

## Impact case study (REF3)

<b>Institution:</b> University of Leeds		
<b>Unit of Assessment:</b> 2		
<b>Title of case study:</b> Improving the management of cancer related pain		
<b>Period when the underpinning research was undertaken:</b> 2009–2016		
<b>Details of staff conducting the underpinning research from the submitting unit:</b>		
<b>Name(s):</b>	<b>Role(s) (e.g. job title):</b>	<b>Period(s) employed by submitting HEI:</b>
Michael Bennett	Professor of Palliative Medicine	July 2011-present
(Susan) Jose Closs	Professor of Nursing	April 1998-March 2018
Lucy Ziegler	Associate Professor	June 2012-present
Matthew Mulvey	University Academic Fellow	Nov 2012-present
<b>Period when the claimed impact occurred:</b> August 2013–July 2020		
<b>Is this case study continued from a case study submitted in 2014?</b> N		
<b>1. Summary of the impact</b> (indicative maximum 100 words)		
<p>Cancer causes 9,600,000 annual deaths worldwide (160,000 in UK) and half of all patients experience moderate to severe pain in the year before they die. Even in developed countries, inadequate assessment and treatment of pain leads to 30% of patients experiencing poor pain management before death, despite analgesia being available.</p> <p>Research led by University of Leeds has been used by many national and international organisations to ensure patients with cancer and other advanced diseases receive appropriate and effective pain management before they die. For example, the Care Quality Commission used it to develop inspection standards for cancer-related pain within NHS hospitals in England, while the World Health Organisation (WHO) changed the International Classification of Diseases (ICD) in 2018 to include the classification of cancer-related pain. ICD is adopted by health care systems in 117 countries to improve diagnosis and customise treatment.</p>		
<b>2. Underpinning research</b> (indicative maximum 500 words)		
<p>Research at the University of Leeds, led by Professor Michael Bennett with international collaborations has:</p> <p>(a) <b>Improved international assessment and classification of pain</b>  A systematic review of international literature [1] established the first actual prevalence and causes of neuropathic pain (pain from nerve damage, the most difficult type of pain to control) in cancer patients. The review identified 22 studies involving 13,683 patients. For these studies, researchers performed sensitivity analyses on the prevalence estimates using different clinical assessment criteria. An international cohort study [2] from 17 European centres recruited 1,051 patients and used standardised measures to reveal new insights into the adverse impact of neuropathic pain in cancer patients. These papers were internationally significant as the first research to highlight the importance of identifying this pain type in clinical practice to ensure more tailored treatment.</p> <p>(b) <b>Determined effectiveness of and access to analgesia</b>  A Cochrane systematic review and meta-analysis identified 17 studies that randomised 1,390 patients and was the first to establish that two commonly used strong opioids for cancer pain, oxycodone and morphine, were equally effective [3]. This paper was also cited in NICE guidance for Opioids in palliative care. Detailed analysis of adverse effects gave clinicians clear evidence, for the first time, that either drug could be used as initial treatment. A further systematic review [4]</p>		

used a novel mixed treatment meta-analysis to indirectly compare data from 5 randomised controlled trials (RCTs) on the relative effectiveness of rapid-onset oral fentanyl formulations against morphine and a placebo for exacerbations of cancer pain (called episodic pain). No clinical trials had compared all three directly, which provided high quality evidence to include these reviews in clinical prescribing guidelines for cancer pain of European and North American cancer organisations such as the European Society for Medical Oncology and the National Comprehensive Cancer Network, respectively.

A retrospective cohort study [5] linked routine data on diagnosis, health care resource use, and opioid prescribing in 6,050 patients who died from cancer. Overall access to strong opioids corresponded to that of other international literature but the study found that access occurred only a few weeks before death. It also uncovered significant inequalities in access to, and duration of, opioid treatment for older patients. This evidence was used in British Medical Association guidance to ensure that access to appropriate pain relief in palliative care is not affected by a patient's age.

**(c) Established the importance of support for self-management**

A systematic review and meta-analysis [6] was the first to demonstrate that interventions which support self-management lead to significantly improved pain outcomes for cancer patients. These interventions consist of helping patients to understand pain and educating them in how to manage their medicines and get appropriate help, aspects that are often overlooked in routine care. The review included 21 RCTs which randomised 3,501 patients and provided a clear and significant estimate of effectiveness. Thus, we provided granular reports on the variations of effectiveness through sensitivity analyses of single dose with multiple dose studies, and of intervention with different methods of control.

