

Institution: University of Dundee		
Unit of Assessment: UoA4 Psychology, Psychiatry and Neuroscience		
Title of case study: Opioid prescribing in Scotland: stemming the epidemic		
Period when the underpinning research was undertaken: 2011 to 2020		
Details of staff conducting the underpinning research from the submitting unit:		
Name(s):	Role(s) (e.g. job title):	Period(s) employed by submitting HEI:
Blair Smith	Professor	2011 to date
Lesley Colvin	Professor	2018 to date
Period when the claimed impact occurred: 2013 to 2020		
Is this case study continued from a case study submitted in 2014? N		

1. Summary of the impact

Despite a lack of evidence for the effectiveness of opioids in the long-term management of pain, prescribing rates have risen in recent years leading to the so-called 'opioid epidemic'. Dundee-led research investigating the prevalence and impact of chronic pain resulted in the first comprehensive evidence-based guideline for the assessment and management of chronic pain, SIGN 136. Since publication of the guideline, opioid prescribing has reduced by 19% across Scotland, with similar reductions observed locally in Tayside and Fife. This research on the benefits and risks of opioids prescribed for chronic pain in Scotland has informed the recent (2019) revision and update of SIGN 136 and has contributed to other local, national and international prescribing strategies.

2. Underpinning research

Opioids are very effective for managing short-term (acute) pain, but there is no evidence for their efficacy as a long-term treatment: in fact there is increasing evidence of harms, such as adverse physical or emotional effects, misuse, addiction or death, from long-term use. The Chronic Pain Research Group, established by Smith in 2011 and co-led by Colvin since 2018 has investigated the prevalence and impact of chronic pain, including neuropathic pain (pain caused by somatosensory system damage or disease), for which opioids are often used despite little evidence of effectiveness. Smith and colleagues demonstrated that neuropathic pain is common and impacts on all aspects of health and life, (with 17% of sufferers describing extremely low associated quality of life, equivalent to "worse than death") [R1].

Working with the Scottish Government National Chronic Pain Steering Group, Smith and Colvin identified the need for evidence-based guidance on chronic pain management in Scotland. A proposal to produce such guidance was therefore taken to the Scottish Intercollegiate Guideline Network (SIGN). One of the main challenges identified by stakeholders was the use of opioids for chronic non-cancer pain; this became a key question in SIGN 136 [E3], which remains the only comprehensive evidence-based guideline for chronic pain assessment and management available globally.

Comprehensive community-based prescribing data for Tayside were obtained through the Health Informatics Centre and used to conduct a cross-sectional patient-level analysis. This identified an 18-fold increase in the rate of strong opioid prescribing in NHS Tayside over a 15-year period (1995-2010), and the patient factors associated with this (older age, female gender, polypharmacy) [R2]. Although this increase was largely driven by Tramadol (which was classified as a strong opioid in this study), established strong opioids, such as morphine and fentanyl, showed 5-fold increases.

Further work identified a research gap around rates and consequences of opioid prescribing in Scotland, which were quantified year-by-year from 2003 to 2012, again using national high quality routine prescribing, linked and research-derived datasets. Potentially dangerous prescribing was scrutinised particularly closely [R3]. The rate of strong opioid prescribing doubled during the study period; in Scotland ~18% of the population were prescribed an opioid in 2012. Gender and deprivation increased risk for both prescribing and potentially dangerous co-prescribing of benzodiazepines. Systematic reviews also demonstrated the incidence of iatrogenic opioid misuse/addiction when prescribed for pain (pooled estimates as high as 4.7%) and associated factors [R4], as well as evidence for opioid induced hyperalgesia and associated factors [R5]. Separately, Smith co-led the opioids section in a detailed systematic review of all available pharmacological treatments for neuropathic pain [R6], conducted as a major update on previous treatment guidelines identified by the Neuropathic Pain Special Interest Group (NeuPSIG) of the International Association for the Study of Pain. This found weak evidence for the effectiveness of strong opioids, and none to support their long-term use.

