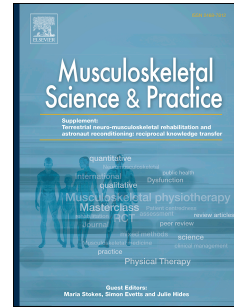


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Title:

Avoiding Nocebo and Other Undesirable Effects in Chiropractic, Osteopathy and
Physiotherapy: An Invitation to Reflect

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Competing Interests Statement

DHS works at several osteopathic education institutions and has received consultancy fees from Altern Health Ltd., an enterprise developing digital therapeutics for pain management. OT receives fees for delivering courses on low back pain communication and podcasting. GR leads education programmes on placebo, nocebo effects, and contextual factors in healthcare to under- and postgraduate students along with private CPD courses. MM has received travel expenses and/or honoraria as an invited speaker regarding therapeutic relationship from San Diego Pain Summit, Physio Austria, and Münster University of Applied Sciences. DN has no conflicts of interests to declare in relation to this work. LR receives fees for delivering communication courses and is currently working on a research project funded by Pfizer. LV has received consulting fees from Lundbeck. JDR receives fees for delivering pain management courses.

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Authors' background

David Hohenschurz-Schmidt, MOst, MSc, is a practising osteopath and a researcher at Imperial College London. He holds an MSc in neuroscience and is completing a PhD in pain research and clinical trial methodology. He investigates placebo effects mainly in the context of nonpharmacological clinical trials and is leading several projects on nocebo effects and language in osteopathic practice. David also investigated communication and management in the context of remote consultations, now contributing to the development of digital pain management programmes. Through presentations and teaching engagements, David is communicating the role of treatment context on various pain-related mechanisms and, eventually, clinical outcomes.

Oliver Thomson PhD, MSc, is a practicing osteopath in London and an Associate Professor at The University College of Osteopathy. His main research interests are using qualitative methodologies to understand the language, clinical reasoning, beliefs, and behaviours of MSK health professionals. He has published over 50 peer-reviewed papers in these areas. He is also host of The Words Matter Podcast where he has critical discussions with leading academics, philosophers, and clinicians across healthcare on topics related to person-centred care, clinical communication, evidence-based practice, and the biopsychosocial model.

Jerry Draper-Rodi, DProf (Ost), PG Dip, PG Cert, DO, is a Senior Research Fellow at the University College of Osteopathy and Director of the National Council for Osteopathic Research. His own research centres

on the translation of evidence into practice including training experienced osteopaths in the biopsychosocial management of patients with low back pain, evaluating the impact of this training on osteopaths' attitudes to back pain, their reported behaviours, and patient outcomes. Jerry provides pain management professional training for clinicians from COP and other professions, using a person-centred approach with a focus on communication skills and shared decision-making.

Giacomo Rossetini, PhD, PT, is a clinical physiotherapist, researcher, and lecturer from Italy. He earned his PhD at the Department of Neuroscience, Rehabilitation, Ophthalmology, Genetics, Maternal and Child Health - University of Genova in 2018, with a thesis on "Contextual Factors, Placebo And Nocebo Effects In Physical Therapy: Clinical Relevance And Impact On Research". Giacomo Rossetini is the author of over 60 peer-reviewed publications in physiotherapy journals. He has given over 50 presentations at universities and national and international conferences. His didactic, clinical, and scientific interests concern the field of musculoskeletal rehabilitation, with an emphasis on placebo and nocebo effects, and contextual factors.

Maxi Miciak PhD, BScPT, BPE, is Associate Professor at the University of Alberta. Her research draws upon her experiences as a physiotherapist to probe the factors that influence relational aspects of care. She has advanced knowledge in her field by developing a conceptual framework of the therapeutic relationship specific to physiotherapy. The framework has been used to develop a physiotherapy-specific measurement tool to assess the therapeutic relationship and in entry-to-practice and post-graduate education, with uptake reported in clinical practice. Her work has received significant interest in scientific and clinical communities with numerous citations and invitations to speak at local, national, and international conferences, webinars, and podcasts.

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Abstract

Introduction: While the placebo effect is increasingly recognised as a contributor to treatment effects in clinical practice, the nocebo and other undesirable effects are less well explored and likely underestimated. In the chiropractic, osteopathy and physiotherapy professions, some aspects of historical models of care may arguably increase the risk of nocebo effects.

Purpose: In this masterclass article, clinicians, researchers, and educators are invited to reflect on such possibilities, in an attempt to stimulate research and raise awareness for the mitigation of such undesirable effects.

Implications: This masterclass briefly introduces the nocebo effect and its underlying mechanisms. It then traces the historical development of chiropractic, osteopathy, and physiotherapy, arguing that there was and continues to be an excessive focus on the patient's body. Next, aspects of clinical practice, including communication, the therapeutic relationship, clinical rituals, and the wider social and economic context of practice are examined for their potential to generate nocebo and other undesirable effects. To aid reflection, a model to reflect on clinical practice and individual professions through the 'prism' of nocebo and other undesirable effects is introduced and illustrated. Finally, steps are proposed for how researchers, educators, and practitioners can maximise positive and minimise negative clinical context.

