**Title:**
Harnessing placebo effects in primary care: do we need to use placebos?

**Proposed supervisory team:**
- Professor George Lewith, Professor of Health Research, University of Southampton
- Dr Felicity Bishop, Associate Professor, University of Southampton
- Dr Adam Geraghty, Senior Research Fellow, University of Southampton
- Dave Newell, Anglo-European College of Chiropractic

**Project description:**

**Introduction**
Recent small-scale trials in the US suggest it might be possible to elicit clinically meaningful placebo effects in patients by openly prescribing them placebo pills. These trials of so-called open-label placebos have been published involving patients with IBS, depression, and back pain. We propose exploring the use of open-label placebos in chronic osteoarthritis (OA) pain. In the UK one third of adults over 45 have sought treatment for OA, primarily through general practice, and in 2010 OA was the 11th leading cause of disability. Disability due to OA increased substantially from 1990 to 2010 and will continue increasing with the aging population. NICE Guidelines recommend a patient-centred approach to OA including information and self-management, non-pharmacological interventions (e.g. exercise, manual therapy, aids and devices), and pharmacological management (paracetamol, NSAIDS, corticosteroids, capsaicin, opioids), before considering referral for joint surgery. Non-invasive interventions typically demonstrate small to moderate effects. Opioids and intra-articular corticosteroids may have larger short-term benefits but patients are concerned about adverse effects. While these treatments can help patients, their full potential is often not realised. Although practitioners typically perceive musculoskeletal pain to be well-managed, patients typically report ongoing chronic pain and disability. OA is primarily managed in general practice and increasingly by physiotherapists (although referral to rheumatologists/surgeons occurs in a minority). There is therefore a need to improve primary care management of pain in osteoarthritis. There is also good evidence to suggest that enhancing patients’ placebo effects is both possible and clinically meaningful in OA. Local pain is the primary complaint in OA: analgesic effects of placebos have been demonstrated in healthy and clinical populations and the psychological and neurobiological mechanisms of placebo analgesia are well-described. Furthermore, meta-analyses of clinical trial data suggest that placebos elicit clinically-meaningful effects in OA. However, it would be premature to propose a major trial of open-label placebos for OA pain at this stage. Our research on doctors’ and patients’ attitudes to placebos suggests that open label placebo prescribing would be ethically highly controversial in UK primary care. Patients in our focus groups expressed diverse views on clinical applications of placebos. Some were willing to entertain the idea of GPs prescribing placebos (particularly where the patients believed such placebos would have positive health benefits and in the absence of effective conventional treatments), but others expressed concerns about potentially deceptive prescribing and did not believe that open-label placebos would be effective. We have recently developed a digital intervention that improves patients’ knowledge about placebos and their effects and so changing patients’ attitudes towards these phenomena is one possible way forward. Concerns about societal and regulatory issues were a key theme to emerge from our mixed methods study of GPs’ views. Some GPs were keen to exploit placebo effects to benefit patients but many were adamant that there was no legitimate (i.e., ethical) place for prescribing placebos in UK primary care. It is therefore essential to distinguish between placebo effects and placebos per se. Based on our qualitative data, interventions around placebo effects have much more potential than open-label placebo prescribing to be taken up and implemented in practice to benefit patients. Furthermore, we do not know whether it is actually necessary to use placebos in order to have the desired effect, namely better health outcomes for patients mediated by strengthened placebo effects. Indeed, our earlier work suggests that communication about
treatments might be particularly important in OA and probably contribute to placebo effects observed in clinical studies.

**Aims and Objectives** The overarching research aim is to examine the feasibility of open-label placebo prescribing to reduce pain in adults with chronic osteoarthritis in primary care. The research objectives are 1) to determine the acceptability of open-label placebo-prescribing vs enhancing placebo effects to reduce pain in chronic OA; 2) to provide an initial comparison of the effects on chronic OA pain of two interventions designed to enhance placebo effects, one that involves openly and honestly prescribing placebos and one that involves enhancing the context around prescribing conventional pharmaceutical pain management; and 3) to test the feasibility of conducting a trial of interventions to enhance placebo effects and thus reduce pain in adults receiving prescriptions for chronic OA in primary care. This PhD will thus examine the potential role and durability of open label placebo prescribing for OA in UK primary care.

**Training plan:**

**Methods**

A PPI panel will be convened and will be central to developing this work, especially in relation to the ethics of consent and open label prescribing. To address objective (a), a comprehensive critical review will consider the scope for application of placebo effects in UK primary care. This review will synthesise qualitative and quantitative studies on patients and practitioners’ perspectives as well as published ethical arguments, relevant regulations and policy documents.

To address objectives (2) and (3) a mixed methods pilot feasibility study will test the use of open-label placebos for chronic osteoarthritic pain in primary care (specifically OA hip and knee). A fully factorial design will compare the effects of two factors – placebo intervention (placebo vs a new or changed anti-inflammatory or analgesic for pain) and placebo effect enhancement (usual prescribing narrative vs enhanced prescribing narrative in which prescriber imparts positive expectations and strong rationale for potential benefit). This design will permit us to compare the acceptability and potential effects on pain of using a placebo intervention vs using a placebo effect intervention. We hypothesise that the latter will be more acceptable and more effective. Quantitative measures will include standardised pain and quality of life measures (WOMAC), perceived intervention credibility, outcome expectancies, and perceived empathy (process measures). Patients and practitioners’ perspectives will be captured through semi-structured qualitative interviews.

In summary, this PhD will outline whether open label placebos could be used in UK primary care and critically question the assumption that placebos are needed to harness placebo effects for improved patient outcomes.