When COVID-19 stopped ketamine: the experience of chronic pain patients during the pandemic

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Thesis declaration form

UCL Doctorate in Clinical Psychology

I confirm that the work presented in this thesis is my own. Where information has been derived from other sources, I confirm that this has been indicated in the thesis.

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Overview

Part 1 consists of a systematic review examining the effectiveness of online Cognitive Behavioural Therapy (CBT) for chronic lower back pain (CLBP). Nine papers were included in the review. Significant results in favour of the intervention group were found on pain outcomes in six studies. The design, administration and duration of the online CBT interventions were heterogenous. The results add to literature on the therapeutic benefits of online CBT for CLBP which is increasingly relevant given COVID-19 restrictions to non-urgent face-to-face healthcare provision.

Part 2 comprises an empirical paper investigating the experiences of chronic pain patients having their ketamine infusions halted during the COVID-19 pandemic. It sought to understand patients' subjective pain, emotion and coping strategies during the period of going without their ketamine treatment. Fifteen participants undertook semi-structured interviews and transcripts were analysed using thematic analysis. Five higher-order themes were devised: 1) *Pain increased without ketamine;* 2) *Depression;* 3) *External locus of control;* 4) *Internal locus of control* and 5) *Support from others*. The findings highlight the negative impact on pain, mood and control over pain. During this period some participants described adopting an internal locus of control, increasing self-management strategies and utilising social support from others.

Part 3 is a critical appraisal of the empirical paper which discusses what attracted the researcher to the field of study, researcher assumptions, the impact of COVID-19 on the project and reflections about the research process.

Impact Statement

Chronic pain is a complex biopsychosocial disorder that is treated (or 'managed') using a variety of psychosocial and medical interventions. This thesis focuses on two approaches to helping patients with chronic pain. The systematic review examines evidence for online CBT for chronic lower back pain (CLBP), while the empirical chapter addresses the experiences of patients treated in a pain management centre (PMC) with ketamine during COVID-19.

Findings from the systematic review indicate the potential effectiveness of online CBT interventions for CLBP. In light of COVID-19 there is heightened need for pain services to deliver psychological interventions remotely. Further high-quality research is required to explore the effectiveness of online CBT for CLBP across pain settings in the UK. Future studies could compare online with face-to-face CBT for CLBP to offer insights into the role of direct therapist contact in determining efficacy of CBT for CLBP. Matching online with standard face-to-face duration and number of sessions (weekly for 6 – 12 weeks) would support more direct comparisons of online versus face-to-face CBT. A number of potential mediating relationships were proposed in the review such as adjuncts to online CBT interventions. The removal of adjuncts such as supplementary telephone calls would enable more precise examination of the treatment effects of online CBT alone.

Primary outcomes of pain coping and pain self-efficacy rather than pain reduction would be more appropriate for examining the mechanisms of change of contemporary pain management interventions such as CBT and third-wave approaches such as Acceptance and Commitment Therapy (ACT). Furthermore, self-efficacy may be a potential mediator to pain outcomes so future studies might seek to control for self-efficacy.

The empirical paper, a qualitative study of the experiences of chronic pain patients having their ketamine infusions halted during the pandemic, found that pain and depression

increased when their treatment was terminated. Some participants perceived pain management as externally located, seeing their pain management as being controlled by "powerful others" at the PMC, whilst others described adopting an internal locus of control during their time without ketamine treatment. Further research into locus of control attributions in other chronic pain settings during the pandemic examining psychosocial factors that may augment locus of control attributions would elucidate the findings of this study. Moreover, exploration of the association between internal locus of control and self-management strategies during the pandemic could examine whether closure of services could have increased internal locus of control to foster more positive pain coping strategies compared to pre-pandemic levels.

Both the review and empirical paper found that white females predominated as participants. Future research ought to aim to provide better representation of gender balance and ethnicity to increase the generalisability and better represent chronic pain populations.

Whilst COVID-19 was unforeseen, there are important policy changes in light of the pandemic that could be taken up by stakeholders. Increasing the provision of online and telemedicine could help services to adapt to the needs of chronic pain patients, offering remote medical consultation and remote self-management courses. Moreover, healthcare providers and policy makers would benefit from future planning how pain services can operate safely, given the possibility of future pandemics, to avoid the negative consequences closure has on both patients and services.

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Acknowledgments

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Part 1: Literature review

A systematic review of the effectiveness of online CBT for chronic lower back pain

Abstract

Aim: The COVID-19 pandemic has resulted in an increasing demand for online delivery of psychological therapies. A considerable number of studies examining the effectiveness of online CBT for pain management have emerged over the last 20 years. This systematic review aims to examine the effectiveness of online CBT for chronic lower back pain (CLBP).

Method: A systematic review of PsycINFO, MEDLINE, EMBASE, and Web of Science yielded nine studies (n = 4032) that fulfilled the inclusion criteria for online CBT for CLBP. Data on study characteristics, trial designs and study outcomes were extracted from papers. Risk of bias ratings using the Revised Cochrane risk-of-bias tool for randomised trials (RoB 2) were conducted.

Results: Significant results in favour of the intervention group were found on pain outcomes in six studies. One study was double-blinded and another single-blinded, the seven other studies were unblinded. Three studies cited that they were underpowered. Four studies were rated as having a low risk of bias and five were rated as having some concerns. The design, administration and duration of the online CBT interventions were heterogenous.

Conclusions: These results add to the emergent literature on the therapeutic benefits and cost-effectiveness of online CBT for CLBP which are increasingly pressing in light of COVID-19. Further research is needed to examine potential moderating and mediating relationships to online CBT for CLBP as well as comparing online versus face-to-face, utilising pain self-efficacy and coping outcomes, and greater diversity across demographics.

1. Introduction

Chronic lower back pain (CLBP) is the presence of non-cancer-related musculoskeletal pain in the lower back for a duration of three months or more (Anderson, 1994). CLBP is a prevalent healthcare disability across the world (Wu et al., 2020). As well as physical trauma and genetic degeneration, a complex interaction of psychological and psychosocial factors including distress, depression, trauma and catastrophising can contribute to the development and maintenance of CLBP (Proctor et al., 2000). Moreover, there are significant economic disadvantages that patients with CLBP are more vulnerable to including absence from work, reduced productivity, long-term sick, and claiming benefits (Edwards et al., 2006). Systemically it has wider economic implications for employers and healthcare providers (Baldwin, 2004). Over the last 20 years pain management clinicians and researchers have been increasingly advising that interventions for CLBP should provide self-management and cognitive-behavioural therapy (CBT) provision alongside more classical physiotherapy and pharmaceutical therapy (Jensen et al., 2003). Recent guidance from the National Institute for Health and Care Excellence (NICE) proposes a shift away from pharmacological interventions, instead recommending that going forward non-pharmacological management of chronic pain such as CBT or acceptance and commitment therapy (ACT), a third-wave form of CBT should take precedence (NICE, 2021). It is therefore all the more pressing that good quality psychological interventions for chronic pain management are available.

