Spinal Cord Stimulator Complications Reported to the Australian Therapeutic Goods Administration

To the Editor:

We read, with interest, the recent publication by Jones et al[1] titled "Spinal cord stimulators: an analysis of the adverse events reported to the Australian Therapeutic Goods Administration." We commend the authors for their efforts and offer the following by way of peer review.

Our first point concerns the use of the Medicare Benefits Schedule item numbers 39134 and 39135 to quantify neurostimulator implants and removals, respectively. Although this definition is accurate, relying on raw numbers of use of these codes and the implication that they directly relate to complications of spinal cord stimulation (SCS) therapy (i.e., removal = complication) has resulted in substantial misinterpretation. All implantable neurostimulator batteries have a finite life span, and when an implanted stimulator reaches the end of its battery life, assuming there is a clinical indication to do so, the implantable pulse generator (IPG) would typically be surgically replaced. The item codes for such an operation would include both 39135 (explant of original IPG) and 39134 (implant of new replacement IPG). Therefore, in any given year, the item code 39135 would be expected to occur for 100% of battery replacements occurring in that 12-month period. The actual number of replacement operations compared with explants due to complications cannot be deduced from the number of occurrences of these item numbers alone. Given that SCS has been used in Australia for treatment of chronic neuropathic pain for more than 25 years, it is reasonable to assume that a majority (even a vast majority) of cases using the 39135 item code are for battery/IPG replacements in routine clinical management. For example, in the years 2018 to 2019, it is likely that around 2000 battery changes occurred, which would account for around 40% of implants and almost all (or very many) explants. To suggest that this item code represents a figure of complications requiring explant is therefore erroneous.

Regarding the reported events from the Therapeutic Goods Administration (TGA) and the figure of 520 unique events recorded, there are several points worthy of comment. Considering the numbers of units implanted (26,786) and removed (10,702), there were at least 16,084 devices still implanted over the reporting period. (This number would likely be higher as item code 39135 [removal] may also be used during revision/replacement of an IPG.) From this number, we could draw the (worse case) conclusion that a total of 520 adverse events equates to a relatively small event rate of 3.2% (see Table 1 for further breakdown).

Also, the authors have not mentioned that almost every reported event was documented by an industry representative. In clinical practice, this is routinely undertaken by the field clinical engineer employed by the device company, and they are required by their own company's mandates to report every single issue they become aware of to the TGA, regardless of whether it is related to the therapy or not. The engineer makes no inference on causation in the reporting. This is noteworthy because such reporting almost always accompanies a device explanted for reason other than end of battery life. As such, the figures are likely to be robust and inclusive and represent an explant due to complication rate of around 2% in Australia, which is within the accepted complication rate for such therapies around the world.[2] Once correction for removal of reports that are wholly unrelated (e.g., death due to cancer, which is one example in the TGA database), then the true figure of complications attributable to SCS therapy is likely to be lower still.

Our next points concern the coding and classification of adverse event seriousness and severity. The authors used the Australian National Health and Medical Research Council safety monitoring and reporting in clinical trials involving therapeutic goods guidance to code adverse events as "serious" or "not serious."[3] What they quote is the definition of a serious adverse event for investigational medicinal product trials, which classes any event requiring hospitalization as serious. What they should have used is the definition for medical device trials, which states that any adverse events requiring surgical intervention are only considered serious if the surgery or hospitalization resulted from "serious deterioration in the health of the participant," and where hospitalization was "inpatient or prolonged hospitalization," and where the surgical intervention was required "to prevent life-threatening illness or injury or permanent impairment to a body structure of a body function." The definition also includes a note that "a procedure required by the Clinical Investigation Plan, without serious deterioration in health, is not considered a serious adverse event." By this definition, events such as lead migrations or fractures, for example, would not be coded as serious.

For classification of severity, the authors used the Common Terminology Criteria for Adverse Events developed by the national cancer institute.[4] Certainly, when a complication arises that requires a surgery to treat it (lead fracture, for example), the event would by default meet the "severe" category of the Common Terminology Criteria for Adverse Events. Furthermore, it is a recommended clinical

TABLE 1. Estimate Adverse Event Rates for SCS Devices: TGA-Reported Events From July 2012 to January 2019

Adverse Event (Action Taken/*ICD-10* Code)	Count	%
Total adverse events	520	3.23
Requiring single surgical intervention	383	2.38
Requiring surgical intervention and IV antibiotics	21	0.13
Requiring multiple surgical interventions	16	0.10
Device malfunction	296	1.84
Pain	110	0.68
Infection/inflammatory reaction	55	0.34
Hemorrhage/hematoma	7	0.04
Headache	6	0.04
Puncture/laceration	5	0.03

ICD-10, *International Classification of Diseases, Tenth Revision*; IV, intravenous.

practice to administer perioperative antibiotics intravenously during such procedures to reduce the risk of postoperative infection.[5] As such, to suggest that these adverse events recorded through the TGA are of significant concern because they are categorized as severe by a system that the authors acknowledge was developed for grading toxicity of cancer treatments is a nonsequitur.

With respect to the authors' comments that there is a dearth of published long-term safety data for SCS systems, we agree that this is an area that warrants further attention. We are encouraged that several robust and industry independent registries and databases are currently in existence around the world, such as the United Kingdom's National Neuromodulation Registry and the Neurizon Neuromodulation Database (formerly, Aarhus Neuromodulation Database),[6] and we await publications from these registries in years to follow. We would also hope to see a registry for these devices developed in Australia soon.

Regarding the authorship, it is noteworthy that none of the listed authors use neuromodulation in the clinical management of patients (to the best of our knowledge) and that one of the authors is an investigative journalist for a media company based in Australia. Although this in and of itself in no way distracts from the validity or authenticity of the publication, we believe that it goes a long way to explain how some of the issues noted previously may have been misunderstood during the writing of the manuscript. We recommend a blend of authors that includes experienced practitioners in the field who are intimately familiar with the nuances of both therapy and coding, as well as independent experts.

Overall, we unfortunately have significant reservations regarding the validity of this study and are concerned that a reader who is not familiar with the issues raised previously would draw erroneous conclusions from this article and potentially come away with an unfounded mistrust of the therapy that is not supported by the available data.

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