A STUDY PROTOCOL

EXPLORING CURRENT PRACTICE IN OPIOID PRESCRIBING FOR CANCER PAIN MANAGEMENT BY PALLIATIVE CARE, MEDICAL ONCOLOGY AND GENERAL PRACTICE SPECIALISTS IN AUSTRALIA AND NEW ZEALAND – a cross-sectional survey

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Version: 1

1. Study team

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2. Background

Pain is common amongst cancer patients. The WHO opioid ladder and titration methodology is well embedded as standard practice in supportive and palliative medicine [1]. The recommended use of opioids remains an effective treatment, with increasing evidence for the use of adjuvants.

Evidence suggests that oral morphine, hydromorphone, oxycodone and methadone offer similar pain relief for cancer pain with similar side effects. Morphine remains the first-choice opioid for most opioid-naïve patients, with a current lack of clinical evidence to guide selecting one opioid over another [2].
Switching opioids requires care to achieve equianalgesic dose, adequate analgesia and to avoid toxicity. The current level of knowledge and comfort of Australian and New Zealand doctors when selecting and rotating opioids is uncertain.

Additionally, barriers to prescribing opioids have been described both internationally and in Australia [3, 4]. One recent barrier, experienced by Australian clinicians, concerns the supply, availability and access to various opioids. Previously opioid shortages have been shown to alter prescription patterns and in turn, management of pain [5]. Therefore, by understanding current practice and the rationale behind prescribing decisions, professional bodies and policy makers will be better placed to further develop guidelines and inform policy for the ongoing safety and efficacy of cancer pain management.

3. Study aims

Overall aim:
To describe current practice in opioid prescribing for cancer pain management by palliative care, primary care and oncology specialists in Australia and New Zealand.

Specific Primary aims:

1) To identify the most common primary long-acting opioid(s) utilised for cancer pain
2) To examine patterns in opioid selection and titration for opioid-naïve patients
3) To explore methods and rationale for opioid prescribing and rotation
4) To identify factors influencing prescribing of opioids in Australia

Secondary aims

5) To identify how supply issues have impacted opioid prescribing

4. Method

A cross-sectional study will explore the current opioid prescribing practices of Palliative care, Medical Oncology and General Practice doctors in Australia and New Zealand. This method allows us to gather a convenient cross section of practices from around Australia and New Zealand, revealing insights into the current barriers facing doctors prescribing opioids and guiding future research.

The survey was developed by the research team and guided by a modified Murshid model[6] utilising the following domains concerned with factors that impact prescribing: Marketing effects (drug information, branding), patient characteristics (patient requests, expectations), and contextual factors (physician habit, cost/benefit of a medication, medication characteristics, control measures).

Elements from Knapp and Oeltjen's[7] model looking at the risk/benefit ratio model and how factors impact a physician's prescribing practice have also been included in the survey instrument. These factors include severity of disease, benefits/side effects of medications, a physician's specialty and demographics.

In view of potential qualitative data collection later, participants will be asked to follow a link if they would be willing to contribute to further research. This link will guide the willing participants to a separate form; therefore, all identifiable data will be kept separate from the main survey. Any further action with this data will be by way of ethics amendment.

The survey will be piloted with at least two clinicians for comprehension, logic and flow. These responses will not be used in the analysis.

4.1 Setting

The study will be undertaken online using a survey tool (Qualtrics).

4.2 Data collection

This survey seeks to gather information from a cross-section convenience sample of palliative medicine specialists, Medical oncologists and General practitioners from Australia and New Zealand.
Survey dissemination will be assisted by professional bodies such as the Australian and New Zealand Society of Palliative Medicine (ANZSPM), Clinical Oncology Society of Australia (COSA), and the Royal Australian College of General Practitioners (RACGP). We will also seek to recruit participants through investigators' own networks. An initial email will be sent to the professional bodies to send out to their members requesting participation (appendix 1).
Ideally two reminder emails will be sent at 4 and 6 weeks after the initial email.
The survey will be open for 8 weeks. It is anticipated the data collection period will be open from mid-August 2023 until mid-November 2023, depending on participant uptake and policies of the professional bodies disseminating the survey.
Due to the difficulties of sampling, response times, and working with various organisations, we have chosen to do a convenience sample.
The data will be collated by the investigators.