Introduction - The nocebo effect as a problem

Placebo and nocebo effects are changes in clinical outcomes due to patient expectations or subconscious learning, produced by treatment context rather than the typically considered ‘active’ element of an intervention. While placebo effects produce positive changes, nocebos are negative (Evers et al., 2018). The placebo effect is a recognised contributor to the effectiveness of many therapies (Tuttle et al., 2015; Wartolowska et al., 2017; Vollert et al., 2020; Bosman et al., 2021; Cashin et al., 2021; Tsutsumi et al., 2022), including manual and physical interventions for people experiencing musculoskeletal pain and other conditions (Bialosky et al., 2017, 2009; Chaibi et al., 2017; Dougherty et al., 2014). Expert consortia recommend using the placebo effect to enhance the real-world effectiveness of medical interventions and state the need to minimise nocebo effects (Evers et al., 2018) (Table 1). However, this paper argues that nocebo and other undesirable effects of treatment contexts have not been sufficiently researched. Their full complexity and relevance to clinical practice are potentially underestimated, particularly given that nocebo effects are likely easier to elicit and more impactful than placebo effects (Amanzio et al., 2009; Petersen et al., 2014; Greville-Harris and Dieppe, 2015). Importantly, chronic primary pain patients are arguably particularly vulnerable to nocebo effects due to previous experiences and other influences that may promote negative expectations in a treatment context (Locher et al., 2019). We propose that the prevalent conceptual models in chiropractic, osteopathy, and physiotherapy (COP) hold significant potential for negative cueing of contextual factors within therapeutic encounters and consequently nocebo and other undesirable effects.

Table 1: Definitions, relevant factors, and mechanisms implicated in placebo, nocebo, and other undesirable effects of chiropractic, osteopathy, and physiotherapy (COP).

Terminology	Definition and examples	Relevant factors of COP	Mechanism(s)
Placebo effect	<p>“Placebo and nocebo effects refer to the beneficial or adverse effects that occur in clinical or laboratory medical contexts, respectively, after administration of an inert treatment or as part of active treatments, due to mechanisms such as expectancies of the patient.” (Evers et al., 2018).</p> <p>In clinical practice, placebo and nocebo effects occur in response to factors other than the supposed main treatment action. For example, massaging a muscle may have direct effects on the muscle and nervous system, but ‘massage treatment’ will also have effects through the contextual factors listed in the next column.</p>	<p>Anything that can produce positive or negative expectations, respectively, or lead to learnt responses. For example (Bishop et al., 2017; Daniali and Flaten, 2019):</p> <ul style="list-style-type: none"> - Healthcare setting - Patient–practitioner interaction, such as verbal and non-verbal communication - Patient and practitioner characteristics, such as reputation, roles, and previous positive or negative experiences - Treatment characteristics or treatment ritual, including symbols and actions that convey meaning 	<p>For placebo analgesia (i.e. placebo-related pain reduction), relevant mechanisms are mainly neurophysiological (Benedetti et al., 2022; Colloca and Barsky, 2020):</p> <p>Through positive expectancy and learning, mainly activating the descending pain-modulating network:</p> <ul style="list-style-type: none"> - endogenous opioid system - endocannabinoid system <p>Also:</p> <ul style="list-style-type: none"> - reducing anxiety (mainly amygdala and its functional network) - activating reward mechanisms (mainly dopaminergic)

		<ul style="list-style-type: none"> - Socially conveyed expectations or learning (through communication, media, and observation of others) 	<p>system)</p>
<p>Nocebo effect</p>			<p>Through negative expectancy and learning:</p> <ul style="list-style-type: none"> - Activating the cholecystokinin (CCK) pronociceptive system - Increasing (anticipatory) anxiety (and activation of the hypothalamic-pituitary-adrenal axis) - Memory systems (mainly hippocampus and its functional network) (Bingel et al., 2022)
<p>Other undesirable effects of COP practice</p>	<p>Undesirable and potentially harmful effects beyond nocebo effects that are a direct result of how COP is commonly taught and practised. Examples include:</p> <p>Cognitive and psychological: Reinforcement or creation of false belief, anxieties, and potentially dependencies on treatment providers</p> <p>Behavioural: Development or reinforcement of passive coping mechanisms; Avoidance of more evidence-based therapeutic approaches</p> <p>Physical: Physical adverse events, which, in manual and exercise therapy, mainly include transient muscle soreness and rarely serious adverse events.</p> <p>Social: Reinforcement of the neoliberal focus on the individual as solely responsible for their own health; Depoliticisation of health and illness and thus exoneration of workplace factors and other socioeconomic determinants of health.</p> <p>Financial: Costs associated with ineffective and low-value</p>	<ul style="list-style-type: none"> - Biomedical belief systems of professionals, patients, and the societies of the global North in general - Verbal and non-verbal communication - Media, including advertising and social media - Socioeconomic and cultural context 	<p>Mechanisms are eventually reflected in a person's neurophysiology or health, but upstream mechanisms include cultural, economic, social, and interpersonal factors.</p> <p>Cognitive: Conscious and subconscious creation or reinforcement of beliefs</p> <p>Behavioural responses to such beliefs, and advice, communication, and expectancies created in the clinic</p> <p>(For adverse events) Physical and neurophysiological mechanisms leading to transient increases in pain; Physical tissue injury</p> <p>Social mechanisms and cultural 'acceptability' leading to the limiting of COP practice to the individual or narrow social circle</p> <p>Financial incentives for providers to create dependencies or provide unnecessary care</p>

	treatments (covered by the individual in private COP practice)		
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Like the placebo effect, nocebo effects are mainly mediated through learning and expectation mechanisms acting through descending pain modulatory pathways (Kleine-Borgmann and Bingel, 2018; Benedetti and Piedimonte, 2019; Colloca and Barsky, 2020; Benedetti et al., 2022). In the narrowest sense, nocebo hyperalgesia is the aggravation of pain not due to disease or treatment-inherent factors, but treatment context (Evers et al., 2018) (Table 1). Other nocebo effects can be the experience or aggravation of treatment side-effects, likely tiredness or soreness after COP treatments (Leboeuf-Yde et al., 1997) (although mild side effects may enhance treatment effects via expectancy mechanisms (Berna et al., 2017)). In a broader sense, however, context-dependent negative effects of patient-practitioner interactions go beyond immediate symptom aggravation and include learnt helplessness, fear avoidance, over-reliance on medical care, and other negative sequelae explored below. Although occasionally the mechanisms of classical nocebo effects may be implicated, behavioural and social mechanisms dominate. In particular, behavioural components likely contribute to negative outcomes that arise when biomedico-structural explanatory frameworks are communicated between practitioners and patients, but also in society at large (Table 1). There remains a need to explicitly identify and evidence the impact of nocebic elements within therapeutic encounters, and assess how these may be the result of profession-specific explanatory frameworks (Figure 1, Table 2). The purpose of this masterclass is to raise awareness of such explanatory frameworks amongst clinicians and educators and their potential impact on clinical interactions; and to highlight the need for further investigation to avoid undesirable effects on patients seeking care.