CBT for CLBP is a psychological intervention that aims to target bio-psycho-social factors that may contribute to and maintain CLBP. CBT is traditionally delivered face-to-face in one-to-one sessions or groups. CBT interventions for CLBP are cost-effective, manualised and easily replicable, and help to empower patients to self-manage pain (Smith & Elliott, 2005). CBT for CLBP focuses on psychoeducation and behavioural strategies such as the

importance of exercise, pacing, relaxation, self-management strategies, reducing catastrophising, and addressing over-reliance on analgesics and opioids (Jensen et al., 2003).

The literature attests patients with CLBP who engage in CBT and pain self-management programmes experience a reduction in pain symptoms (Bodenheimer et al., 2002). Furthermore, various studies have found that CBT for CLBP is effective in altering a number of pain outcomes including disability, functioning, catastrophising and coping (Chou et al., 2007; Hoffman et al., 2007; Moore et al., 2000; Von Korff et al., 1998).

The advent of the internet in the early 2000s, not to mention the emergence of the COVID-19 pandemic, has led to the prevailing use of online and internet resources in everyday life. We live in a society where services are increasingly moving online. Through this, patients are ever more using the internet to access healthcare information, research medical options, and find targeted healthcare information on specific conditions. This fosters positive health behaviours and encourages self-management without the need for direct involvement with healthcare workers (Chiauzzi et al., 2010; Webster, 2020).

Online psychological interventions can be defined as interventions that use the internet or online interactive platforms to promote cognitive and behaviour change with some level of feedback that is tailored to the individual (Barak et al., 2009). There are a number of barriers to patients accessing face-to-face CBT for CLBP such as discomfort, time and cost travelling to clinics that are ameliorated when CBT is offered online. Furthermore, online CBT can be accessed at times convenient to the patient and allows people to tailor their treatment around their work, family, and other healthcare appointments. Moreover, traditional face-to-face CBT in the UK is generally offered within working hours, however online CBT can be accessed out of hours at the leisure of the patient's schedule. CBT for CLBP enables patients to develop a greater sense of empowerment and self-efficacy. Self-efficacy is the belief in one's abilities to manage daily life in spite of pain (Chiarotto et al.,

2016). Online CBT encourages patients to be more proactive in engaging with the treatment programme and learning about maintenance and exacerbating factors that might lead to back pain flare ups.

Garg and colleagues (2016) conducted a systematic review of web-based interventions for chronic back pain examining both CBT and self-management interventions which suggested that online CBT for CLBP could help to reduce pain catastrophising. The review examined both CBT and more general non-CBT-informed self-management strategies for CLBP. A number of studies have been published since this review and there is an ever-increasing relevance and demand for online and remote working since the outbreak of the COVID-19 pandemic across the world. E-health and web-based self-management platforms for chronic pain have been recommended as means to treat chronic pain patients in light of the restrictions to face-to-face working brought about by the COVID-19 (Eccleston et al., 2020). Further, as far as the author is aware, there is a gap in the literature for a review that focuses solely on the effectiveness of online CBT for CLBP.

The aims of this review are to examine the effectiveness of online CBT interventions for patients with CLBP. For the purposes of the review, CBT is defined as second-wave and third-wave CBT encompassing ACT and compassion focused therapy (CFT) as there has been increased prevalence of the implementation of both interventions in chronic pain treatment in recent years (Hughes et al., 2017; Penlington, 2019). The review will build upon the literature reviewed in Garg and colleagues' 2016 study with additional studies that have emerged since its publication.

2. Methods

2.1 Data Sources and Searches

The electronic databases of PsycINFO, MEDLINE, EMBASE, and Web of Science with date restriction of 2000 – 2021 were searched using the following search terms on

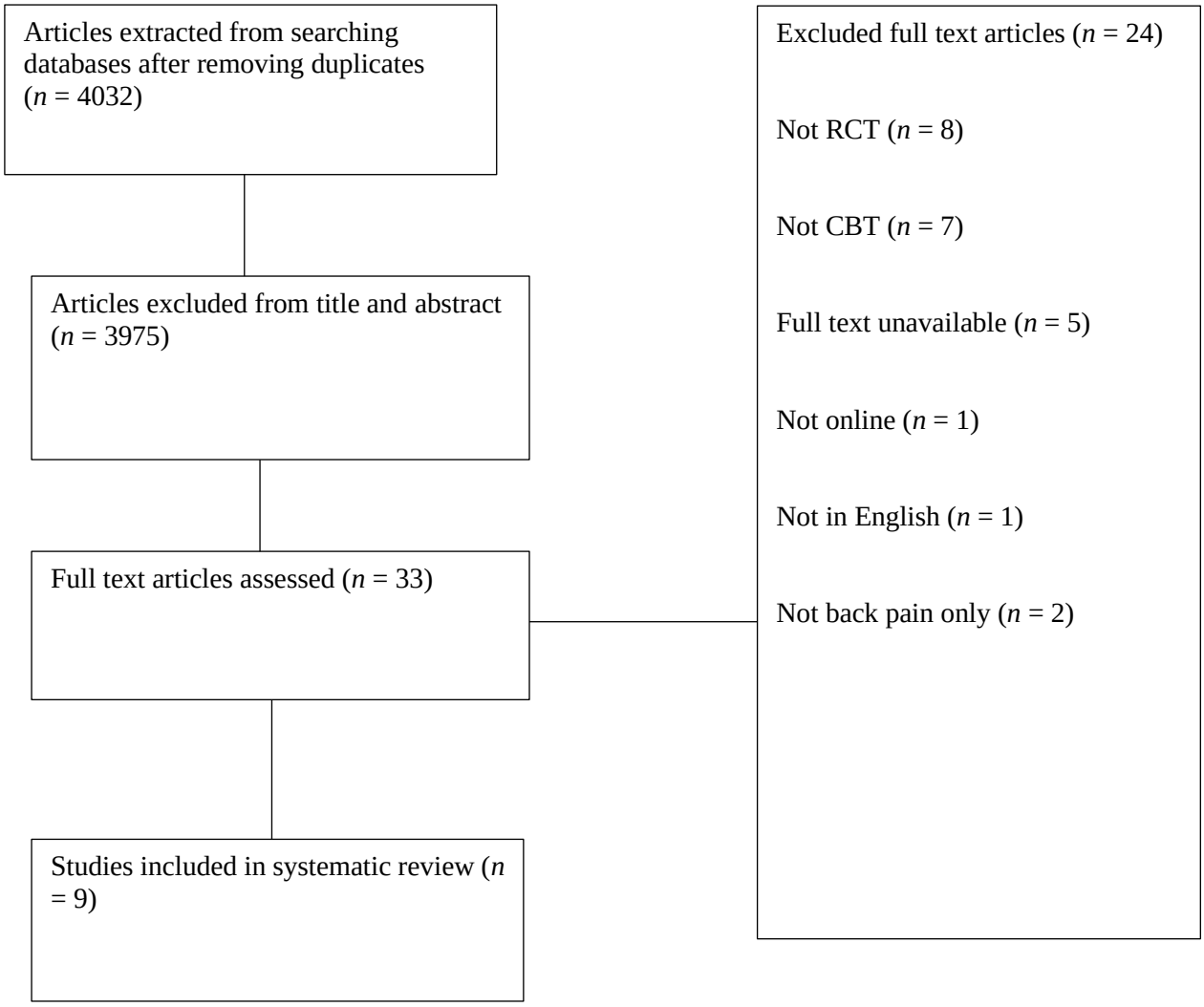
21/01/2021: (Internet* OR guided-internet OR world wide web OR www OR web-based OR website OR online OR email OR e-mail OR (inform* or communicat*) or interactive OR computer or technolog* software) AND (Psychological treatment or Psychological intervention or Psychological or Psychology or psychotherapy or Intervention or CBT or Cognitive Behavioural Therapy or Cognitive or Cognitive intervention or ACT or "Acceptance Commitment Therapy" or Compassion Focused Therapy or CFT or Mindfulness or MBCT or Mindfulness-based or Mindfulness based stress reduction or MBSR) AND (Chronic back pain OR Chronic low* back pain OR Back pain OR Low* back pain OR Chronic Spinal pain OR Spinal pain OR degenerative disc disease OR sciatica OR myofascial back pain OR nonspecific back pain OR lumbosacral region). Papers of interest were randomised controlled trials (RCTs).

