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# **Original Article**

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Subcutaneous administration of drugs and hydration in acute palliative care units: Physician attitudes and beliefs in the United States and Canada

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### **Abstract**

**Objectives.** The objective of this study was to compare the attitudes and beliefs of PCU physicians leaders in the United States versus Canada regarding the subcutaneous method in the administration of medications and hydration in order to gain a better understanding as to why variations in practice exist.

**Methods.** This survey trial took place from November 2022 to May 2023. The MD Anderson Cancer Center institutional review board in Houston, Texas, approved this study. The participants were the physician leaders of the acute palliative care units (PCUs) in the United States and Canada. The survey comprised questions formulated by the study investigators regarding the perceived comfort, efficiency, and preference of using the subcutaneous versus the intravenous method. The consent form and survey links were emailed to the participants.

**Results.** Sixteen PCUs were identified in the United States and 15 PCUs in Canada. Nine US and 8 Canadian physicians completed the survey. Physicians in Canada were more likely to use the subcutaneous route for administering opioids, antiemetics, neuroleptics, and hydration. They preferred subcutaneous over intravenous or intramuscular routes (p = 0.017). Canadian physicians felt their nursing staff was more comfortable with subcutaneous administration (p = 0.022) and that it was easier to administer (p = 0.02). US physicians felt the intravenous route was more efficient (p = 0.013).

**Significance of results.** The study results suggest that exposure to the subcutaneous route influences a physician's perception. Further research is needed to explore ways to incorporate its use to a greater degree in the US healthcare system.

## Introduction

The subcutaneous administration of medications and fluids is a viable parenteral route for institutions worldwide (Anderson and Kralik 2008; Herndon and Fike 2001; Slesak et al. 2003). This route is safe and effective when compared to intravenous delivery of medications and fluids and has several reported benefits in patients with advanced cancer (Challiner et al. 1994; Nelson et al. 1997; Vidal et al. 2016). Advanced cancer may cause symptoms such as dysphagia, nausea, vomiting, and decreased oral intake due to delirium (Hui et al. 2015; Vidal et al. 2016). Intravenous access may be difficult to achieve due to dehydration that may develop (Bartz et al. 2014; Caccialanza et al. 2018; Vidal et al. 2016). The same subcutaneous injection site can be used for 7 days or more so patients do not have to undergo the discomfort of frequent site changes that occur with intravenous access (Fainsinger et al. 1994; Vidal et al. 2016).

This subcutaneous route allows for a seamless transition from inpatient settings to chronic care facilities or home. A significant advantage of this route is that it frees the patient from having to carry poles with infusion pumps in the hospital, since excellent symptom control can be achieved with intermittent injections of opioids or hydration as 1-h subcutaneous boluses (Parsons et al. 2008). Several other drugs, including antibiotics, can also be administered into a subcutaneous indwelling catheter (Walker et al. 2005). Despite all of these benefits, the subcutaneous route as a method to deliver medications and fluids remains underutilized in the United States (Slesak et al. 2003; Tang et al. 2023).

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Acute palliative care units (PCUs), which are specialized inpatient units where palliative care medicine specialists along with interdisciplinary teams provide highly intensive symptom management, are an ideal environment to utilize the subcutaneous route (Eti et al. 2014). These units not only help with providing high-level care at the end of life but can also help facilitate discharge to home or a facility with hospice care (Elsayem et al. 2011). PCUs also provide education for future specialists and contribute to research. However, there is very limited number of PCUs in both the United States and Canada (Hui et al. 2020).

We have previously published a study demonstrating differences in the use of subcutaneous administration of medications and fluids between US and Canadian PCUs (Tang et al. 2023). This was the first study published directly quantifying differences in practices in subcutaneous use between the United States and another country (Tang et al. 2023). The objective of this study was to compare the attitudes and beliefs of PCU physicians leaders in the United States versus Canada regarding the subcutaneous method in the administration of medications and hydration in order to gain a better understanding as to why variations in practice exist.

### **Methods**

The MD Anderson Cancer Center institutional review board approved this survey study. The study took place from November 2022 to May 2023. The participants for this survey were physician leaders of PCUs in the United States and Canada. These participants were identified by contacting known PCUs through email or telephone (Hui et al. 2020). We included physicians in Canada who were leaders in "acute palliative care units" or "tertiary palliative care units," defined as interdisciplinary PCUs located in acute care hospitals. We excluded physicians who practiced only in

inpatient hospice units. The participants were emailed the survey instructions, consent form, and links.