The context-sensitivity of treatment outcomes

Clinical outcomes are context-sensitive: Placebo research has illustrated the powerful impact of patient and practitioner characteristics and beliefs, the healthcare setting, treatment characteristics, and the patient–practitioner interaction (O’Keeffe et al., 2016; Bishop et al., 2017; Benedetti et al., 2018). Clinical practice in COP is often highly participatory, involving the sharing of patients’ narratives, verbal and non-verbal communication with practitioners, and physical interactions, including through touch (Roberts and Bucksey, 2007; Kim et al., 2022). Musculoskeletal practitioners make person/patient-specific judgements, where the solutions to clinical problems are often ambiguous, ill-defined, and not always amenable to the routine use of technical skills and propositional knowledge (Petty et al., 2012; Thomson et al., 2014). Furthermore, practitioners’ interactions with patients and the cues they deliver co-create meaning within the healthcare encounter (Hutchinson and Moerman, 2018; Stilwell and Harman, 2019), also interacting with an individual’s previous experiences (Newell et al., 2017) and the wider societal context. Patients may adapt how they behave, think, and experience their condition in accordance with these meanings.

Due to the contextually rich nature of the therapeutic encounter in COP, many authors recommend enhancing clinical outcomes through honing of contextual aspects that are under the practitioner’s control (Testa and Rossettini, 2016; Bialosky et al., 2017; Evers et al., 2018; Manaï et al., 2019). In these publications, however, the recommendations to avoid nocebo effects are largely a mirror image

of the attempt to 'boost' placebo effects: For example, where empathic communication is recommended to enhance placebo effects, de-validating communication should be avoided as it may lead to nocebo effects (Greville-Harris and Dieppe, 2015; Rossetini et al., 2020a, 2022). Albeit relevant, we argue that this approach is insufficient. Instead, we propose that features inherent in their historical development and underpinning explanatory frameworks make COP professions prone to generating nocebo and other undesirable effects in a systematic fashion. Similar attempts for investigation have been made in psychotherapy (Locher et al., 2019).

COP foundational knowledge: Focussing on the patient body

Body-mind dualism shaped most thinking about health and disease in western societies, and continues to influence patient expectations and medical decision-making (Demertzi et al., 2009; Hofmann, 2016). Musculoskeletal care has an inherent focus on the patient's body, indeed embedded in its name. The biopsychosocial model was proposed over 45 years ago (Engel, 1981) and while professional training and education may be increasingly incorporating psychosocial perspectives, clinical practice is still dominated by physically-focused approaches (Cowell et al., 2018; Macdonald et al., 2018; Oostendorp et al., 2015; Thomson et al., 2014). These approaches rely mostly on biomedical assumptions that are deeply ingrained in COP training (Gliedt et al., 2020) and professional identity.

Scientific interest in the human spine's role in health and disease dates back to ancient times (Sanan and Rengachary, 1996), but merged with Descartes' mechanical philosophy in the 17th century, powerfully postulating that "*all of animal physiology could be explained by mechanics.*" (Naderi et al., 2007). Explicitly referring to the notion of 'the body as a machine', osteopathy's founder, A.T. Still, incorporated this philosophy into his understanding of illness and therapy, with the osteopath as the 'mechanic' who tests the machine for signs of stress, strain, and deviations from the norm to then manually correct those 'lesions' (Liem, 2016; Still, 1908). From their inception, influences from spiritual vitalism and naturopathy are apparent in osteopathy and chiropractic. Nonetheless, such influences only led osteopaths to relocate the mechanical 'fulcrum' to the energetic realm (e.g., 'biodynamics') and chiropractors to 'remove neuromechanical interference' to facilitate the metaphysical flow of a universal life force (Simpson and Young, 2020). Mechanistic principles continue to dominate the teaching in craniosacral therapies (Liem, 2009; Sergueef, 2007) and chiropractic (Marcon et al., 2019). Explanatory frameworks in physiotherapy were influenced by regional phenomena, such as gymnastics, massage, and naturopathic traditions in Germany and Scandinavia (Hüter-Becker, 2004; Schiller, 2021) or the rehabilitation of injured soldiers in wartime Britain and the U.S. Furthermore, the quest for scientific validation in the 20th century (Nicholls, 2017) and a strong link to athletic performance science promoted the extensive measurement and classification of the body's structure and function. Throughout the 20th century, the COP professions have played their part in promoting a 'compulsory able-bodiedness', the hegemonic preferability of ableness at the expense of supposedly 'abnormal' people, including people living with some form of 'disability' or the normal effects of ageing (MacMillan, 2021; McRuer, 2010). For example, manual therapists and their institutions have at times promoted an obsession with 'good posture' (Hüter-Becker, 2004; Linker, 2005, 2021). Contemporary trends such as fascia-based concepts (Myers, 2012; Tozzi, 2012) or functional biomechanics ("Gray Institute - Blog," n.d.) are modern manifestations of an excessive focus on physicality and of a continuing body-mind dualism. Chiropractic Functional Neurology, an approach characterised by the finding and fixing of functional neurological 'lesions', alludes to the same

mechanical ‘tweaking’ but at nerve level (Meyer et al., 2017). Despite overwhelming evidence to the contrary (Lederman, 2011), the notion of normative body-mechanics is deeply embedded in the COP professions’ teaching models. As we argue below, this may underpin many undesirable effects of COP practice.

