Inconsistencies in the 2017 Canadian Guideline for Opioids for Chronic Noncancer Pain

With the *2017 Canadian Guideline for Opioids for Chronic Noncancer Pain* (the guideline) currently undergoing an independent assessment of the rigour that went into its development, it is surprising that the health care community has not publicly commented on the many inconsistencies that shroud its content.[1]

The content of Table 3 (p. 28), "Practical Info," in the full guideline[2] is highly disturbing. First, *codeine* is devoid of any comment. Codeine's potency relative to morphine, the fact that codeine is a prodrug that is converted to morphine in a highly variable fashion, and that codeine should be avoided in renal insufficiency are all missing. In 2008, Health Canada endorsed important safety information on (Tylenol with) codeine products by nursing mothers and ultrarapid metabolizers of codeine.[3] Second, the comment regarding tramadol is inaccurate. Tramadol is not a prodrug, as both the parent molecule (serotonin–norepinephrine reuptake inhibitor–like + opioid) and the M1 metabolite (opioid) have analgesic properties.[4] Granted, in animal models, the M1 metabolite (which is converted from the parent molecule in a highly variable fashion) is thought to have higher affinity binding to the opioid receptors than the parent molecule.[4] Finally, "available in a tamper-resistant formulation" is stated for the opioids: oxycodone, hydromorphone and tapentadol. As per the March 2017 CADTH summary on *Opioid Formulations With Tamper-Resistance or Abuse-Deterrent Features*,[5] Health Canada has not approved tamper-resistant labelling for any opioid formulation marketed in Canada. How can we now stop the pharmaceutical industry from taking advantage of the current messaging in Table 3?

Page 13 of the full guideline states: "The Panel also endorsed three *good practice statements*, actionable guidance regarding interventions with compelling indirect evidence of large net benefits. Input from medical regulators guided our selection of *good practice statements*." Unfortunately, the wording "*best practice statements*" is found in the guideline's table of contents (p. 3), on page 7, and where the practice statements are located (p. 77). "Best" is the superlative of "good," as in "good, better, best."[6] With this important inconsistency in language, how will regulators and educators be able to potentially incorporate these practice statements into standards, and how might this inconsistency in language be used by lawyers in the future?

Guidance statement 2 (p. 78) contains potentially misleading information. The last sentence reads: "Individuals misusing opioids favour immediate-release (IR) opioid preparations, regardless of the route of administration." It is my opinion that, by excluding the second line from the conclusions of the reference cited in the guideline,[7] "…initiatives to restrict the diversion and abuse of prescription opioids may be just as important for *both* IR and ER [extended-release] (CR [controlled-release]/SR [sustained-release]) opioids," and conclusions from other current articles,[8] "For the greatest public health benefit, future interventions to decrease prescription opioid abuse should focus on *both* IR and ER (CR/SR) formulations," the new guideline may erroneously lead clinicians to think that CR/SR opioid formulations are safer than IR formulations. In addition, as these statements are based on US data, the guideline panel has overlooked the fact that generic CR oxycodone is available and prescribed in Canada, and that many fewer opioid formulations with potentially abuse-deterrent or tamper-resistant properties are available and used in Canada compared with the US.

Other inconsistencies in the full guideline include the variable language regarding urine drug screening and urine drug testing and the differing statements: "… there is likely a dose-dependent increase in the risk of nonfatal opioid overdose. There is an increased risk of fatal opioid overdose with higher doses" (p. 64) versus "a clear dose–response relationship was demonstrated for the outcomes of fatal and nonfatal overdose" (pp. 62, 65).

On a more positive note, evidence in the new guideline may necessitate reconsideration by many authors of their opinions on the subjects of the dose–response relationship of opioids and the outcomes of addiction and diversion, as it states, "no evidence was found for a dose–response relationship between opioid dose and the outcomes of addiction and diversion. The studies that informed these two outcomes included patients on a variety of opioid doses. We therefore assume that the risks presented are applicable to all doses of opioids."

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Competing interests: Erica Weinberg has received speaker fees from Sea Courses. She is also a national faculty member of the Michael G. DeGroote National Pain Centre.