Please see the Explanatory statement (appendix 2) and survey questions (appendix 3)

4.3 Inclusion and exclusion criteria

Inclusion criteria:

- Advanced trainees and specialists in Palliative medicine, medical oncology, and general practice AND
- Currently practicing in Australia/New Zealand

Exclusion criteria:

- Nurse practitioners and registered nurses OR
- Doctors practicing outside of the above specialties
- People outside of Australia/New Zealand

4.4 Consent and Withdrawal

The survey is voluntary, and consent is implied by participation.
Prior to submitting their survey response participants can withdraw by not completing/submitting their form.
Given that there are no identifiers collected with the survey responses, once a survey response is submitted that participant will be unable to request their withdrawal.

5. Storage, access, and destruction of data

Qualtrics will be used as the electronic data collection platform and complies with the security and privacy standards of Monash Health and Monash University due to enforceable contract obligations.
All electronic data will be stored on secure Monash Health servers. Monash Health policies governing the access and storage of research data will be adhered to in line with The National Statement. Only named investigators will have access to any raw data, and the team is experienced in secure data storage and data management. Data held by Monash will be kept for 7 years, after which it will be destroyed. The destruction of all data held by Monash Health will be irreversible with no chance of recovery later. Digital data will be destroyed by deleting or overwriting information, purging magnetic media through degaussing (exposure to a strong magnetic field) or destroying the physical media.

6. Privacy and confidentiality

The generated data will be kept confidential according to the National Statement on Ethical Conduct in Human Research 2007 (updated 2018) and the Australian Code for Responsible Conduct of Research 2018.
The research team are experienced in the conduct of research and confidential data management.

7. Analysis plan

Data will be initially exported to Excel for cleaning. The analysis will occur in SPSS, Stata or other appropriate statistical analysis software. Survey results will be summarised using descriptive statistics and reported using frequencies, means/medians, standard deviations/interquartile ranges as appropriate. Data will also be analysed to assess associations between clinical specialities and prescribing practises appropriate statistical analyses.

8. Reporting of study results

These findings may be published in a peer-reviewed journal, and presented at conferences, societal meetings or other professional gatherings. The professional bodies involved in distributing our survey will be provided with an infographic and summary of results on completion of the study to inform members of the findings.
At no time will the results presented be identifiable.

9. Budget

This is an unfunded study being undertaken by staff as part of their role.

10. References

1. Organization WH. WHO guidelines for the pharmacological and radiotherapeutic management of cancer pain in adults and adolescents. 2018.

2. Hanks GW, Conno FD, Cherny N, Hanna M, Kalso E, McQuay HJ, et al. Morphine and alternative opioids in cancer pain: the EAPC recommendations. British Journal of Cancer. 2001;84(5):587-93.
3. Gallagher R, Hawley P, Yeomans W. A Survey of Cancer Pain Management Knowledge and Attitudes of British Columbian Physicians. Pain Research and Management. 2004;9(4):188-94.
4. K R. Sustainable access to appropriate opioids for palliative care patients in Australia-preventing the need for crisis management. J Pain Palliat Care Pharmacother. 2020;34(1):13-21.
5. Haider A, Qian Y, Lu Z, Naqvi S, Zhuang A, Reddy A, et al. Implications of the Parenteral Opioid Shortage for Prescription Patterns and Pain Control Among Hospitalized Patients With Cancer Referred to Palliative Care. JAMA Oncology. 2019;5(6):841.
6. Murshid MA, Mohaidin Z. Models and theories of prescribing decisions: A review and suggested a new model. Pharm Pract. 2017;15(2):990.
7. Knapp DE, Oeltjen PD. Benefits-to-risk ratio in physicians use when prescribing. Am J Public Health. 1972;62(10):1346–1347.

Appendix 1

Invitation email template to be provided to professional bodies to assist with survey dissemination

Monash Health are inviting you to participate in a confidential survey (10-15min) exploring the current practice of opioid prescribing for cancer pain.