**3. References to the research** (indicative maximum of six references)

Research from Leeds has made important contributions to the field of cancer pain management at an international standard, has contributed important knowledge and ideas and is published in the highest ranked peer-reviewed pain and palliative care journals in these fields:

[1] **Bennett MI**, Rayment C, Hjermstad M, Aass N, Caraceni A, Kaasa S. Prevalence and aetiology of neuropathic pain in cancer patients: a systematic review. *Pain* 2012; 153(2): 359-365. DOI: [10.1016/j.pain.2011.10.028](https://doi.org/10.1016/j.pain.2011.10.028)

➤ *Systematic review widely cited in international cancer pain guidelines.*

[2] Rayment C, Hjermstad M, Aass N, Kaasa S, Caraceni A, Strasser F, Heitzer E, Fainsinger R, **Bennett MI**. Neuropathic cancer pain: prevalence, severity, analgesics, and impact from the European Palliative Care Research Collaborative Computerised Symptom Assessment study (EPCRC-CSA). *Palliative Medicine* 2013; 27(8): 714-721. DOI: [10.1177/0269216312464408](https://doi.org/10.1177/0269216312464408)

➤ *International cohort analysis that quantified impact of neuropathic pain.*

[3] Schmidt-Hansen M, **Bennett MI**, Arnold S, Bromham N, Hilgart JS. Oxycodone for cancer-related pain. *Cochrane Database of Systematic Reviews* 2015; Feb 27; DOI: [10.1002/14651858.CD003870.pub5](https://doi.org/10.1002/14651858.CD003870.pub5)

➤ *First meta-analysis to show equivalence of oxycodone and morphine relating to efficacy and adverse effects, widely cited in international cancer pain guidelines.*

[4] Jandhyala R, Fullarton JR, **Bennett MI**. Efficacy of rapid-onset oral fentanyl formulations versus oral morphine for cancer-related breakthrough pain: a meta-analysis of comparative trials. *Journal of Pain and Symptom Management* 2013; 46(4): 573-580. DOI: [10.1016/j.jpainsymman.2012.09.009](https://doi.org/10.1016/j.jpainsymman.2012.09.009)

➤ *First network meta-analysis to compare relative efficacy of placebo, morphine and fentanyl for breakthrough pain.*

[5] **Ziegler LE**, **Mulvey MR**, Blenkinsopp A, Petty D, **Bennett MI**. Opioid prescribing for cancer patients in the last year of life: a longitudinal population cohort study. *Pain* 2016; 157(11): 2445-

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2451. DOI: [10.1097/j.pain.0000000000000656](https://doi.org/10.1097/j.pain.0000000000000656)

- *Cohort study demonstrating inequalities in access to opioids, widely cited in cancer pain guidelines and policy documents.*

[6] **Bennett MI**, Bagnall AM, **Closs SJ**. How effective are patient-based educational interventions in the management of cancer pain? Systematic review and meta-analysis. *Pain* 2009; 143(3): 192-9. DOI: [10.1016/j.pain.2009.01.016](https://doi.org/10.1016/j.pain.2009.01.016)

- *First meta-analysis to show impact of educational interventions on cancer pain relief, widely cited in international cancer pain guidelines.*

**Grants:** **Bennett MI**, IMPACCT Programme Grant by NIHR, 2010-2018, approx. GBP2,200,000 including extension

#### 4. Details of the impact (indicative maximum 750 words)

Our research has made an impact on health through cancer-related pain management in the UK, and on international health policy through the WHO and cancer organisations across Europe and United States. These organisations influence international healthcare professional behaviour, benefitting patients living with and beyond cancer. Even so, it is difficult to provide robust data on patient impact because pain severity is not a routinely recorded health care outcome.

#### IMPACT ON HEALTH

##### Care Quality Commission Inspection framework for end of life care

Bennett, as member of the National Institute for Health and Care Excellence (NICE) original guidance committee on opioids for palliative care, led the dissemination of the original guideline in 2012 [A]. He was also invited to chair NICE evidence committee to update the guidance in 2014 and 2016 [B], which cites research in Leeds [C]. The purpose of NICE guidance is to provide 'evidence-based recommendations to improve health and social care' in the UK. The NICE guideline on opioids for palliative care remains in place. It recommends that healthcare professionals provide verbal and written information on strong opioid treatment to patients and carers, and supports self-management. Additionally, since oxycodone and morphine are equally effective, the latter is cheaper and therefore to be used first line.

Bennett was also invited by the Faculty of Pain Medicine (FPM) in 2015 to lead development of NHS core standards for cancer-related pain, "Core Standards for Pain Management Services in the UK (CSPMS)". The FPM is the professional body responsible for the training, assessment, practice and continuing professional development of specialist medical practitioners in the management of pain in the UK. The FPM standards for cancer-related pain incorporated Leeds evidence on supporting self-management and focus on pain assessment; including access to analgesia, assisting patients and referral to specialist help [D].

Subsequently, the Care Quality Commission (CQC) developed an *inspection framework* in 2016 which incorporated both the NICE guidance on opioids in adult palliative care and the FPM standards for cancer-related pain [E]. CQC is the independent regulator of health and adult social care services in England; ensuring patients receive safe, effective and high-quality care. Since 2016, all NHS Hospital Trusts must provide evidence of how they meet these standards and guidance; directly driving improvements in pain outcomes for cancer patients within the NHS.