The survey consisted of a questionnaire with 33 questions. The first section included physician demographics and the characteristics of their PCUs, and the second section assessed physician perceptions. The study investigators formulated the questionnaire. In order to determine the likelihood of using an administration route, the participants were asked to respond to, "Out of 100 patients in your palliative care unit, how many would receive (opioids/ antibiotics/neuroleptics/ antiemetics/ hydration) via (subcutaneous/ intravenous/ intramuscular/ rectal)."

Continuous variables were summarized using mean, median, standard deviation, quartiles, minimum, and maximum, while discrete variables were likewise summarized using frequency with percentage; Likert-scale variables were summarized as both continuous and discrete. As appropriate, differences between countries were assessed using two-sample *t*-tests and Mann–Whitney tests or by Chi-square tests.

Logistic regression models were used to model the proportions (out of 100) reported for each drug category administration route with relation to country. Differences between countries were reported as odds ratios with 95% confidence intervals. Model-adjusted proportions for each country were reported as percentages with  $\pm$ standard error intervals. Statistical analyses were performed using R statistical software version 4.2.2. A two-sided alpha of 0.05 was utilized in all statistical tests. Catseye plots were produced using the "catseyes" package (Andersen 2020; Cumming 2014).

### **Results**

Nine physician leaders of 16 PCUs identified in the United States and 8 physician leaders of 15 PCUs identified in Canada completed the survey, for an overall response rate of 55%. There were no

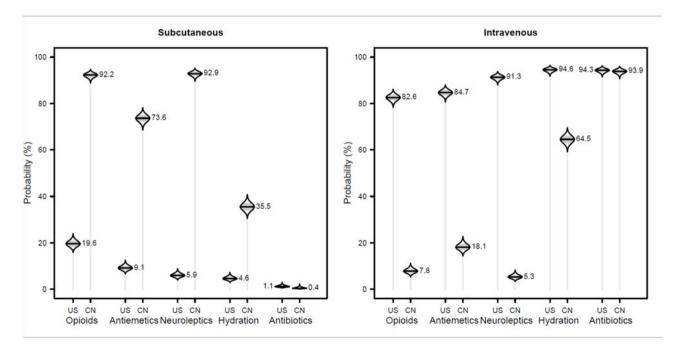


Figure 1. Likelihood of subcutaneous use versus intravenous use for medications and hydration in the United States and Canada. Model-adjusted probability by country. Catseye plots illustrate the normal distributions of the model-adjusted means, with shaded ±standard error intervals, transformed from the log-odds to the probability scale.

statistically significant differences when comparing the age, gender, location of practice (urban, suburban, or rural), and number of years practiced. Respondents in Canada had spent more years practicing palliative medicine (median value of 16 vs 11 years, p=0.044). All 8 physicians in Canada estimated that, on average, greater than 40% of the patients in their PCUs have cancer, compared to only 3 US physicians (p=0.033). PCUs in the United States more often required a Do Not Resuscitate or Allow Natural Death order for admission, 6 versus 1 (p=0.0498).

Figure 1 shows the logistic regression-based model-adjusted probability of using subcutaneous versus intravenous administration of medications and fluids based on location. Physicians in Canada were more likely to use the subcutaneous route for opioids, antiemetics, neuroleptics, and hydration (p < 0.0001 in each case), while those in the United States were more likely to use the intravenous route in these conditions (p < 0.0001 in each case). There was no significant difference between countries in subcutaneous or intravenous use of antibiotics (p = 0.10 and 0.69, respectively).

Table 1 shows the survey responses. Physicians from Canada agreed to the statement, "I prefer using subcutaneous route over other parenteral routes" more often than US physicians (p=0.017). US physicians agreed to the statement, "I prefer using intravenous route over other parenteral routes" more often than Canadian physicians (p=0.002). Canadian physicians felt that their nursing staff was more comfortable with subcutaneous administration (p=0.022), while physicians in the United States felt that intravenous was a more efficient route (p=0.013).

### **Discussion**

Our study provides insight as to why variations in practice may exist. Both US and Canadian physicians reported familiarity and comfort with the subcutaneous route. Notable differences were that the US physicians felt that the IV route was most efficient, whereas Canadian physicians felt that the subcutaneous route was easier to administer than other routes. US physicians also felt that their nursing teams were more comfortable administering medications and hydration intravenously rather than subcutaneously, while the opposite was true for Canadian physicians.