Examining clinical COP practice for potential nocebo and other undesirable effects

In the case of COP, nocebo effects have been attributed to contextual factors, briefly reviewed below (also Table 1). We add to the discussion behavioural features of practitioners and patients, also broadening the perspective by not only looking at pain and function in relation to nocebo effects but adding upstream mediators of poor health outcomes and a socioeconomic discussion of incentive structures.

The role of language and nonverbal communication

In the area of language, there are attempts to acknowledge the link between the nocebo effect and common clinical reasoning frameworks of COP practitioners. Stewart and Loftus (2018) promote “*an improved understanding of the frequently hidden influence that language can have on musculoskeletal rehabilitation*” (p.519) and draw attention to the fact that potentially harmful language may be linked to underlying concepts of health and disease. Especially, reconceptualising pain as a complexly influenced and emergent phenomenon rather than a linear consequence of tissue damage is warranted. A meta-analysis suggests that effect sizes related to verbally induced nocebo can be substantive (Petersen et al., 2014). Verbal cues can be either specifically designed as negative (“this will be painful”, as in experiments) or incidental within clinical settings such as the use of negative words to describe a non-threatening situation; for example, diagnostic descriptions of imaging reports perceived by patients as implying an increased severity of their condition (Farmer et al., 2021). Importantly for this discussion, COP vocabulary is replete with terms that medicalise normal anatomy (‘lesion’, ‘dysfunction’, ‘subluxation’, ‘asymmetry’, ‘scoliosis’, ‘blockage’, etc.) and physiological processes (e.g., ‘degeneration’). The negative impact of diagnostic labels has been further shown amongst patients experiencing low back pain: diagnostic labels which allude to specific pathoanatomy (e.g., ‘joint degeneration’ or ‘disc bulge’) led to more imaging and second-opinion consultations compared to those de-emphasizing anatomical structures and damage (e.g., ‘episode of back pain’, ‘lumbar sprain’, and ‘non-specific low back pain’)(O’Keeffe et al., 2022). Such reconceptualization is the aim of several biopsychosocial management strategies for patients with musculoskeletal pain (Leventhal et al., 2016; Carnes et al., 2017; Keefe et al., 2018; O’Sullivan et al., 2018; Ashar et al., 2021), most strikingly expressed in pain education approaches (Moseley and Butler, 2015; Traeger et al., 2018). Educating patients in an evidence-based manner is also concordant with many patients’ desire for explanation and diagnosis (McRae and Hancock, 2017). If a definite ‘label’ is desired by the patient, it nonetheless needs to be evidence-based and can be complemented by reassurance and education.

The not-so-therapeutic relationship

The therapeutic relationship is the shared affective affinity between practitioner and patient, formed by establishing personal and professional connections within a safe environment (Miciak et al., 2018, 2019; McCabe et al., 2021). Albeit often assumed to be inherently beneficial, therapeutic relationships

are complex social endeavours in which patients and clinicians are continually responding and reacting to a slew of emergent personal (e.g., emotions, expectations), intersubjective (e.g., power dynamics), and institutional (e.g., performance measures) factors. Given this complexity, ruptures are expected consequences of therapeutic relationships (Gelso and Kline, 2019; Miciak and Rossettini, 2022; Safran and Kraus, 2014). Ruptures are relational tensions that range from minor rifts to major breaches (Gelso and Kline, 2019; Safran and Kraus, 2014). Ruptures are implicit to all relationships, therapeutic or otherwise. Their presence within the clinical encounter implies nocebo effects (Blease, 2022) and nonadherence.

COP professional ways of practicing can cause relational ruptures. Although biopsychosocial and person-focused care models are promoted as 'the way' to practise (Gibson et al., 2020; Hutting et al., 2022), and would seem to mitigate relational breakdowns (Ekman et al., 2011), implementation is often conflicted, inconsistent, or mechanised (Ekman et al., 2011; Synnott et al., 2015; Cowell et al., 2018; Ng et al., 2021; Gibson et al., 2020). Clinicians' failure to connect with patients in a humanistic way (Gibson et al., 2020; Godfrey, 2020) or acknowledge the influence of their own emotional reactions on clinical decisions (Langridge et al., 2016; Miciak and Rossettini, 2022), could result in patients withdrawing from or becoming confrontational with clinicians, which if unaddressed can negatively influence the therapeutic process and clinical outcomes (Safran and Kraus, 2014). Further, disagreements on goals (Miciak and Rossettini, 2022) and potentially unmet patient expectations (Schemer et al., 2020) may cause ruptures. This is why Nijs et al. (2013) recommend exploring patients' attitudes and beliefs as the basis for clinical decision-making and the addressing of false beliefs.

Similarly, professional 'scripts', although efficient, can trigger such tensions when incongruent with patient needs. Scripts are professionally sanctioned ways of engaging based on 'written and unwritten' (Gibson et al., 2020) texts, such as best practice guidelines, outcome measures, and documentation practices (Gibson et al., 2020). In COP, most such scripts remain biomechanically focused (Cowell et al., 2018; Macdonald et al., 2018; Oostendorp et al., 2015; Thomson et al., 2014). Even clinicians trained in psychosocially oriented approaches to care might default to such scripts when they feel uncomfortable within the clinical interaction or need to be validated professionally. For example, clinicians under duress may automatically revert to biomedical aspects of care, become transactional versus relational in their approach, or engage in paternalistic ways of being (Ekman et al., 2011; Gibson et al., 2020; May et al., 2004).