3. References to the research

[R1] Torrance, N., Lawson, K. D., Afolabi, E., Bennett, M. I., Serpell, M. G., Dunn, K. M. & Smith, B. H. (2014). Estimating the burden of disease in chronic pain with and without neuropathic characteristics: Does the choice between the EQ-5D and SF-6D matter? *Pain*, Vol. 155, pp. 1996-2004. DOI: [10.1016/j.pain.2014.07.001](https://doi.org/10.1016/j.pain.2014.07.001).

[R2] Ruscitto, A., Smith, B. H. & Guthrie, B. (2015). Changes in opioid and other analgesic use 1995-2010: Repeated cross-sectional analysis of dispensed prescribing for a large geographical population in Scotland. *European Journal of Pain*, Vol. 19, No. 1, pp. 59-66 DOI: [10.1002/ejp.520](https://doi.org/10.1002/ejp.520).

[R3] Torrance, N., Mansoor, R., Wang, H., Gilbert, S., Macfarlane, G. J., Serpell, M., Baldacchino, A., Hales, T. G., Donnan, P., Wyper, G., Smith, B. H. & Colvin, L. (2018). Association of opioid prescribing practices with chronic pain and benzodiazepine co-prescription: A primary care data linkage study. *British Journal of Anaesthesia*, Vol. 120, No. 6, pp. 1345-1355 DOI: [10.1016/j.bja.2018.02.022](https://doi.org/10.1016/j.bja.2018.02.022).

[R4] Higgins, C., Smith, B. H. & Matthews, K. (2018). Incidence of iatrogenic opioid dependence or abuse in patients with pain who were exposed to opioid analgesic therapy: A systematic review and meta-analysis. *British Journal of Anaesthesia*, Vol. 120, No. 6, pp. 1335-1344 DOI: [10.1016/j.bja.2018.03.009](https://doi.org/10.1016/j.bja.2018.03.009).

[R5] Higgins, C., Smith, B. H. & Matthews, K. (2019). Evidence of opioid-induced hyperalgesia in clinical populations after chronic opioid exposure: A systematic review and meta-analysis. *British Journal of Anaesthesia*, Vol. 122, No. 6, pp. e114-e126 DOI: [10.1016/j.bja.2018.09.019](https://doi.org/10.1016/j.bja.2018.09.019).

[R6] Finnerup, N. B., Attal, N., Haroutounian, S., McNicol, E., Baron, R., Dworkin, R. H., Gilron, I., Haanpää, M., Hansson, P., Jensen, T. S., Kamerman, P. R., Lund, K., Moore, A., Raja, S. N., Rice, A. S., Rowbotham, M., Sena, E., Siddall, P., Smith, B. H. & Wallace, M. (2015). Pharmacotherapy for neuropathic pain in adults: A systematic review and meta-analysis. *Lancet Neurology*, Vol. 14, No. 2, pp.162-173 DOI: [10.1016/s1474-4422\(14\)70251-0](https://doi.org/10.1016/s1474-4422(14)70251-0).

4. Details of the impact

Colvin and Smith's work on SIGN 136 influenced Scottish policy and practice with regard to chronic pain (e.g. level and duration of opioid prescribing). Their research highlighted the need for local and national guidelines and strategies in order to reduce rates and improve the safety and appropriateness of opioid prescribing in chronic pain not caused by cancer (for which there is a different prescribing strategy). This led to the National Chronic Pain Prescribing Strategy

[E1, E2]. Changes in the evidence base led Smith and Colvin to revise the SIGN 136 section on opioids in 2019 **[E3]**.