2.2 Inclusion and Exclusion Criteria

Papers eligible for inclusion were full paper articles of RCTs published after the year 2000 of online interventions for adults with chronic back pain. Exclusion criteria were: persons under 18, referred back pain due to pathological processes not involving the musculoskeletal system, back pain that existed for less than 6 weeks, case-control studies, cohort, cross-sectional studies, case reports, systematic reviews, meta-analyses, and meeting/congress reports. Studies with incomplete information or only title and abstract were excluded. Studies that were not published in English were also excluded.

After the search had been applied to the databases, papers were exported to Endnote for screening. Duplicates were removed. Papers were initially screened based on titles and abstracts. Papers then underwent full paper screening, where nine papers matched the inclusion criteria for this review. See Figure 1.

Figure 1: PRISMA Flow diagram



2.3 Data Extraction

Title and abstract screening and full paper screening was conducted by the author. Study characteristics and study statistical outcomes were extracted by the author. Risk of bias ratings using the Revised Cochrane risk-of-bias tool for randomised trials (RoB 2) and corresponding RoB 2 cribsheet (Sterne et al., 2019). Risk of bias ratings examined the domains of randomisation, assignment, missing outcomes, measurement of the outcome, reported result and an overall risk of bias rating. Bias ratings were corroborated with a second reviewer where discrepancies were discussed and resolved. (See Appendices 1.A – 1.H. for full details of how the researcher arrived at risk of bias ratings).

3. Results

The literature search identified nine RCTs that examined the effectiveness of online CBT for CLBP. Study characteristics and trial design can be found in Tables 1 and 2 respectively. Table 3 displays study outcomes. Risk of bias ratings can be found in Table 4.

The sample size of participants in studies ranged from 51 to 597 with a mean of 180 participants and an interquartile range of 123 (1^{st}Q 76 & 3^{rd} Q 199) participants. Women formed a larger proportion of participants in studies (50%-100%).

Buhrman and colleagues (2004) deployed internet CBT with supplementary telephone support for the intervention of treating chronic back pain. The control group was waitlist control. The authors noted that they would need to recruit 95 participants to achieve 80% power, however they enrolled 51, indicating that the study was underpowered. The primary outcome measure was a subscale of the Coping Strategies Questionnaire (CSQ; Stewart et al., 2001) which was chosen to measure the construct of pain catastrophising defined as irrational thoughts pertaining to the extent of pain. The CSQ catastrophising domains included: diverting attention, reinterpret pain sensations, coping self-statements, ignore pain sensations, praying or hoping, catastrophising, increased activity level, control over pain, and ability to decrease pain (Rosenstiel & Keefe, 1983). The secondary outcome measures were the Multidimensional Pain Inventory (MPI; Kerns et al., 1985) which measures the psychosocial and behavioural impact of pain. Domains included: pain severity, interference, life control, affective distress, support, punishing responses, solicitous responses and distracting responses. A further secondary outcome measure was the Pain and Impairment Relationship Scale (PAIRS; Riley et al., 1988) which measures attitudes and thoughts about pain and beliefs about how one can function in spite of pain.

Participants in the intervention group had weekly access to online CBT modules and physical therapy and coping strategy guidance for 12 weeks. In conjunction they were also

provided with weekly telephone calls with therapists where they could discuss goals, relaxation, coping strategies, exercise and stretching guidance. The intervention group showed significant reductions on the CSQ, MPI and PAIRS at eight weeks. Both intervention and control groups showed a reduction in average and highest pain ratings over time on the pain diary. Moreover, 39% of the participants in the intervention group reported clinically significant improvement on the CSQ compared to 14% in controls. However, due to the addition of telephone support, it is difficult to determine how much of the effect is associated with the online aspect of the intervention or the telephone support.

Buhrman and colleagues (2011) conducted a later study which was similar to their earlier study with the difference of not providing telephone support in the intervention group. The study included 54 participants and was also noted to be underpowered by the authors. The outcome measures were the same as their previous study listed above. A significant effect was found for catastrophising on the CSQ however results for the MPI and PAIRS were not significant in the intervention group. However, both groups showed reductions on the PAIRS over time. Furthermore, 58% of participants in the intervention group reported clinically significant improvement on the CSQ, compared to 18% in controls. Despite not receiving telephone support, the intervention participants were provided supplementary email support. Therefore, again, it is difficult to determine how much of the effect is associated with the online modules of the intervention over the email support.

Table 1: Study characteristics

Author, year	Location	Study Design	ITT or PP	*n* of participants	Mean Age	Sex %	Drop-out % (n)
Buhrman et al., 2004	Sweden	RCT	PP	51	44.6	M (37.5) W (62.5)	9 (5)
Buhrman et al., 2011	Sweden	RCT	ITT	54	43.2	M (26.9) W (73.1)	4 (7.4)
Carpenter et al., 2012	USA	Pilot RCT	PP	141	42.5	M (17) W (83)	23 (16.3)
Chiauzzi et al., 2010	USA	RCT	ITT	199	46.1	M (24) W (76)	10 (5)
Irvine et al., 2015	USA	RCT	ITT	597		M (42.7) W (58.3)	2.8 (17)
Petrozzi et al., 2019	Australia	RCT	ITT	108	50.4	M (50) W (50)	10.7 (10)
Sander et al., 2020	Germany	RCT	ITT	295	52.8	M (38.6) W (62.4)	12.5 (37)
Schlicker et al., 2020	Germany	Pilot RCT	ITT	76	50.78	M (45) W (55)	36 (27)
Strom et al., 2019	Denmark	RCT	ITT	114	65.0	W (100)	3.1 (5)