With regard to efficiency, there are studies that demonstrate the pharmacokinetic properties are similar whether given intravenously or subcutaneously (Lipschitz et al. 1991; Penson et al. 2002). We have demonstrated that caregivers without previous medical training can learn how to set up and deliver hydration at home with 60 min of training and reported minimal difficulty in use (Vidal et al. 2016). Despite this evidence, it appears that US physicians perceived the intravenous route to be more efficient.

This response may reflect several factors. Due to a lack of familiarity, there are multiple administrative barriers to implementing the use of subcutaneous lines in the hospital prior to transitions of care. The US reimbursement model favors a "buy-and-bill" method of payment (Epstein 2021). Administration of fluids solely by the subcutaneous route may not increase the acuity level of patients for insurance companies, affecting reimbursement (Remington and Hultman 2007). Physicians may also be concerned about the comfort levels of nursing staff placing and maintaining subcutaneous lines. Finally, there is a possibility that training programs in the United States do not accurately portray the ease of setting up and using a subcutaneous delivery method. Many of these beliefs may be modified if US physicians had more exposure and used the subcutaneous method more often.

Table 1. Survey responses

able 1. Survey responses	United	Canada	
	States (n, %)	(n, %)	p Value*
Completely agree/ Partially agree			
Prefer to use the subcutaneous route over other parenteral routes	1 (11)	7 (88)	0.017
Prefer to use the intravenous route over other parenteral routes	8 (89)	1 (13)	0.002
The nursing staff is more com- fortable with administration of medications/hydration via a subcutaneous route	2 (22)	6 (75)	0.022
I am comfortable with using the subcutaneous route to administer hydration	8 (89)	6 (75)	0.62
I am comfortable with using the subcutaneous route to administer medications	8 (89)	8 (100)	1
I believe the intravenous route is most efficient route of administration	8 (89)	1 (13)	0.013
Subcutaneous route is better tolerated by patients when compared to other parenteral routes	2 (22)	6 (75)	0.064
Subcutaneous route is easier to administer as compared to other parenteral routes	2 (22)	8 (100)	0.02
Subcutaneous route causes more discomfort compared to intravenous route	1 (11)	1 (13)	0.45
Familiarity with subcutaneous route			
Familiar with the subcutaneous route of administration			0.2
Not familiar	0 (0)	0 (0)	
Somewhat familiar	2 (22)	0 (0)	
Extremely familiar	6 (88)	8 (100)	
Level of education/ training where first learned about the subcutaneous route			0.62
Medical school	0 (0)	1 (13)	
Residency/Fellowship	5 (56)	5 (63)	
Post training work experience	4 (44)	2 (25)	

\*Statistical testing was based upon a 5-point Likert scale (completely agree/partially agree/neither agree nor disagree/partially disagree/completely disagree). This summary collapses categories (completely agree/partially agree) for clarity and ease of presentation. The bolded values indicate statistical significance of a p value less than 0.05.

There are limitations to this study. We discovered that there were several eligible PCUs that had closed because of the pandemic and had not reopened. A larger sample size may have detected more differences in perceptions. Also, the survey questions provide us insight into differences in opinions between physicians in the 2 countries but do not establish causality into the underutilization of subcutaneous administration in the United States.

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Our findings suggest that the differences in perceptions between the physicians of the 2 countries are due to exposure to using the route. Further research is needed in this area to explore ways to incorporate subcutaneous administration of drugs and hydration into the US healthcare system.

**Author contributions.** Michael Tang and Rida Khan contributed equally to the manuscript.

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**Competing interests.** None of the authors have any conflicts of interests to disclose