Therapeutic relationships can empower or disempower patients in their experience of pain by cultivating a sense of safety or threat with and within their own bodies (Arandia and Di Paolo, 2021; Miciak et al., 2019). This may foster expectancies about symptom development, although the direction of the effect may depend on the specific example (Peschken and Johnson, 1997; McMurtry et al., 2006; Pincus et al., 2013). Safety as a function of relationships is ingrained in social hierarchies. For example, children gain trust in themselves when parents show trust in them (Ryan et al., 1994; Otto and Keller, 2014; Brummelman et al., 2019). A child trying to balance the branch of a tree is looking to their parent for encouragement and is more likely to hesitate or even fall if they are met with a worried expression (Gershgoren et al., 2011) - as would be the case if the parent thinks the branch might break at any point. The socially learnt expectation of threat or safety is a key mediator in placebo and nocebo effects, making improvement or deterioration more likely, respectively (Arandia and Di Paolo, 2021). Like a child to their parents, patients look to their clinician for an indication of safety or danger, for example when performing a movement, likely more so when the provider has fostered a hierarchical paternalistic relationship as is inherent in traditional COP thinking.

The clinical ritual

COP are highly ritualistic therapies, often with treatments delivered in clinical settings full of symbols of health and life, through repeated visits, routine 'skilful' examination, and treatment methods that convey professional and clinical expertise (Kaptchuk, 2011). This ritual is often accompanied by visible totems of hierarchised specialisation and expertise which the patient is invited to trust (titles, certifications, anatomical wall charts and models). At home, and like a reminder of the ritual, patients are encouraged to perform little rituals themselves (e.g., exercises). There is not necessarily any harm in such rituals. Indeed, they are part and parcel of all medical interventions, Western or otherwise, and science is beginning to recognise their healing potential (Jonas, 2018). However, while these rituals are *supposed to mean* 'healing' (Hutchinson and Moerman, 2018), their meaning is open to interpretation. Rituals can become problematic in various scenarios: When they are elevated to represent the only possible source to alleviate somebody's suffering, they can create dependency and potential for exploitation. An example is the idea of 'killer subluxations' which can only be removed by chiropractors (Carter, 2000). Also, clinicians need to be aware of the possibility of adverse conditioning, including from previous experiences with COP (Locher et al., 2019).

Social learning and the social context of practice

Social learning is strong (Sorensen, 2006) and COP clinicians regularly drive nocebic learning. YouTube content with men in white coats wielding a plasticine model of a spine whilst red flashes indicate the 'source' of the pain, may have more views than most public outreach campaigns, undoing valuable educational work (Maia et al., 2021; Hornung et al., 2022). These social media agitators, together with the disciples of traditionalist or secular schools of musculoskeletal care, keep the circles of social learning going. Indeed, this may constitute a negative social contract between patients and the treating professions, where outdated beliefs are kept alive and erroneous models communicated continuously by professionals to patients; the effect being that these explanatory frameworks then drive demand by patients. Together with their often appealingly simplistic logic, the continued spreading of such narratives ensures that an individual's symptomatic improvement is ascribed to the treatments – again perpetuating false beliefs.

Satisfaction does not equal effective care

Patient satisfaction with COP is high but does not correlate clearly with effectiveness: in a UK osteopathy survey, about 90% of patients were satisfied one week after their treatment with only 3% describing themselves as recovered (Fawkes and Carnes, 2021) (Also see Field and Newell (2016)). Satisfaction and clinical effectiveness interact in complex ways (Chen et al., 2019; Rossetini et al., 2020b), and arguments for the value of patient satisfaction are increasingly made (Morris et al., 2013; Tinetti et al., 2016). In private COP practice and elsewhere, however, incentives exist for practitioners to mainly provide what is likely to satisfy patients, not what constitutes evidence-based care. As outlined above, prevalent COP explanatory frameworks may facilitate such decision-making. Examples include patients preferring a 'simple' mechanistic diagnosis or patients with uncomplicated primary low back pain demanding (referral for) imaging (Blokzijl et al., 2021; Jenkins et al., 2016, 2018a): The clinician can decide to not satisfy the patient's wish, thus acting in line with current evidence, or to

comply and risk nocebo effects from relational ruptures or incidental imaging findings (Kendrick et al., 2001; Rajasekaran et al., 2021). Importantly, satisfaction may increase healthcare costs and contribute to worse clinical outcomes, including mortality (Fenton et al., 2012), although the evidence is conflicting (Anhang Price et al., 2014). Therefore, despite potential benefits, satisfaction should not be used as a proxy for effectiveness nor dominate clinical decision-making. Future research should evaluate its relationship with COP concepts and low-value care (Moynihan et al., 2012), and how clinicians can best negotiate patient expectations that conflict with evidence.

The economic context of clinical practice

Physiotherapy for musculoskeletal pain, in particular, can be delivered at relatively low cost individually or in group settings, potentially facilitating physiotherapy's integration into many public healthcare systems. Contrastingly, osteopathy and chiropractic are practised almost exclusively in private settings ("Chiropractic," 2017; "Osteopathy," 2017). However, compared to many biomedical interventions for pain, these are still relatively low-cost interventions, posing the question of why their integration into healthcare systems is not more advanced. While there are quality concerns with underlying efficacy and effectiveness research (Hohenschurz-Schmidt et al., 2021b, 2022a), spinal manipulation-based interventions, for example, show some beneficial effects, and underlying sham-controlled studies are plentiful (Hohenschurz-Schmidt et al., 2022b; Rubinstein et al., 2019). Therefore, the focus on private practice models may have additional reasons, and, apart from historical reasons, underlying thought models are a likely culprit: Concepts in osteopathy and chiropractic imply long-term treatment, including in the absence of symptoms – an approach that decision-makers in public healthcare systems are unwilling to support. Conversely, these models may appeal to people who can or would like to afford externalising responsibility for their health to practitioners.