This impact has, to date, mostly occurred within Scotland, although there is evidence that it is beginning to extend further afield **[E10]**. Colvin and Smith proposed and led development of the 2013 SIGN guideline on Management of Chronic Pain **[E3, E4]**. SIGN clinical practice guidelines are always based on rigorous systematic reviews and appraisals of evidence **[E5]**. SIGN's Key Recommendations are important benchmark standards for care and, since its publication, SIGN 136 has formed the basis of pain service provision and improvement in Scotland **[E4]**. Its 2013 edition includes evidence-based guidance on safe and effective opioid prescribing, including the recommendation for prescribers to seek pain specialist review when prescribing reached morphine equivalent doses >180mg/day. This was used as the basis for the Scottish Government's strategy to reduce opioid-related harms **[E4]**. The National Prescribing Strategy for Chronic Pain was produced in collaboration with the Scottish Government Effective Prescribing and Therapeutics Branch **[E1, E2]** and has been used along with SIGN 136 and general practice-based feedback on opioid prescribing rates to drive reductions in numbers and doses of opioid prescriptions across Scotland, as confirmed by the Healthcare Quality and Improvement Directorate **[E4]**:

[SIGN 136] has been at the centre of all clinical decisions relating to Scottish Government and NHS policy and practice relating to pain management since its publication. It was central to the subsequent Scottish National Pain Prescribing Strategy (2018), to which [Smith and Colvin] provided additional important input. Its updated Opioids Section (2019) continues to inform policy and practice across the country.

Recently, we have seen opioid prescribing rates beginning to fall across the country, and we are grateful for the work that Professors Colvin and Smith have led and undertaken to help with this.

Smith represents NHS Tayside on the national group overseeing implementation of this strategy. Smith and Colvin sit on the Scottish Government Short Life Working Group on Prescription Medicine Dependence and Withdrawal in Scotland, which aims to guide and support safe prescribing and de-prescribing of medicines that can cause dependence or withdrawal **[E1, E2, E4]**.

Noting increasing evidence concerning the harms and lack of long-term effectiveness of opioids, Colvin and Smith proposed and conducted a revision of the opioids section of SIGN 136 **[E3]**. Published in 2019, this provides more detailed evidence-based guidance and recommendations on safe and effective prescribing and referral for specialist review with morphine equivalent doses >90mg/day. The Chair and Programme Lead of SIGN write **[E5]**:

Professors Lesley Colvin and Blair Smith... have played a key role in advancing understanding of opioid use in chronic pain, underpinning the opioid guidance in SIGN 136 and its recent update (2019).

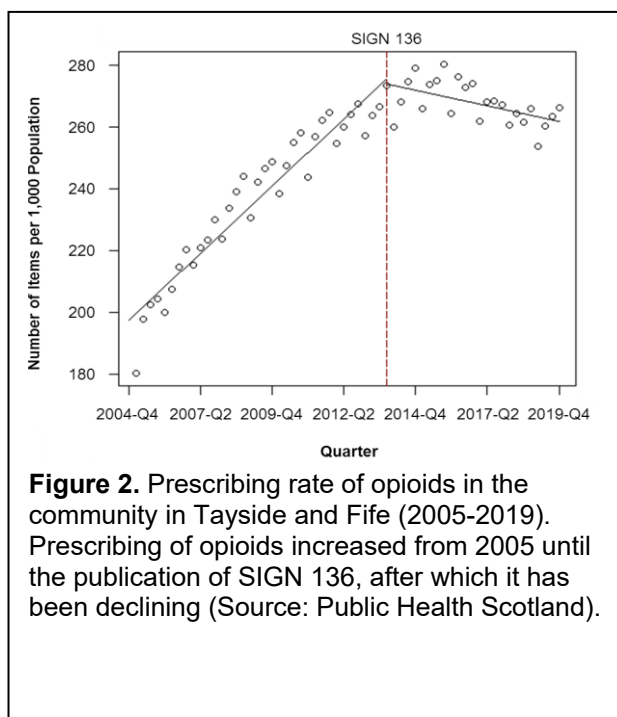
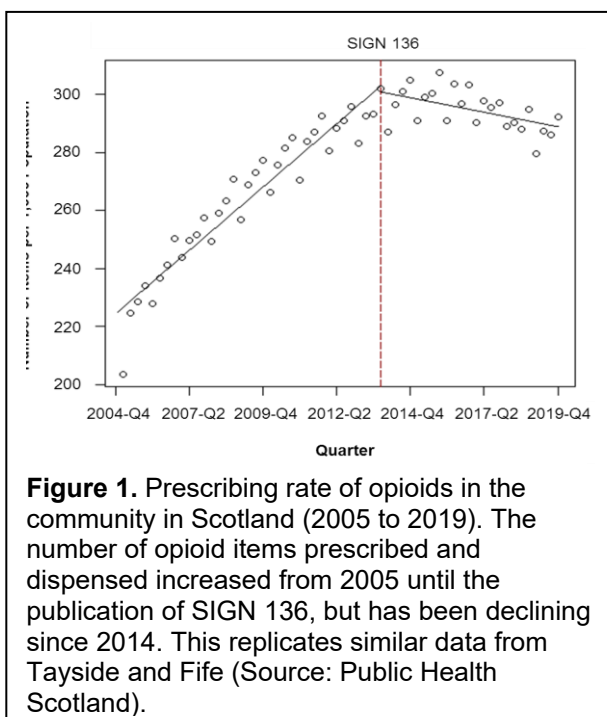
The Royal College of Anaesthetists has incorporated the SIGN 136 approach (as the only guideline in this area) into their new Quality Improvement Compendium **[E6]**. This includes a chapter (Section 10.5, by Colvin and Smith) on long-term opioid use in chronic pain. This book is distributed to every UK NHS anaesthetics department and is freely available to all online.