Pain is common amongst cancer patients, for which the recommended use of opioids remains an effective treatment. There has been an increase in opioid prescribing in Australia over the past decade. Concurrently various changes to government regulations, and more recently, increasing issues with supply, have created challenges to prescribers with implications for patients with cancer pain. This study aims to explore current practice in Australia and New Zealand in primary selection of long-acting opioids for cancer pain management, and to identify the impact of barriers on opioid prescribing.

At the end of the survey, we are interested in your thoughts regarding the current issues with availability, supply and withdrawals of opioid medications and how they are impacting your practice.

We will not be asking about breakthrough opioid dosing, rather focusing on background opioids and challenges around prescribing.

The results from this survey will help to inform further research, identify current issues, and support requests for change.

This survey has been reviewed and approved as a Quality Assurance activity at Monash Health (ethics approval: RES-23-0000-489Q)

For the explanatory statement and to start the survey please follow this link: <link>

For more information please contact Dr Rachel Everitt- Rachel.everitt@monashhealth.org

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Appendix 2

Explanatory statement

Welcome and thank you for your interest in this survey.

We are seeking to understand the current practice in opioid prescribing for cancer pain by palliative care, medical oncology and general practice specialists in Australia and New Zealand.
The focus will be on primary opioid selection in opioid-naive patients, opioid rotation and titration, as well as potential barriers to opioid prescribing.
We will not be asking about breakthrough medications in this survey.

At the end of the survey, we are interested in your thoughts regarding the current issues with the availability, supply and withdrawals of opioid medications and how they are impacting your practice.

Participation in this survey is voluntary.

The survey will take around 10-15 minutes to complete. You are eligible to complete this survey if you are a doctor working in Palliative Medicine, Medical Oncology, or General Practice. Completing any part of the survey implies your consent to participate. All survey responses are anonymous, and all data will be stored on a secure online platform. Only the research team will have access to the data. *This study has been reviewed and approved as a Quality Assurance activity at Monash Health* (ethics approval: RES-23-0000-489Q).

This research has been initiated by Dr Rachel Everitt (Palliative Care Fellow, Monash Health)
Other investigators involved in this research include:
A/Prof Peter Poon (Supportive and Palliative Care Unit, Monash Health)
Dr Catriona Parker (Monash University, School of Clinical Sciences at Monash Health)
Ms Jade Hudson (Supportive and Palliative Care Unit, Monash Health)

If you have any questions about the research or require further information, please contact Dr Rachel Everitt (Rachel.everitt@monashhealth.org)

If you wish to lodge a complaint about the survey you may do so via the Human Research Ethics Committee Executive Officer via 03 9594 4611 or research@monashhealth.org

Appendix 3:

Survey questions:

Demographics:

Q1 What is your age?

o 20-29 years (1)

o 30-39 years (2)

o 40-49 years (3)

o 50-59 years (4)

o 60 + years (5)

Q2 What is your gender?
o Male (1)
o Female (2)
o Non-binary / third gender (3)
o Prefer not to say (4)

Q3 Where is your most common place of practice?

- o New Zealand (1)
- o New South Wales (2)
- o Queensland (3)
- o South Australia (4)
- o ACT (5)
- o Victoria (6)
- o Western Australia (7)
- o NT (8)
- o Tasmania (9)

Q4 How would you describe your place of practice?
o Regional/rural (1)
o Metro (2)

Q5 What is your current role?
(Please select any/all that apply)
o Palliative Care Registrar (1)
o Palliative Care specialist (2)
o Medical Oncologist/ registrar (3)
o General Practitioner/ registrar (4)
o Other (5) _____

Q6 For Palliative care specialists: What palliative medicine qualification did you complete?

- o Fellowship of the Australasian Chapter of Palliative Medicine (1)
- o Clinical Diploma in Palliative Medicine (2)

Q7 For how many years have you worked in your current specialty? (Including training time)
o0-5 years (1)
o5-10 years (2)
o10-20 years (3)
o20 + years (4)

Q8 How comfortable do you feel initiating the following medications for cancer pain?