Maintenance care is an example of patient passivity even in the absence of symptoms. It is common practice in osteopathy and chiropractic (Axén et al., 2019), probably mainly in pockets of the professions that adhere to traditional schools of thought (Gíslason et al., 2019). Although Eklund et al. (2018) have shown comparable effects for maintenance visits and symptom-driven visits in patients with persistent low back pain, these authors acknowledged the possibility that positive outcomes associated with ongoing visits could result from meeting and interacting with the clinician rather than the spinal manipulative therapy itself. Although there are some arguments for regularly 'checking in' with a healthcare professional (Axén et al., 2019; Volz et al., 2021), maintenance concepts may over-emphasise reliance on others rather than promoting health through self-management and a healthy lifestyle. At the same time, biomedical models of disease obscure socio-political causes of disease (Kriznik et al., 2018; Marmot, 2020) - an effect, however, that can be criticised in the biopsychosocial model or behavioural interventions, too (Nunan et al., 2021; Shakespeare et al., 2017). In addition, passive approaches may further increase the divide between those able to self-fund COP therapies and those who cannot: By blending into private practice business models that depend on returning patients for income, biomedical thinking turns otherwise relatively low-cost healthcare into an exclusive provision to those able to afford a series of appointments (McGill et al., 2015; Nunan et al., 2021), as reflected by the demographic profiles of patients seeking chiropractic (Beliveau et al., 2017; Herman et al., 2018; Mior et al., 2019) and osteopathic care (Burke et al., 2013; Fawkes et al., 2014; Alvarez Bustins et al., 2018; Fawkes and Carnes, 2021). Ideally, COP act as advocates for patients,

lobbying for availability of evidence-based interventions, integrations with public services, and reduction of socioeconomic disparities (Nunan et al., 2021).

Table 2: Examples of profession-specific sources of nocebo and other undesirable effects, their clinical manifestations, and potential implications

Clinical action or event	Potentially harmful consequences	Possible sources in the profession's core tenets or history
Shared across COP professions		
Ambiguous, fear-evoking or contradictory advice (Osborn-Jenkins and Roberts, 2021)	Confusing patients, limiting their chance to engage with active self-management strategies	Existence and propagation of numerous contradictory explanatory models
Use of unhelpful diagnostic labels such as 'chronic' and 'degeneration' (Roberts and Langridge, 2018)	Promotion of fear of movement and direct nocebo effects (through negative expectancies)	Physical focus of many thought models, medicalising normal anatomy and physiology
Failure to promote positive attributes of structure and function of the human body (Marcum, 2005; Stewart and Loftus, 2018)	Promotion of catastrophisation Distorting a person's own perception of their body and its ability to adapt.	The body is conceptualised as a machine that breaks down if all 'parts' are not 'aligned' and operating 'optimally' or 'properly'
Lack of recognition of 'non-traditional' explanatory factors, such as heritability and socioeconomic determinants of health (Nunan et al., 2021)	Increasing the onus on individual patients, with the potential to impact upon their self-esteem and self-efficacy or obscuring of other important contributors to illness	Embeddedness in private practice models (in many cases), relying on patients to return for income Commitment to bio-reductionist model of care
Physiotherapy		
Excessive attention to tissue modification induced through treatment (e.g., "The massage will normalise your fascia and trigger points") (Nicholls and Gibson, 2010)	Promoting beliefs in mechanistic causes of pain or disability Reinforcing dependence on the clinician who represents the protagonist of patients' care Discouraging patients from self-management strategies and active management of their clinical conditions	Dependence on a paternalistic model of care that reinforces patient passivity Commitment to bio-reductionist model of care Emphasis on biomechanical view of the body
Over-emphasis on teaching 'proper' static (e.g., "Avoid sitting slouched") and active postures (e.g., "Keep your back straight at all times during lifting") (O'Sullivan et al., 2012; Korakakis et al., 2019)	Promoting beliefs in mechanistic causes of pain or disability Limiting options for the patients to adapt within their contexts	Over-reliance on mechanistic spine-centric models and ergonomic models of pain or disability

	Triggering anxiety/fear regarding movement (e.g., performing 'right or wrong' positions)	
Overuse of low-value-based therapies (e.g., electrotherapy, ultrasound) not recommended by international guidelines for musculoskeletal conditions (Kharel et al., 2021; Zadro et al., 2020)	Waste of public and private economic resources Delayed recovery with persistence of pain and disability Failure to provide the best evidence to encourage the patient's active involvement in decision-making about their health (e.g., exercise, self-management)	Poor propensity to adopt clinical guidelines within care settings Biomechanical / reductionist thinking (ultrasound may be attractive if one thinks the problem is mainly 'in the tissue')
Osteopathy		
Communicating undue or excessive beliefs in the "body's capacity to heal itself" (Paulus, 2013)	Promoting anti-science beliefs and harmful treatments or treatment avoidance (in extreme cases). Illustrated, for example, by current intra-professional vaccine hesitancy (Thomson et al., 2021)	Historic incorporation of vitalistic concepts and a mistrust in mainstream medicine (likely justified at the time but often still adopted unquestioned) Contemporary affinity for and professional overlap with other naturopathic professions and homeopathy in some countries (e.g., Germany)
Communicating concepts of "(Somatic) Dysfunction" to patients (Fryer, 2016)	Promoting beliefs in mechanistic causes of non-specific pain or disability (Medicalisation of non-specific problems)	Historic over-reliance on mechanistic spine-centric models of health and disease
Cranial osteopathy models communicated to patients in an imprudent manner	Promoting beliefs in mechanistic causes of non-specific pain or disability (Medicalisation of non-specific problems) Reducing patient agency by not providing self-management strategies Inappropriate distraction from evidence-based explanations and solutions Catastrophising (via ambivalent or catastrophic language, e.g., "the base of your skull is twisted")	Mechanistic thinking of founding fathers applied to the skull
Chiropractic		
Excessive and inappropriate use of	Reinforcing patients' false beliefs	Historical adherence to mechanical