Colvin sits on the MHRA Opioid Expert Working Group. Following pre-publication sharing of the SIGN 136 opioid update **[E5]**, the MHRA published new guidance on the safe use of opioids, including changes to patient information leaflets, product characteristics and packaging **[E7, E8, E9]**. The impact of these changes on opioid prescribing rates in England is yet to be assessed.

Internationally, Smith's involvement with the Neuropathic Pain Special Interest Group, NeuPSIG (Management Committee 2010 to 2020, Chair 2016 to 2018), has included analysis of evidence-

based guidance for pharmacological treatment of neuropathic pain [R6], which has contributed to and been cited in other international guidelines [E10], as well as the SIGN 136 revision [E3]. Locally, Smith led the development of pathways for managing chronic pain in NHS Tayside, which are used by all prescribers there [R6, E1, E2, E3].

Opioid prescribing rates have become one of NHS Scotland's key national therapeutic indicators [E4] and, following the demonstration that they exhibit wide geographical variation [R3], will also feature in Scotland's Atlas of Healthcare Variation [E4]. From 2005 to 2013, opioid prescribing rates increased steadily in Scotland, but this trend has changed significantly coincident with the publication of SIGN 136 (Fig. 1). Between Q4 2013 and Q1 2020 there was an 18.8% reduction in the number of people prescribed an opioid [E11]. This change has also been observed at local level since 2014 (Fig. 2), in contrast to the UK as a whole. Smith and Colvin's team established that ~250,000 individuals (18% of the Scottish population) were prescribed an opioid in one year [R3], placing ~11,750 (4.7%) at risk of dependence or abuse [R4]. An 18.8% reduction in this figure could equate to ~2,200 fewer people/year experiencing this outcome, with substantial population benefits in reduction of other harms and improved Quality of Life [E3].



The impact of the work undertaken by Smith and Colvin on policy and practice relating to opioid prescribing in Scotland is acknowledged at the highest level [E2]:

Over the last decade, the Government and NHS in Scotland have worked to reduce harms associated with the prescribing of opioids. To do this, we have developed strategies to reduce both the number of people receiving an opioid prescription, and the overall doses that are prescribed.

Professors Colvin and Smith have contributed importantly to this work and success, through their roles in developing and disseminating SIGN 136 (2013 and 2019), their contributions to the National Prescribing Strategy, and their membership of the Scottish Government Short Life Working Group on Prescription Medicine Dependence and Withdrawal.