	Extremely uncomfortable (1)	Somewhat uncomfortable (2)	Neither comfortable nor uncomfortable (3)	Somewhat comfortable (4)	Extremely comfortable (5)
Morphine (1)	○	○	○	○	○
Oxycodone (2)	○	○	○	○	○
Targin (oxycodone/naloxone) (3)	○	○	○	○	○
Hydromorphone (4)	○	○	○	○	○
Fentanyl (5)	○	○	○	○	○
Buprenorphine (6)	○	○	○	○	○
Methadone (7)	○	○	○	○	○
Pregabalin (8)	○	○	○	○	○
Gabapentin (9)	○	○	○	○	○

Duloxetine (10)	○	○	○	○	○
TCAs such as Nortriptyline (11)	○	○	○	○	○
Steroids such as dexamethasone (12)	○	○	○	○	○
Ketamine (13)	○	○	○	○	○
Lignocaine (14)	○	○	○	○	○
Ketorolac (Parenteral) (15)	○	○	○	○	○
Tapentadol (16)	○	○	○	○	○
Other (17)	○	○	○	○	○

Q9 On average, how often do you commence a patient on a long-acting opioid

- o Daily (1)
- o Once a week (2)
- o Once a month (3)
- o Never (4)
- o Other (0) _____

Q10 Please rank the following opioids in order of how frequently you prescribe them for cancer pain (1-7)

- o Morphine (1) _____
- o Oxycodone (2) _____
- o Targin (oxycodone/naloxone) (3) _____

- Hydromorphone (4) _____
- Fentanyl (5) _____
- Buprenorphine (6) _____
- Methadone (7) _____

Q11 For what reason(s) do you select your highest ranked option?
(Select any/all that apply)

1. It is most effective (1)
2. Fewer side effects/ well tolerated (2)
3. In line with my colleagues' practice (3)
4. Cost (4)
5. Availability (5)
6. As per guidelines (specify which) (6)
   _____
7. Other (7) _____

Q12 Regarding the highest ranked opioid above, what would be the most common starting dose in an opioid-naive patient?
State name of opioid and dose.
(Assume normal renal function, age <80 and AKPS >70)

_____

Q13 How often would you typically review/titrate your highest ranked long-acting opioid dose after commencement in an opioid-naive patient?

	Daily (1)	Every 3 days (2)	Every 5 days (3)	Weekly (4)	Fortnightly (5)	None of these (0)
REVIEW in an inpatient setting (1)	○	○	○	○	○	○
TITRATE in an inpatient setting (2)	○	○	○	○	○	○
REVIEW in an outpatient setting (3)	○	○	○	○	○	○

TITRATE in an outpatient setting (4)	○	○	○	○	○	○

Q14 Are there any long-acting opioids you would never prescribe in your practice? (select any/all that apply)

- ☐ Morphine (1)
- ☐ Oxycodone (2)
- ☐ Targin (oxycodone/naloxone) (3)
- ☐ Hydromorphone (4)
- ☐ Fentanyl (5)
- ☐ Buprenorphine (6)
- ☐ Methadone (7)
- ☐ Other (8) _____

Q15 What are the reason(s) for not prescribing the above opioid(s)?

- ☐ Ineffective (1)
- ☐ Poorly tolerated (2)
- ☐ Cost (3)
- ☐ Not available (4)
- ☐ Stigma (5)
- ☐ Lack of experience prescribing that opioid (6)
- ☐ Other (7) _____

Q16 How often do you prescribe the following weak opioids before considering stronger opioids for cancer pain?

	Often (1)	Sometimes (2)	Rarely (3)	Never (4)
Codeine Phosphate (1)	○	○	○	○
Tapentadol (2)	○	○	○	○
Tramadol (3)	○	○	○	○

Other (4)	○	○	○	○	

Q17 Please state how strongly you agree/disagree with the following statements

	Strongly disagree (1)	Disagree (2)	Neutral (3)	Agree (4)	Strongly agree (5)
I am very experienced in prescribing opioids (1)	o	o	o	o	o
I have a good level of knowledge about prescribing opioids (2)	o	o	o	o	o
I am aware of opioid options/alternatives (3)	o	o	o	o	o
I am concerned about side effects when prescribing opioids (4)	o	o	o	o	o
I am concerned about addiction when prescribing opioids (5)	o	o	o	o	o
I am concerned about professional/ legal repercussions when prescribing opioids (6)	o	o	o	o	o

I have a good knowledge of current restrictions on prescribing (eg PBS) (7)	o	o	o	o	o

Q18 How significant are the following *patient/medication* factors when selecting background opioids for cancer pain in opioid naive patients?