#### References

- Andersen C (2020) Catseyes: Create catseye plots illustrating the normal distribution of the means. https://cran.r-project.org/web/packages/catseyes/ catseyes.pdf
- Anderson BA and Kralik D (2008) Palliative care at home: Carers and medication management. Palliative and Supportive Care 6(4), 349–356. doi:10.1017/S1478951508000552
- Bartz L, Klein C, Seifert A, et al. (2014) Subcutaneous administration of drugs in palliative care: Results of a systematic observational study. *Journal of Pain* and Symptom Management 48(4), 540–547. doi:10.1016/j.jpainsymman. 2013.10.018
- Caccialanza R, Constans T, Cotogni P, et al. (2018) Subcutaneous infusion of fluids for hydration or nutrition: A review. Journal of Parenteral and Enteral Nutrition 42(2), 296–307. doi:10.1177/0148607116676593
- Challiner YC, Jarrett D, Hayward MJ, et al. (1994) A comparison of intravenous and subcutaneous hydration in elderly acute stroke patients. Postgraduate Medical Journal 70(821), 195–197. doi:10.1136/pgmj.70. 821.195
- **Cumming G** (2014) The new statistics: Why and how. *Psychological Science* **25**(1), 7–29. doi:10.1177/0956797613504966
- Elsayem A, Calderon BB, Camarines EM, et al. (2011) A month in an acute palliative care unit: Clinical interventions and financial outcomes. American Journal of Hospice and Palliative Medicine 28(8), 550–555. doi:10.1177/1049909111404024
- Epstein RS (2021) Payer perspectives on intravenous versus subcutaneous administration of drugs. ClinicoEconomics and Outcomes Research 13, 801–807. doi:10.2147/CEOR.S317687
- Eti S, O'Mahony S, McHugh M, et al. (2014) Outcomes of the acute palliative care unit in an academic medical center. *American Journal of Hospice and Palliative Medicine* **31**(4), 380–384. doi:10.1177/1049909113489164

- Fainsinger RL, MacEachern T, Miller MJ, et al. (1994) The use of hypodermoclysis for rehydration in terminally ill cancer patients. *Journal of Pain and Symptom Management* 9(5), 298–302. doi:10.1016/0885-3924(94) 90187-2
- **Herndon CM and Fike DS** (2001) Continuous subcutaneous infusion practices of United States hospices. *Journal of Pain and Symptom Management* **22**(6), 1027–1034. doi:10.1016/S0885-3924(01)00365-7
- Hui D, De La Rosa A, Chen J, et al. (2020) State of palliative care services at US cancer centers: An updated national survey. Cancer 126(9), 2013–2023. doi:10.1002/cncr.32738
- Hui D, Dev R and Bruera E (2015) The last days of life: Symptom burden and impact on nutrition and hydration in cancer patients. *Current Opinion in Supportive & Palliative Care* 9(4), 346–354. doi:10.1097/SPC. 00000000000000171
- **Lipschitz S, Campbell AJ, Roberts MS**, *et al.* (1991) Subcutaneous fluid administration in elderly subjects: Validation of an under-used technique. *Journal of the American Geriatrics Society* **39**(1), 6–9. doi:10.1111/j.1532-5415.1991.tb05898.x
- Nelson KA, Glare PA, Walsh D, et al. (1997) A prospective, within-patient, crossover study of continuous intravenous and subcutaneous morphine for chronic cancer pain. *Journal of Pain and Symptom Management* 13(5), 262–267. doi:10.1016/S0885-3924(96)00329-6
- Parsons HA, Shukkoor A, Quan H, et al. (2008) Intermittent subcutaneous opioids for the management of cancer pain. Journal of Palliative Medicine 11(10), 1319–1324. doi:10.1089/jpm.2008.0155
- Penson RT, Joel SP, Roberts M, et al. (2002) The bioavailability and pharmacokinetics of subcutaneous, nebulized and oral morphine-6-glucuronide. British Journal of Clinical Pharmacology 53(4), 347–354. doi:10.1046/j.1365-2125.2002.01554.x
- Remington R and Hultman T (2007) Hypodermoclysis to treat dehydration: A review of the evidence. *Journal of the American Geriatrics Society* **55**(12), 2051–2055. doi:10.1111/j.1532-5415.2007.01437.x
- Slesak G, Schnürle JW, Kinzel E, *et al.* (2003) Comparison of subcutaneous and intravenous rehydration in geriatric patients: A randomized trial. *Journal of the American Geriatrics Society* **51**(2), 155–160. doi:10.1046/j.1532-5415. 2003.51052.x
- Tang M, Abdelaal M, Lau J, et al. (2023) Subcutaneous vs intravenous administration of medications and fluids for patients with cancer in the US and Canada. *JAMA Oncology* 9(5), 717–719. doi:10.1001/jamaoncol.2023.0239
- Vidal M, Hui D, Williams J, et al. (2016) A prospective study of hypoder-moclysis performed by caregivers in the home setting. Journal of Pain and Symptom Management 52(4), 570–574.e579. doi:10.1016/j.jpainsymman. 2016.04.009
- Walker P, Neuhauser MN, Tam VH, et al. (2005) Subcutaneous administration of cefepime. Journal of Pain and Symptom Management 30(2), 170–174. doi:10.1016/j.jpainsymman.2005.03.007