5. Sources to corroborate the impact

[E1] Harrison, H., Cameron, P., Colvin, L., Cormack, J., Gilbert, S., Hurding, S., Kirkpatrick, D., Lannigan, N., Lim, P., Rae, C., Smith, B., Steven, D. & Wallace, H. (2018). *Quality prescribing*

for chronic pain: A guide for improvement 2018-2021. Scottish Government, Realistic Medicine, NHS Scotland. R6 is cited under Early Assessment on p12 (Footnote 11). Available at: <https://www.therapeutics.scot.nhs.uk/wp-content/uploads/2018/03/Strategy-Chronic-Pain-Quality-Prescribing-for-Chronic-Pain-2018.pdf>. [Accessed 26 March 2021]

[E2] Head of Effective Prescribing & Therapeutics Scottish Government 2020. To whom it may concern. *Letter of Support, 9th December 2020*.

[E3] Scottish Intercollegiate Guidelines Network. (2013), revised and updated 2019. SIGN 136: *Management of chronic pain: A national clinical guideline* Edinburgh: Scottish Intercollegiate Guidelines Network [Online]. Colvin chaired the group, Smith was a member. Smith and Colvin are identified as having developed the 2019 update, to which they contributed Section 10.3 *Opioids* on behalf of SIGN. R3 and R4 are cited (References 201 and 229). Available at: https://www.sign.ac.uk/media/1108/sign136_2019.pdf [Accessed 16th March 2021].

[E4] Team Leader (Neurological Conditions Chronic Pain and Long-Term Conditions), Scottish Government; Head of Effective Prescribing and Therapeutics Branch, Scottish Government; and Interim Chief Medical Officer for Scotland 2020, Scottish Government. Healthcare Quality and Improvement Directorate. To whom it may concern. *Letter of Support, 10th November 2020*.

[E5] Chair and Programme Lead, SIGN 2020. To whom it may concern: REF impact case study: Opioid prescribing: Stemming the epidemic. *Letter of Support, 23rd November 2020*. SIGN aims to improve patient care through developing and disseminating guidelines.

[E6] Cheresheva, M., Johnston, C., Colvin, J. R. & Peden, C. J. (2020). *Raising the standards: RCoA quality improvement compendium*. 4th ed. Incorporation of SIGN 136 into clinical practice. Smith and Colvin contributed Section 10.5, *Opioid use in Chronic Pain*. R3 is cited (Section 10.5, Ref 1). Available at: https://rcoa.ac.uk/sites/default/files/documents/2020-08/21075%20RCoA%20Audit%20Recipe%20Book_Combined_Final_25.08.2020_0.pdf [Accessed 26 March 2021]

[E7] Medicines & Healthcare products Regulatory Agency (2020). *Drug safety update: Latest advice for medicines users*. Vol. 14, No. 2. Commission on Human Medicines in response to the Opioid Expert Working Group, of which Colvin was a member; cites SIGN 136. Available at: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/920770/Sept-2020-DSU-PDF.pdf [Accessed 26 March 2021]

[E8] Medicines & Healthcare products Regulatory Agency, September 2020. Patient Information Leaflet: *Opioid medicines and the risk of addiction*. Available at: <https://assets.publishing.service.gov.uk/media/5f6a078ed3bf7f7238f23100/Opioid-safety-leaflet-v1-Sep2020.pdf> [Accessed 26 March 2021]

[E9] Medicines & Healthcare products Regulatory Agency, September 2019. *Additional warning statements for inclusion on the label and/or in the leaflet of certain medicines*. Available at: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/835489/Warning_Statements.pdf The section on opioids is at p37-38. [Accessed 26 March 2021]

[E10] Past Chair, NeuPSIG 2020. To whom it may concern. *Letter of Support, 20th October 2020*.

[E11] Hebert, H. L., Morales, D. R., Torrance, N., Smith, B. H. & Colvin, L. A. (2021). Assessing the impact of sign 136 on opioid prescribing rates in Scotland: An interrupted time series analysis *medRxiv*, 2021.02.19.21251770. DOI: [10.1101/2021.02.19.21251770](https://doi.org/10.1101/2021.02.19.21251770)