Analysis of CQC inspection reports from 2016 onwards demonstrates that these standards have influenced inspection outcomes [F]. Each of the following quotes, from various hospital inspection reports, corresponds to a CQC quality outcome which illustrates how pain was monitored and treated at end of life care:

- a) "Pain assessments and pain scores were not completed consistently." (CQC outcome 'Requires improvement');
- b) "Staff assessed and monitored patients regularly to see if they were in pain and gave pain

- relief in a timely way.” (CQC outcome ‘Good’);
- c) “The specialist palliative care team worked with the specialist pain team, that included a combined multidisciplinary team meeting fortnightly to discuss patients with complex pain needs.” (CQC outcome ‘Outstanding’).

The Dean of FPM has confirmed Bennett’s role in the development of the FPM Core Standards, and the influence of his work to the CQC framework, “*Prof Bennett’s contribution has been instrumental in articulating the Care Quality Commission (CQC) Inspection Framework in 2016: FPM standards for cancer-related pain were incorporated in the CQC inspection framework and facilitated optimisation of pain management of patients in end-of-life care.*” [G].

## IMPACT ON INTERNATIONAL HEALTH POLICY

### WHO International Classification of Diseases (ICD), 11<sup>th</sup> revision ICD-11, Classification of chronic pain

WHO is responsible for publishing the ICD since 1948. The ICD is regularly revised to keep up to date with health science and medical practice; ICD-11 is the latest revision of the guidelines. Bennett was invited to serve on the international pain classification committee for ICD-11, and to lead work on cancer pain taxonomy, as pain had not previously been represented within ICD. The inclusion of pain classification in the *ICD-11 guidelines* represents a substantial international policy change [H,I].

ICD is used by 117 countries to define and study disease patterns, manage health care, and allocate resources. About 70% of the world’s health expenditures are allocated using ICD for reimbursement and resource allocation. ICD is the international standard for defining and reporting diseases and health conditions, for all clinical and research purposes. The inclusion of a cancer pain taxonomy provides a common language which allows health professionals to compare and share health information about cancer-related pain across the globe. This is a significant and far-reaching step forward for global recognition and coding of cancer-related pain, driving international improvements in clinical care and research. Bennett is first author on the published taxonomy [I], which also cites Leeds research, including papers on assessment of neuropathic pain and episodic pain in cancer patients. Taskforce Chair of the International Association for the Study of Pain has acknowledged Bennett’s role in the ICD-11, “*Thanks to Michael Bennett’s work, the mechanism (neuropathic) and periodicity (episodic) features of cancer pain are now distinctly recognised in the classification system. This has benefitted standards of pain management in cancer patients and paved new way to the development of pain treatment and classification systems of pain.*” [J].

Using headache as an exemplar, having a common language and terminology has accelerated advancements in research regarding headache mechanisms, and type-specific headache treatments. With an improved understanding of characteristics specific to a headache type, deriving an accurate headache diagnosis has substantially improved treatment outcomes through mechanism- and evidence-based treatment strategies.

### 5. Sources to corroborate the impact (indicative maximum of 10 references)

[A] Prescribing strong opioids for pain in adult palliative care: summary of NICE guidance. *BMJ* 2012; 344. DOI: [10.1136/bmj.e2806](https://doi.org/10.1136/bmj.e2806)

[B] NICE Guidance: Opioids in palliative care (Group membership, p. 16)  
<https://www.nice.org.uk/guidance/cg140/documents/cg140-opioids-in-palliative-care-evidence-update2>

[C] Surveillance proposal consultation document:  
Surveillance report 2016 – Palliative care for adults: strong opioids for pain relief  
<https://www.nice.org.uk/guidance/cg140/documents/surveillance-review-proposal> (Leeds research cited p. 7; also, page 21: reference #5)

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[D] Core Standards for Pain Management Services in the UK (Leeds research cited p. 109)  
<https://fpm.ac.uk/standards-publications-workforce/core-standards>

[E] Care Quality Commission Inspection framework for end of life care (20160905 p. 15-16)

[F] CQC Inspection reports

[G] Testimonial letter from Dean of the Faculty of Pain Medicine of the Royal College of Anaesthetists, 14/01/2021

[H] ICD-11 for Mortality and Morbidity Statistics: Chronic cancer related pain  
<https://icd.who.int/browse11/l-m/en#/http%3a%2f%2fid.who.int%2fid%2fentity%2f785363034>

[I] Pain taxonomy classification: **Bennett MI**, Kaasa S, Barke A, Korwisi B, Rief W, Treede RD, and the ICD-11 task force. The IASP classification of chronic pain: Chronic cancer-related pain. *Pain* 2019; 160(1):38-44. DOI: [10.1097/j.pain.0000000000001363](https://doi.org/10.1097/j.pain.0000000000001363)

[J] Testimonial letter from Taskforce Chair of the International Association for the Study of Pain, 19/10/2020