<p>routine medical imaging (Jenkins et al., 2018a, 2018b)</p>	<p>about the need for imaging for diagnosis, thus contributing to more disability, cost and inadequate medical treatments (Lemmers et al., 2019)</p>	<p>paradigms that posit potential identification of spinal lesions or spinal deformities on imaging (originally x-ray) supposedly associated with 'dis-ease'</p>
<p>Contracts for long-term care (with payments in advance for excessive amounts of treatment, where patients' needs are not assessed on an ongoing basis or changes in care not considered as symptoms change)</p>	<p>Along with potential economic harm to patients, high treatment frequencies together with high use of x-ray imaging, absence of routine diagnosis, and vaccine mistrust are associated with ultra-unorthodoxy (i.e., associated with worldviews that oppose allopathic medical practice) (Gislason et al., 2019)</p>	<p>Historical adherence to theories (or leverage of for financial gain) that posit spinal mechanical or neural 'interferences' to optimum health that can only be removed by 'chiropractic adjustments', and that these lesions will return without permanent and ongoing care.</p>
<p>Fear-inducing explanatory paradigms (such as 'subluxation degeneration', 'spinal decay' or 'bone out of place', with the suggestion 'deterioration' is inevitable without chiropractic or intensive and/or long-term care (Carter, 2000))</p>	<p>Reducing self-efficacy. Additionally, these ideas can be used to induce fear leveraging further dependency, risk of chronicity, ongoing pain, and economic harm</p>	<p>Similar to above, a historical paradigm that invokes spinal lesions (subluxations) as impediments to health and as originators of disease and ill-health, that can only be removed by a chiropractor using 'specific chiropractic adjustments'.</p>

Making the most of COP: Maximising placebo and minimising harm

COP are well-placed to provide primary health care that reduces requests for imaging, strong analgesic medications, and invasive pain treatments, and to mitigate the commonly-held belief that where there is pain there must be an injury. COP practitioners could do so by triaging, providing patient-focussed communication and supportive relationships, helping to re-engage in physical activity and providing short-term symptom relief, and by increasing their focus on advocacy for patients. To effectively redirect patients' journeys away from provider-shopping and consecutive disappointments, long-term educational efforts at profession-level need to be paired with public outreach campaigns and the disincentivizing of passive low-value care.

The first step: raising awareness

For too long, the placebo effect was seen as an undesirable nuisance or somewhat impure means of enhancing health outcomes. Trying to overcome this aversion, researchers are now communicating that placebo effects are inherent, neurophysiologically grounded parts of healthcare (Evers et al., 2021), likely more so in inherently social and complex interventions such as COP (Rossetini et al., 2020a; Testa and Rossetini, 2016). These effects should be embraced rather than dismissed (Evers et al., 2018; Kleine-Borgmann and Bingel, 2018). Indeed, COP curricula now place more emphasis on relationship-building and communication skills.

Nonetheless, a similar shift in awareness cannot be observed with regards to nocebo effects. Contrary to placebo effects, they do not need to be positively reframed. Quite the opposite, they may have to be actively demonised, owing to their potential for harm (and barring the need for further research). Initiatives for change need to address multiple levels: practitioners and students, educational institutions, healthcare systems and policy makers, and the public. Often, clinicians will find contextual factors easily modifiable, for example by adjusting the wording of a prognosis or avoiding negative behaviours (e.g., frowning) at the sight of a person's not-so-straight back. Contemporary academic discussions of COP have largely overcome structural models of health and disease (Alvarez et al., 2021; Bialosky et al., 2009; Draper-Rodi et al., 2018; Esteves et al., 2020; Hutting et al., 2022; Lederman, 2017; Stilwell and Harman, 2019) and can be used to design awareness campaigns. Irrespective of the impact of these behaviours on the patient, following these suggestions will make for a more positive atmosphere in the clinic as contemporary practice becomes less influenced by traditional COP concepts.

To aid reflection, we propose to consider clinical practice and individual professions through the 'prism' of nocebo and other undesirable effects (Figure 1), also drawing on content of table 2.

