Pharmaceutical Benefits Scheme in Australia[12] have both implemented public coverage for DOACs, without requiring an initial trial of warfarin.

There are several things that we could do to mitigate the confusion around this subject. First, if the cost-effectiveness data are convincing, then the discussion should be over. We need a position statement that draws on expertise from both clinicians and health economists to analyze the existing research and make relevant conclusions for the Canadian context. The guidelines by cardiovascular societies focus on the clinical aspect of therapy, but our publicly funded health care system requires an assessment of whether DOACs provide value for money. Necessarily, this assessment will need to address directly the detailed cost-effectiveness analysis (and caveats) used by CADTH to generate its initial recommendations.[13] Stone et al made such an appeal to public funding agencies in the *Canadian Journal of Cardiology* in 2014,[14] and Leong-Sit and Healey made a more focused recommendation in the same journal in 2016 (funding DOACs for patients with CHA_2DS_2-VASc scores >2)[15]; although governments will reserve the right to make final spending decisions, physicians deserve to see a transparent response, either broadening coverage or maintaining the status quo.

Second, if individual physicians or groups are convinced that DOACs ought to be covered as first-line therapy for most patients with atrial fibrillation, and that government regulations are unconscionable, then we should be overt about our acts of civil disobedience. Permitting practitioners to select (with relative ease and impunity) which restrictions can be set aside creates a worrying precedent in a democratic society, putting (unelected) physicians in the position of rewriting public policy. If advocating for change is considered insufficient, physicians could send a letter to the provincial drug program, outlining their concerns with the current restrictions, and indicating that they will be deliberately flouting the rules in order to obtain better outcomes for their patients. This would have 2 advantages: it would delimit a clear moral position for the prescribing physician, and it would eliminate the ability of ministries of health to "look the other way" (through absent enforcement of existing policies), which allows them to maintain a semblance of fiscal restraint. To be sure, embedded in the notion of civil disobedience is the element of risk, including potential sanctions by governments or regulatory bodies; as philosopher John Rawls observed, "the willingness to accept the legal consequences of one's conduct" is part of what defines civil disobedience as a particular form of societal protest.[16]

Conclusion

At a time when various groups are calling for a national public pharmacare program,[17,18] it is more important than ever that we have a clear and equitable process for getting medications to the patients who will benefit from them. While physicians might cast themselves as patient champions by undermining a restrictive regulatory regime, it is worth considering whether these actions jeopardize a larger project: if public payers cannot trust mechanisms that rely on the good-faith assessment of physicians, they will implement increasingly bureaucratic processes. Ultimately, if governments are holding the purse strings, then they are necessary partners with us as health care providers. The DOAC dilemma is not the first of its kind, and will not be the last; we should see this as an opportunity to clarify our obligations on all sides. Politicians, patient advocates, and taxpayer coalitions will be watching closely.

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Competing interests
None declared

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