	Not significant (1) (1)	(2) (2)	(3) (3)	(4) (4)	Very significant (5) (5)
Mechanism of patient's pain (1)	○	○	○	○	○
Breakthrough medications available (2)	○	○	○	○	○
Cost (3)	○	○	○	○	○
Renal function (4)	○	○	○	○	○
Liver function (5)	○	○	○	○	○
Available routes of medication- ie oral, injectable, transdermal (6)	○	○	○	○	○
Availability/shortages of specific opioids (7)	○	○	○	○	○

Patient requests/expectations (8)	○	○	○	○	○
Stigma regarding opioids (9)	○	○	○	○	○
Patient health literacy (10)	○	○	○	○	○
Side effect profile (11)	○	○	○	○	○
Marketing/promotion of certain brands (12)	○	○	○	○	○
Potential medication interactions (13)	○	○	○	○	○
Patient/caregiver compliance (14)	○	○	○	○	○
Other (15)	○	○	○	○	○

Q19 How likely would the following factors trigger a conversion to a different opioid in your practice?

	Extremely unlikely (1)	Somewhat unlikely (2)	Neither likely nor unlikely (3)	Somewhat likely (4)	Extremely likely (5)
Intolerable side effects (1)	○	○	○	○	○
Poor pain control despite large doses (2)	○	○	○	○	○

Change in mechanism of pain (3)	○	○	○	○	○
Mode of delivery unacceptable to patient (4)	○	○	○	○	○
Frequency of dosing (5)	○	○	○	○	○
Patient request (6)	○	○	○	○	○
Other (7)	○	○	○	○	○

Q20 What strategies do you employ when rotating opioids in cancer pain patients who require a change in medication?
(Select all that apply)

- ☐ Seek advice from a pharmacist (1)
- ☐ Seek advice from a medical colleague (2)
- ☐ Search guidelines (please specify) (3)
  _____
- ☐ Refer to a specialty team (please specify) (4)
  _____
- ☐ Own knowledge (5)
- ☐ Other (6) _____

Q21 Which three long-acting opioids do you most commonly rotate between for cancer pain?
(Please select 3 options)

- ☐ Morphine (1)
- ☐ Oxycodone (2)
- ☐ Targin (oxycodone/naloxone) (3)
- ☐ Hydromorphone (4)

- ☐ Fentanyl (5)
- ☐ Buyprenorphine (6)
- ☐ Other (7) _____

Q22 Are there any opioids that are currently unavailable in your place of practice that you would like to be able to use?

- ○ Yes (specify which) (1)
- ○ No (2)

Q23 Please describe why you would like to use the above opioid.

_____

Q24 The following questions relate to the current and impending issues regarding opioid supply. We are aware of several common opioids being withdrawn, and/or becoming less available in certain formulations. We are interested in how these issues have impacted your practice and the care of your patients with cancer pain.

Has the supply/availability of opioids impacted your practice this year?

- ○ Yes (1)
- ○ No (2)

Q25 If yes, how has your practice been impacted by the above?
(select any/all that apply)

- ☐ I am less willing to prescribe opioids (1)
- ☐ Changing from preferred choice to a less preferred opioid option (2)
- ☐ Patients self-ceasing medications due to not being able to access (3)
- ☐ Change to dose due to formulations being unavailable (ie liquid) (4)

Other (5) _____

Q26 In your opinion, does there need to be a stronger government policy for opioids/analgesics to protect supply?

- ○ Yes (1) _____
- ○ No (2)

Q27 Do you have any further comments or anything you would like to add?

_____
_____
_____
_____

_____

Q28 Finally, in the future, we might undertake some qualitative interviews to improve our understand some of the findings from this survey. We don't have the details about this yet, but if you are interested in participating or hearing more please let us know by clicking HERE. You will be taken to a different survey, so we keep your survey responses and your identifying information separate and your above survey responses remain anonymous.

Future qualitative interviews will be part of a research study that will be submitted to the Monash Health Human Research Ethics Committee for review and approval.