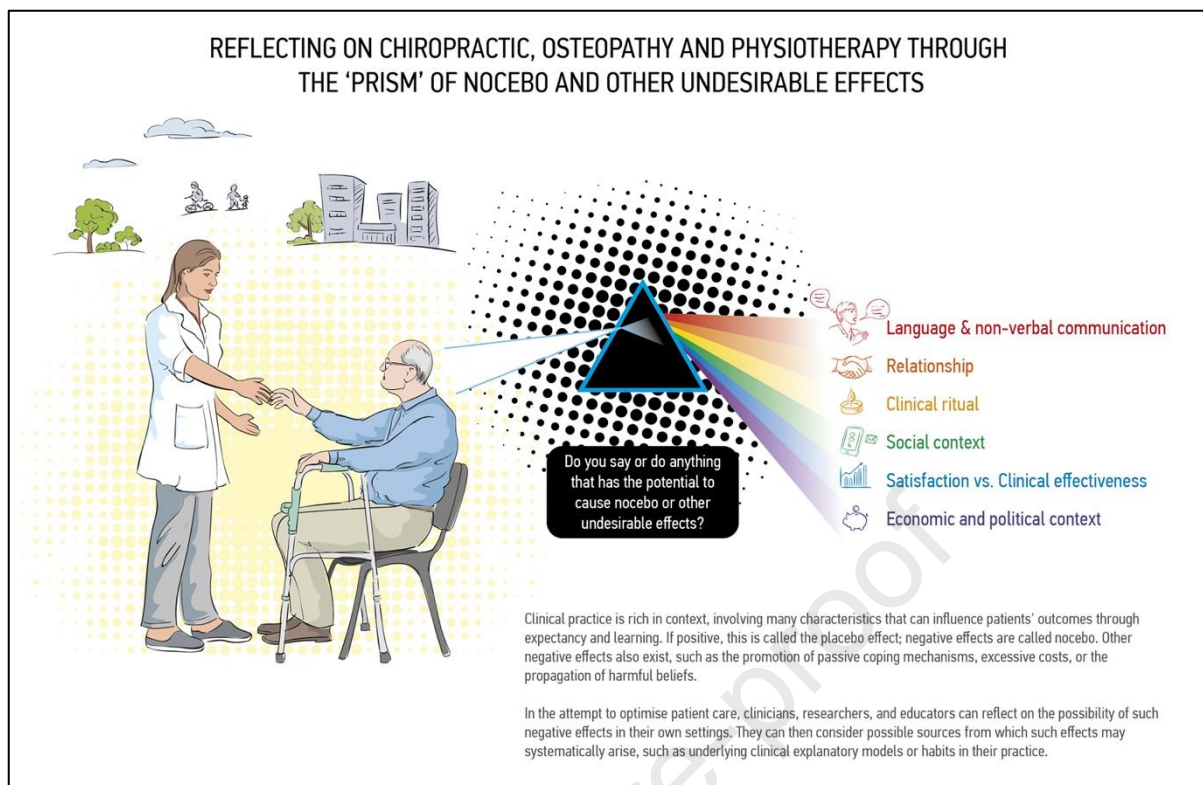


Figure 1: The image illustrates the clinical encounter and its context (left-hand side of image), postulating that the context-rich nature of chiropractic, osteopathic, and physiotherapy practice requires reflection on the possibility of nocebo and other undesirable effects (i.e., reflecting through the 'nocebo prism', centre). These effects can arise from and occur in various domains (right-hand side). Illustration by Ihor Protsenko via Upwork.com. [Note: PLEASE PRINT IN COLOUR]

The second step: Research

With the explosion of the placebo research field (JIPS database, n.d.), research into nocebo effect has also increased. So far, the evidence indicates that nocebo effects can be powerful under certain circumstances, with some studies providing conflicting evidence (e.g., Coleshill et al., 2021). When studied not in a purely experimental setting, however, the evidence is clear that contextual factors such as communication (Howick et al., 2018), the therapeutic relationship (Bishop et al., 2021), and the promotion of salutogenic upstream behaviours (Wang et al., 2018; Williams, 2018) have small to moderate effects on patient health (Howick et al., 2018; Blease, 2022) and may have greater effects in combination (Sherriff et al., 2022). It remains to be studied how these insights play out in the COP context.

Randomised clinical trials (RCTs) usually evaluate adverse events. In trials of COP, adverse effects commonly include transient post-treatment soreness and infrequent serious medical complications (Carnes et al., 2010; Hebert et al., 2015; Walker et al., 2013). Rarely do COP RCTs, however, study upstream mediators of negative health outcomes, such as increases in fear-avoidance behaviour, negative health beliefs, and effects on pain coping mechanisms. In doing so, especially in real-world settings and monitoring such effects long-term, RCTs could provide important information to whether COP are indeed associated with nocebo and other undesirable effects (Hohenschurz-Schmidt et al.,

2021a). Quantitative and qualitative assessments of potential changes in healthcare utilisation may be additional indicators of whether COP promoted active versus passive coping.

The third step: Implementation

The implementation of beneficial change must be based on educational media campaigns that change how we perceive musculoskeletal pain at a societal level (Gross et al., 2012; Hodges et al., 2021). Change is certainly driven most effectively by reforming institutional curricula and targeted professional training at practitioner level. However, clinical guidelines and incentive structures need to become better at curbing unnecessary use while allowing for evidence-based long-term care where needed (Buchbinder et al., 2020). Once reformed and having filled with life a new evidence-based whole-person model of care, practitioners and educational institutions are in a better position to take leading roles in highlighting the role of organisations and healthcare systems as well as systemic socio-economic determinants of ill-health or poor outcomes, and advocating for the people most affected (Nunan et al., 2021).

Conclusion

This article focused on an inherently negative phenomenon. Whilst this may have been challenging at times, we would like to finish on a positive note: By actively screening theory and practice for potential sources of nocebo, new avenues open to understand and enhance the positive potential routinely observed in clinicians' care of individuals with musculoskeletal pain. Such reflection allows us to draw on a contemporary framing of manual and physical approaches and integrate them with psychologically-informed best-practice (Keefe et al., 2018). Seeing this as a maturing and learning process, the question is not whether COP interventions are better than sham treatments for certain conditions, but rather how we can optimise and individualise these complex interventions to maximise the benefit for suffering individuals and for society. Overall, many contemporary treatment approaches for pain can be interpreted as the attempt to reduce nocebo effects by creating positive expectations, unlearning of pain conditioning, and addressing psychosocial predictors of long-term pain. In addition to the honest and careful examination of their treatments for the inadvertent creation of nocebo effects, COP clinicians should increasingly incorporate such a rationale into their treatments to enhance the salutogenic potential of COP care for the benefit of their patients.

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