ITT = intention-to-treat. PP = per-protocol

Table 2: Trial design of studies

Author, year	Intervention	Control	Duration	Measurement times	Outcomes
Buhrman et al., 2004	Internet CBT	WLC	8 weeks	BL, 8 weeks & 3 months	CSQ, MPI & PAIRS
Buhrman et al., 2011	Internet CBT	WLC	12 weeks	BL & 12 weeks	CSQ, MPI & PAIRS
Carpenter et al., 2012	Internet CBT	WLC	3 weeks	BL, 3 weeks & 6 weeks	SOPA, FABQ, PCS, RMDQ, PSEQ, PAQ
Chiauzzi et al., 2010	CBT website	Back pain workbook	6 months	BL, 1 month, 3 months	BPI, ODQ, PCS, PSEQ, FABQ
Irvine et al., 2015	Online CBT app	1. Back pain website 2. TAU	8 weeks	BL, 8 weeks, 16 weeks	MPI, BPI, SOPA, TSK
Petrozzi et al., 2019	Internet CBT	TAU	8 weeks	BL, 8 weeks, 6 months, 12 months	PSEQ, RMDQ, PCS & NRS
Sander et al., 2020	Internet CBT	TAU	9 weeks	BL, 9 weeks, 6 months, 12 months	NRS, ODQ, PSEQ
Schlicker et al., 2020	Internet CBT	WLC	9 weeks	BL, 9 weeks, 6 months	NRS, ODQ, PSEQ
Strom et al., 2019	Internet CBT	TAU	3 months	BL, 2 days, 3 months, 6 months	LBPRS & ODQ

MPI = *Multidimensional Pain Inventory*. BPI = *Brief Pain Inventory*. *NRS* = pain intensity. LBPRS = *Low Back Pain Rating Scale*. PAIRS = *The Pain Impairment Relationship Scale*. SOPA = *Survey of Pain Attitudes*. RMDQ = *Roland-Morris Disability Questionnaire*. ODQ = *Oswestry Disability Ques*tionnaire. FABQ = The *Fear Avoidance Beliefs Questionnaire*. CSQ = *The Coping Strategies Questionnaire*. PCS = *Pain Catastrophising Scale*. TSK = *Tampa Scale for Kinesiophobia* (pain catastrophising). PSEQ = *Pain Self-efficacy Questionnaire. PAQ = pain assessment questionnaire.* WLC = waitlist control. TAU = treatment as usual

Carpenter and colleagues (2012) conducted a study which comprised on online self-help CBT intervention for CLBP which randomised 141 participants. The primary outcome measure was the Survey of Pain Attitudes (SOPA; Jensen & Karoly, 1992; Jensen et al., 1999) which measures beliefs and attitudes about pain. Domains include control over pain, disability from pain, harm-exercise, emotion, medication, solicitude, and medical cure. Secondary outcome measures were: *The Roland-Morris Disability Questionnaire* (RMDQ; Roland & Morris, 1983) measuring pain-related physical disability, the *Pain Self-efficacy*

Scale (PSEQ; Lorig et al., 1989), measuring one's level of self-efficacy over pain, the *Fear Avoidance Beliefs Questionnaire* (FABQ; Waddell et al., 1993), measuring beliefs about the effects of physical activity and work on back pain, PCS, and *Demographics and Pain Assessment Questionnaire* (PAQ; Carpenter et al., 2012), which asked participants to rate their average, highest, and lowest level of pain over the previous week.

Participants in the intervention group were given access to an online "wellness workbook" based on CBT for three weeks. The control group was waitlist control but were given access to the online wellness workbook three weeks after baseline along with the intervention group. At three weeks post-intervention, a statistically significant effect was found for SOPA, RMDQ, PSEQ, FABQ and PCS. Results for PAQ were non-significant. At six weeks when the control group had also been given access to the wellness workbook alongside the intervention group there were found to be no significant differences between groups. This indicates that the intervention had been effective in treating pain across all outcome measures except the PAQ.

Chaiuzzi and colleagues (2010) conducted a study in which participants in the intervention group received access to on online self-help website called painACTION based on CBT principles for four weeks with five monthly booster sessions after the initial four weeks. The control group were given a hardcopy workbook about back pain self-management. The study randomised 202 participants but 10 were found ineligible so the final study sample was 199 participants. The outcome measures used were the *Brief Pain Inventory* (BPI; Cleeland & Ryan, 1994) which measures pain severity and function and constructs pain domains in terms of worst, least, average, current, relief and interference and the Oswestry Disability Questionnaire (ODQ; Fairbank et al., 1980) which measures functional impairment of back pain containing domains: pain intensity, personal care, lifting, walking, sitting, standing, sleeping, sex life, social life, and travelling. Other pain outcomes

were PCS, PSEQ and FABQ. A significant effect was found for worst pain and average pain on the BPI for the intervention group. No other significant effects were found for other pain outcomes. Within the intervention group, 12.3% of participants reported clinically significant change in pain from baseline to post-intervention compared with 7% in controls.

Irvine and colleagues (2015) used a three-arm trial in which participants in the intervention group were given access to FitBack, an online app based on CBT principles, which provided tailored guidance on self-management of lower back pain over an eight-week period. The alternative care group received eight emails encouraging them to access links to six internet resources on lower back pain. The control group received usual care. The study randomised 597 participants. Participants were blinded to treatment allocation during the trial. Outcome measures were MPI, BPI, SOPA and pain catastrophising measures using the *Tampa Scale for Kinesiophobia* (TSK; Burwinkle et al., 2005). Significant effects were found in the intervention group on MPI, BPI and SOPA. At follow up participants in the alternative care group were 1.6 times more likely to report current back pain compared with FitBack participants and participants in the control group were 1.7 times more likely to report current back pain than Fitback participants.

Petrozzi and colleagues (2019) reported a study in which participants in the intervention group received MoodGYM, an online CBT programme for CLBP, alongside standard care of physical treatment for CLBP for eight weeks. The control group received standard care alone. The study randomised 108 participants. Participants and assessors were blinded to treatment allocation during the trial. Primary outcome measures were PSEQ and RMDQ. Secondary outcomes were PCS and pain *Numerical Rating Scale* (NRS; Jensen & Karoly, 1992). No significant effects were observed for any of the outcomes. As well as receiving online CBT the intervention group also received physical treatment which makes it harder to distinguish the effects of online CBT alone from physical therapy.

Sander and colleagues (2020) conducted a study of a guided web-based self-help intervention based on CBT to treat depression in patients with CLBP. Intervention participants were given access to eSano BackCare-DP which consisted of six mandatory and three optional online modules as well as an e-coach who gave them tailored feedback about their progress. The control group received treatment as usual. The study randomised 295 participants. Primary outcomes were depression measures, so these have not been reported. Secondary outcome measures pertaining to pain were NRS, ODQ and PSEQ. Small to medium effect sizes in favour of the intervention group were found for ODQ and PSEQ however p values of these outcome measures were not reported. No significant effects were found for NRS.

Schlicker and colleagues (2020) reported a study of a web- and mobile-based CBT intervention called Get.Back for patients with recurrent depression who also had CLBP who were on sick leave. The intervention group were given online access to Get.Back for nine weeks which contained seven modules on psychoeducation, behavioural activation, cognitive restructuring and content around returning to work. The intervention group were also assigned e-coaches for support and encouragement around engagement. Furthermore, participants received daily standardised text messages reinforcing learning and adherence to the intervention. Participants received a booster module four weeks after the intervention ended. The control group were waitlist control. The study randomised 76 participants. The authors noted that the study was underpowered due to a smaller sample size than intended. Primary outcomes were depression measures. Secondary outcomes for pain were NRS, ODQ and PSEQ. No significant effects were found between groups for any of the pain outcomes.

Strom and colleagues (2019) conducted a study of an animated web-based CBT platform to treat anxiety and depression in patients undergoing surgery for lumbar spine fusion. The intervention group were given access to W-SPIINA, an animated internet CBT

programme, a patient support group and a pain diary. Participants in the control group received treatment as usual. The study randomised 114 participants. Primary outcomes were anxiety and depression measures. Secondary outcomes pertaining to pain were the *Low Back Pain Rating Scale* (LBPRS; Manniche et al., 1994) measuring both back and leg pain and ODQ. No significant differences were observed between groups on pain outcomes. Minimum clinically important difference (MCID) six months after surgery was found on the ODQ for 44% of participants in the intervention group, with 9% worsening. In the control group 43% improved on the ODQ and 21% worsened. MCID for average back pain was 74% in the intervention and 66% in the control group.

Table 3: Study outcomes

Author, year	Outcomes	BL M (SD)	T1 M (SD)	T2 M (SD)	T3 M (SD)	p	Effect size
Buhrman et al., 2004	CSQ						
	Catastrophising	13.6 (7.7)	8.6 (5.2)	9.3 (5.2)		0.005	-0.56
	Praying/ hoping	12.0 (6.9)	9.8 (5.1)	10.5 (7.1)		0.032	-0.22
	Control	2.8 (1.0)	3.9 (0.7)	3.6 (1.1)		0.001	0.80
	Decrease pain	3.0 (0.8)	3.9 (0.9)	3.7 (0.9)		0.001	0.88
	MPI						
	Life control	3.1 (1.1)	3.9 (1.0)	3.6 (1.1)		0.001	0.46
	Punishing responses	1.0 (1.4)	0.7 (1.1)	0.7 (1.0)		0.05	-0.21
	PAIRS	55 (10.9)	53.2 (10.2)	51.7 (13.9)		0.01	-0.30
Buhrman et al., 2011	CSQ						
	Catastrophising	14.3 (6.1)	9.5 (5.5)			0.001	-0.79
Carpenter et al., 2012	SOPA						
	Control	2.1 (0.7)	2.9 (0.6)	3.0 (0.7)		0.001	0.89
	Disability	2.5 (0.9)	2.1 (0.9)	2.0 (0.7)		0.001	-0.72
	Harm-exercise	1.6 (0.8)	1.1 (0.7)	1.1 (0.8)		0.001	-0.80
	Emotion	2.6 (0.9)	3.2 (0.7)	3.2 (0.7)		0.001	0.82
	Medication	2.5 (0.9)	1.9 (1.0)	2.0 (1.0)		0.001	-0.88
	Solicitude	2.2 (0.9)	2.0 (0.9)	1.9 (1.0)		0.001	-0.39
	RMDQ	16.3 (5.3)	13.5 (5.8)	11.9 (5.9)		0.001	-0.45
	PSEQ	4.9 (2.0)	7.0 (1.8)	7.0 (1.7)		0.001	0.89
	FABQ						
	Physical activity	3.7 (1.2)	2.7 (1.5)	2.6 (1.4)		0.001	-0.80
	PCS						
	Rumination	2.1 (1.0)	1.6 (1.0)	1.4 (1.0)		0.001	-0.59
	Magnification	1.8 (1.0)	1.3 (0.9)	1.0 (0.8)		0.001	-0.63
	Helplessness	1.6 (0.9)	1.0 (0.8)	0.9 (0.7)		0.001	-0.77
Chiauzzi et al., 2010	BPI						-0.68
	Worst pain	7.0 (0.2)	6.5 (0.2)	6.4 (0.3)	6.5(0.3)	0.05	
	Least	5.6 (0.2)	5.1 (0.2)	5.0 (0.2)	4.8(0.3)	0.05	
Irvine et al., 2015	MPI & BPI						
	Severity	1.0 (1.3)	0.8 (1.2)	0.6 (1.0)		0.010 (MPI & BPI)	0.02
	Frequency	2.9 (0.9)	2.6 (1.0)	2.2 (1.1)			
	Intensity	2.6 (1.2)	2.2 (1.2)	2.1 (1.5)			
	Duration	2.5(1.0)	2.3 (1.1)	2.0 (1.0)			
	Function & QoL	3.8 (1.9)	3.3 (1.7)	3.0 (1.9)			
	SOPA						
	Control	3.2 (0.9)	3.7 (0.8)	3.9 (0.8)		0.001 (SOPA)	0.04
	Emotion	3.0 (1.3)	3.3 (1.3)	3.4 (1.2)			
Sander et al., 2020	ODQ	27. 3(12.4)	23.4 (11.7)	22.0 (11.3)	20.2 (10.6)	nr	-0.58
	PSEQ	39.8 (11.1)	42.9 (9.89)	41.9 (10.4)	44.8 (9.7)	nr	0.19

1. Significant results have been displayed for intervention groups only. No significant results were found for Petrozzi et al. (2019), Schlicker et al. (2020) and Strom et al. (2019).
2. nr = not reported
3. Effect size estimates were calculated from differences within participant change from BL to follow up/ final timepoint.
4. Effect size estimates were calculated for statistically significant timepoints only.

3.1 Risk of bias

Table 4: Risk of bias ratings using RoB2

Author, year	ITT/ PP	Randomisation	Assignment	Missing outcomes	Measurement of outcome	Reported result	Overall risk of bias
Buhrman, 2004	PP	Low	Low	Low	Low	Low	**Low**
Buhrman, 2011	ITT	Low	Low	Low	Low	Low	**Low**
Carpenter, 2012	PP	Some concerns	Low	Some concerns	Low	Low	**Some concerns**
Chiauzzi, 2010	ITT	Low	Low	Some concerns	Low	Low	**Some concerns**
Irvine, 2015	ITT	Low	Low	Low	Low	Low	**Low**
Petrozzi, 2019	ITT	Low	Low	Low	Low	Low	**Low**
Sander, 2020	ITT	Low	Low	Some concerns	Low	Low	**Some concerns**
Schlicker, 2020	ITT	Low	Low	Some concerns	Low	Low	**Some concerns**
Strom, 2019	ITT	Some concerns	Low	Some Concerns	Low	Low	**Some concerns**

Four studies were rated as low risk of bias on the RoB2, however, Buhrman (2004) used a per-protocol analysis which is problematic as this may have increased the bias of the study (Sterne et al., 2019). Five studies were rated as having some concerns regarding risk of

bias. The major reason for this rating was due to missing outcome data which were imputed using methods such as multiple imputation or "last-observed-carried-forward" which the RoB2 deems to increase results bias. Additionally, Carpenter et al. (2012) and Strom et al. (2019) raised some concerns with the randomisation process noting gender imbalances between groups were likely not random and may have influenced estimated effects. Finally, Carpenter et al.'s (2012) study, which was rated as some concerns due to the aforementioned reasons, also used a per-protocol analysis which may have further increased the risk of bias in this study.

4. Discussion

4.1 Overview

Nine RCTs were included in this systematic review which examined the effectiveness of online CBT interventions to treat chronic lower back pain. One study was double-blinded and another single-blinded, the seven other studies were unblinded. Three studies cited that they were underpowered. Four studies were rated as having a low risk of bias and five were rated as having some concerns in terms of risk of bias. The design, administration and duration of the online CBT interventions were heterogenous. All but one study reported follow up data. Three of the studies reported depression/anxiety measures as the primary outcome measure and were predominantly interested in these outcomes over and above pain outcomes.

4.2 Summary of results

Significant results in favour of the intervention group were found on pain outcomes in six studies. Burhman et al. (2004) found significant differences in CSQ, MPI and PAIRS. Burhman et al. (2011) found significant results for pain catastrophising subscale of the CSQ only. Carpenter et al. (2012) found significant differences on SOPA, RMDQ, PSEQ, FABQ and PCS. Chiauzzi et al. (2010) found significant improvements on the average and worst

pain subscales of the BPI only. Irvine et al. (2015) found significant differences in favour of the intervention group for MPI, BPI and SOPA. Sander et al. (2020) found significant results for ODQ and PSEQ. Three studies did not find significant differences in pain outcomes after the intervention (Petrozzi et al., 2019; Schlicker et al., 2020; Strom et al., 2019).

4.3 Comparison to other interventions

All of the studies included control allocation in their randomisation, with one study including a three-arm allocation. Four of the studies applied waitlist control (WLC) in their study designs. WLC can be problematic in terms of evaluating the size of effects as they tend to inflate the effect size. Three of the studies deployed treatment as usual (TAU) as the control conditions, which is preferential to WLC but can pose challenges to internal and external validity of the results. However, type of control allocation ultimately comes down to both methodological and practical restrictions of the setting. TAU for the Petrozzi et al. (2019) study consisted of physical therapy for CLBP. TAU for Sander et al. (2020) and Strom et al. (2019) consisted of access to primary care practitioners and general practitioners for the treatment of subclinical or mild depression and anxiety. Given that the primary outcomes for these studies did not pertain to pain this makes these comparator interventions less appropriate for comparison for the purposes of this review looking at pain outcomes. Chiauzzi et al. (2010) used a back pain workbook containing information about back pain self-management as the comparator condition. When looking at the effectiveness of online CBT for CLBP this appears to be a better fit for a comparator. Irvine et al. (2015) utilised a three-arm design with the alternative care group receiving access to six online web-resources on CLBP self-management and the control group received TAU.

All studies except Burhman et al. (2011) included follow up outcomes. Most studies assigned one follow up time point, however two studies contained two follow up time points (Chiauzzi et al., 2010; Sander et al., 2020). The duration of time from baseline to follow up

varied across studies; with four studies having shorter follow up ranging from six weeks to 16 weeks (Burhman et al., 2004; Carpenter et al., 2012; Chiauzzi et al., 2010; Irvine et al., 2015) and four studies having a longer duration of time ranging from six to 12 months (Petrozzi et al., 2019; Sander et al., 2020; Schlicker et al., 2020; Strom et al., 2019). Studies with shorter follow up reported a greater number of significant results than those with longer term follow up. One explanation for this is that treatment effects taper off post-treatment after longer-term follow up.

4.4 Mediating and moderating relationships

A number of mediating and moderating relationships were noted in the studies. Adjuncts to online CBT interventions were included in six studies. The various adjuncts included: supplementary telephone support, email support, physical therapy, e-coach feedback, online peer support group and a pain diary (Burhman et al., 2004; 2011; Petrozzi et al., 2019; Sander et al., 2020; Schlicker et al., 2020; Strom et al., 2019). The degree to which these adjuncts could have influenced the true value of the outcomes will vary. However, it is likely that these are potential moderators to pain outcomes which means that generalisability from these studies should be considered with caution as it cannot be known if the effects were attributable to online CBT for CLBP alone. Across all studies the majority of participants were female. It is known that women are more likely to seek psychological support than males (Unruh, 1996). In this way gender (female) may also be a moderator for pain outcomes.

Patient characteristics that lead to better adherence and treatment outcomes for online CBT for CLBP such as self-efficacy was not discussed as a potential mediator to the results. The literature suggests that patients with higher levels of self-efficacy are more likely to respond better to self-management strategies for pain (Buenaver et al., 2006). Self-efficacy

has been found to mediate the relationship between pain intensity and disability in chronic pain patients (Arnstein et al., 1999; Chiarotto et al., 2016). Self-efficacy was found to have a mediating relationship between function at discharge for CLBP patients who receive physical therapy (Riley et al., 2020). Therefore, self-efficacy could serve as a mediator to pain outcomes for CBT for CLBP.

The duration and dose of online CBT for CLBP varied significantly across studies. Duration of intervention ranged from three weeks to six months and dosages of CBT varied in terms of prescribing weekly access to online CBT versus unlimited access to online CBT resources. Some of the interventions also provided boosters after the initial intervention. The heterogeneity in duration and dose of CBT may moderate the relationship between intervention and pain outcomes across the studies.

4.5 Strengths and limitations of reviewed studies

According to the authors, six studies had sample sizes sufficient to reach a significance level of <0.05 with power of 0.80 (Carpenter et al., 2012; Chiauzzi et al., 2010; Irvine et al., 2015; Petrozzi et al., 2019; Sander et al., 2020 & Strom et al., 2019). Three studies had smaller sample sizes which rendered them underpowered in terms of being able to detect a medium effect size or higher. However, all authors of these studies acknowledge this as a limitation and Schlicker et al, (2020) noted that the sample size should be considered within the context of a pilot RCT.

Another strength is that all of the studies monitored engagement to increase adherence to interventions. This took various forms including monitoring website or in-app usage, reminder emails and telephone calls to encourage adherence where participants might have appeared to not be conducting treatment modules. This helped with reducing attrition rates within the studies.

A potential limitation is that five of the nine studies were rated as having some concerns regarding risk of bias relating to imputation of missing data and randomisation. This leads onto another limitation on the grounds of attrition as these five studies had high levels of drop out. Carpenter et al. (2012) and Chiauzzi et al. (2010) make reference in their limitations section that valuable data on the factors that determine why participants might drop out was lost. Moreover, they noted that control participants were more likely to drop out than those in the intervention group. Conversely, Strom et al. (2020) acknowledged that attrition was higher in the intervention condition amongst those with greater severity of depression and cautioned that this was likely not due to random effects, instead related to the true value.

Further limitations in reporting ethnicity demographics were noted in six of the studies (Buhrman et al, 2004; 2011; Petrozzi et al., 2019; Sander et al., 2020; Schlicker et al, 2020; Strom et al., 2019). Given that Black, Asian, and minority ethnic (BAME) persons are often under-represented in clinical research (Smart & Harrison, 2017), it seems important to note this as a shortcoming as pain-related outcomes can vary across ethnicities (Campbell & Edwards, 2012). Additionally, some studies made reference to the samples being over-representative of persons with higher socio-economic status (Chiauzzi et al., 2010; Irvine et al., 2015; Petrozzi et al., 2019) and how this is not reflective of the general chronic pain population.

Another limitation is that six of the studies used adjuncts to online CBT alone in their intervention conditions. To this end, one cannot dissociate whether significant effects were attributable to these adjuncts or online CBT alone.

A final limitation is that none of the studies account for other physical health comorbidities that co-occur in many patients with CLBP such as diabetes, heart and vascular disease (Ramanathan, et al., 2018), and indeed Buhrman et al. (2004; 2011) excluded

participants who had heart and vascular disease. Whilst homogeneity of the samples increases internal validity, the reality is that CLBP patients have multiple comorbidities which decreases the external validity of the results.

4.6 Strengths and limitations of this review

The review used a systematic search strategy across a number of relevant databases and risk of bias ratings were corroborated by a second assessor. A variety of different pain outcome measures were included. A review by Eccleston and colleagues (2009) revealed that pain reduction outcomes demonstrate mixed results in RCTs of CBT and self-management for chronic pain. The inclusion of pain coping and self-efficacy measures in this review is supported by that of Eccleston and colleagues who did not use pain measures as primary outcomes by virtue of the fact that CBT interventions are not designed to reduce pain per se but improve pain coping.

Three of the studies included in this review were primarily interested in the effectiveness of online CBT for CLBP to reduce depression and anxiety and used these as the primary outcomes, with pain as a secondary outcomes. Whilst these studies did pay attention to pain, in retrospect it may have been better to have excluded these studies to increase the homogeneity of the included studies. However, due to having a small number of included studies, excluding these studies this would have created issues with the generalisability of the findings of this review.

4.7 Future research

In light of the COVID-19 pandemic there is increased uptake and need for psychological therapies for chronic pain to be delivered online (Eccleston et al., 2020). Future studies would benefit from comparing online CBT with face-to-face CBT for CLBP to

gain further insights into the potential differences in treatment outcomes and effectiveness. Further, given that treatment effects taper off post-treatment, future studies would benefit from including longer-term follow up data in their reporting. Another recommendation for future research is that mediating factors such as adjuncts to online CBT interventions be removed so that the treatment effects of online CBT alone can be examined with greater precision. Similarly, duration and dose of online CBT interventions ought to be better matched to that of face-to-face CBT interventions (once weekly sessions for 6-12 weeks) to further expound the effectiveness of online versus face-to-face CBT for CLBP.

Future studies and reviews might seek to employ pain coping and pain self-efficacy outcome measures as their primary outcomes over those of pain reduction outcomes given that the mechanisms of CBT for CLPB are seeking to improve pain in these domains as opposed to intrinsically reducing pain. Moreover, self-efficacy could serve as a mediator to pain outcomes for CBT for CLBP so future studies should seek to isolate or control for self-efficacy. Women are more likely to seek pain-related healthcare than their male counterparts (Unruh, 1996). Although this may reflect the epidemiology of pain, future research ought to aim to provide better participant representation in terms of gender balance, ethnicity and socioeconomic status to help to increase the generalisability and applicability of the findings and examine whether any of these demographics play a moderating role in the effectiveness of online CBT for CLBP.

5. Conclusion

Six of nine studies in this review reported reductions in pain outcomes in participants receiving online CBT for CLBP. These results add to the nascent body of literature on the benefits on online CBT for physical health problems and offers some persuasive evidence to consider implementing online CBT for CLBP as a cost-effective alternative to face-to-face

CBT in the ever-increasing parsimony of healthcare provision. Moreover, the COVID-19 pandemic has highlighted the demand and need for online delivery of psychological therapies. More research is needed in this area comparing online versus face-to-face, studies employing primary outcomes of pain self-efficacy and coping, and greater diversity across demographics to increase generalisability.

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Part 2: Empirical paper

When COVID-19 stopped ketamine: the experience of chronic pain patients during the pandemic

Abstract

Aims: This study investigated the experiences of chronic pain patients having their ketamine infusions paused during the COVID-19 pandemic. It sought to understand the impact on patients' subjective pain and emotion. Further, it explored the wider impact of going without ketamine and how patients coped during this period and aspects lost or gained from the absence of ketamine.

Method: Chronic pain patients receiving ketamine infusions at a London specialist pain management service were recruited using convenience sampling. Fifteen participants took part in semi-structured interviews over video conferencing or telephone. Data was transcribed and analysed using thematic analysis methods.

Results: The thematic analysis yielded five higher-order themes related to the experience of patients having ketamine infusions paused: 1) *Pain increased without ketamine;* 2) *Depression;* 3) *Perceiving pain management as externally located;* 4) *Adopting an internal locus of control* and 5) *Support from others*.

Conclusions: The findings highlight the deleterious impact on pain, mood and control over pain experienced by participants who were without their ketamine infusions. In spite of these difficult circumstances, at times, some participants were able to adopt an internal locus of control, increase self-management strategies and utilise social support from others in their system. The findings contribute to the nascent body of research on the impact of COVID-19 on chronic pain patients. Further mixed methods research would be of benefit to examine the experiences of terminating ketamine infusions in other pain clinics.

1. Introduction

1.1 Chronic Pain

Chronic non-cancer-related pain is defined as persistent pain that endures for three months or longer (International Association for the Study of Pain, 1986). The most prevalent forms of chronic pain are back pain, neuropathic pain, fibromyalgia and headache (Williams et al., 2020). Chronic pain is a global healthcare concern (Rice et al., 2016) with estimates of occurrence being approximately 20% of the European adult population (Eccleston et al., 2018). Chronic pain has a pervasive impact on quality of life, physical functioning, and increases risks of suffering from mental health difficulties such as depression (Breivik et al., 2006; 2013). Moreover, chronic pain is associated with decreased work ability and productivity, work absence and taking early retirement (Nielsen, 2013; Patel et al., 2012). The overall economic burden of chronic pain in some European countries has been estimated between €1800 and €10,200 per patient per year (Williams et al., 2020). Treatments for chronic pain are best provided by a multidisciplinary pain team including pharmacological management, psychological interventions including cognitive-behavioural therapy (CBT), and physiotherapy (Scascighini et al., 2008).

1.2 Ketamine

Ketamine is a non-competitive N-methyl d-aspartate (NMDA) antagonist receptor hypothesised to increase the release of glutamate from presynaptic neurons (Moghaddam et al., 1997). Ketamine is used in veterinary and human medicine for anaesthesia and analgesia. It is recognised by The World Health Organisation (WHO, 2016) as an essential medicine and used widely in emergency medicine and paediatrics (Holloway et al., 2000) due to its rapid analgesic onset, reduction in response to pain stimuli and limited side effects (Doyle, 2002).

1.3 Ketamine and chronic pain

There is a growing body of literature attesting to the analgesic efficacy of sub-anaesthetic ketamine for chronic pain, particularly neuropathic pain (Niesters et al., 2014; Nourozi et al., 2010). Neuropathic pain is pain emanating from lesions or dysfunction in the nervous system (IASP, 1994). Patients with chronic pain are believed to have over-activity in the NMDA receptors which leads to central sensitistion known as "wind up" which heightens pain sensitivity (Truini & Cruccu, 2006). Sub-anaesthetic doses of ketamine may inhibit NMDA receptors thus reducing sensitization to pain (Fisher, et al., 2000).

1.4 Pain and depression

Patients with chronic pain have increased risk of suffering with depression and research posits that duration of chronic pain heightens the incidence of depression (Bair et al., 2003). Whilst the coexistence of pain and depression is well documented (Gerrits et al., 2015) and changes in neuroplasticity are seen as a potential causal link between the two, it remains unclear how chronic pain and depression are connected (Sheng et al., 2017).

1.5 Ketamine and depression

A review found that ketamine has efficacy in treating severe and treatment resistant depression (Caddy et al., 2015). The rapid-onset (40 minutes) antidepressant effects of intravenous ketamine show great promise for research in this field (Zarate et al., 2012). However, the antidepressant effects of single-dose ketamine are short lived and wear off after 1 – 2 weeks (Corriger & Pickering, 2019). Therefore, Caddy and colleagues (2015) recommended further research on the antidepressant effects of repeated ketamine doses. That withstanding, ketamine has demonstrated dual efficacy for treating pain and depression (Kryst et al., 2020; Nourozi et al., 2010) which opens up promise for further research exploration into co-morbid chronic pain and depression.

1.6 Opioids for pain management

Opioids are a group of analgesic medications that effectively reduce pain. In the UK, they are most commonly prescribed for acute, post-operative, cancer and palliative pain (National Institute for Health and Care Excellence; NICE, 2012). Additionally, opioids have been prescribed to manage chronic pain (Fishman, 2014; Ruscitto et al., 2014). However, in recent years there has been mounting concern about the efficacy and adverse effects of long-term opioid prescribing to chronic pain patients (Els et al., 2017). Adverse side effects range from constipation and nausea (Kalso et al., 2004) to hyperalgesia (Lee et al., 2011) and addiction (Juurlink & Dhalla, 2012). The opioids crisis in the US, which has led to over 33,000 opioid-related deaths per year; with approximately half from prescription opioids (Soelberg et al., 2017), has emphasised the need for greater restrictions on long-term usage. Awareness of the long-term implications of prescribing opioids has increased moving towards limiting and de-prescribing opioids and suggesting alternative pain management interventions (Owen et al., 2018). The most recent NICE recommendations propose a departure from opioids towards non-pharmacological management of chronic pain (NICE, 2021).

1.7 The impact of COVID-19 on pain management services

In March 2020 the UK went into national lockdown due to concerns about the rising COVID-19 infection rates. The government mandated the closure of schools, non-essential workplaces, and non-urgent healthcare provision. Where practicable non-urgent healthcare was delivered remotely however, non-urgent procedures that could not be administered remotely were terminated with no clear end date. Healthcare staff in these settings were often redeployed to intensive care units to support colleagues in the over-burdened wards filled with COVID-19 patients. Pain management services were closed, and patients were left

unable to access their usual treatments and had to rely solely on self-management strategies. Chronic pain patients were likely to experience increased severity of COVID-19 due to other comorbidities, disruption to usual care, and disproportionate secondary consequences of closure of wider support, such as social and community services (Eccleston et al., 2020; Zambelli et al., 2021). The closure of pain services was predicted to have short- and long-term negative consequences for both patients and healthcare providers exacerbating the complexity, severity and incidence of chronic pain (Eccleston et al., 2020).

1.8 Self-management strategies

Self-management strategies are the development of skills to manage symptoms, treatment, physical and psychosocial aspects of pain management (Barlow et al., 2002). Patients with musculoskeletal pain and depression who underwent a pain self-management programme with antidepressant therapy showed an increase in self-management behaviours and self-efficacy (Damush et al., 2016). Moreover, a review of 20 studies on musculoskeletal pain revealed marginal short-term effects in favour of self-management on physical function and pain intensity and longer-term effect for self-efficacy. However, it was noted that there was large heterogeneity across studies (Elbers et al., 2018).

The closure of pain management centres (PMCs) due to COVID-19 had the unintended consequence of propelling self-management strategies as the primary means of managing pain during this period. Patients who hold beliefs about the advantages of self-management are more likely to find benefit from self-management approaches than those who place greater emphasis on medical and pharmacological management (Burns et al., 2005). Self-management programmes require the adoption of lifestyle changes and a conviction and motivation to change and engage in the proposed benefits of self-management (Liddle et al., 2007). It is also suggested that patients with higher levels of self-efficacy are likely to respond better to self-management strategies (Buenaver et al., 2006). Self-efficacy

demonstrated a mediating relationship between pain intensity and disability in patients with chronic lower back pain (Chiarotto et al., 2016).

The British Pain Society recommends the provision of pain management programmes for patients with persistent pain including skills training and activity management, physical exercise, education and CBT-informed approaches targeting graded activation and exposure, methods to enhance acceptance, mindfulness and psychological flexibility (British Pain Society, 2013). This is further supported by the most recent NICE recommendations for a move towards non-pharmacological management of chronic pain (NICE, 2021). Moreover, the context of COVID-19 forced patients to rely exclusively on self-management strategies in the absence of other pain management options.

1.9 Rationale and aims of the current study

Given the recency of the COVID-19 pandemic there are few studies exploring the impact of the COVID-19 pandemic on chronic pain patients. Whilst there is some emerging research on the general impact of closure of PMCs there is no research exploring the closure on specific pain treatments such as sub-anaesthetic ketamine infusions. Further, there is no existing research on the impact of the pandemic on subjective pain, emotion and coping in chronic pain patients receiving ketamine infusions. This study attempts to address these gaps in the literature to better understand the experiences of chronic pain patients having their ketamine infusions terminated during the pandemic. The study will examine the experience of ketamine infusions being halted for patients in a specialist London pain management service.

The following research questions will be addressed:

1. How did the absence of ketamine treatment impact patients emotionally during the pandemic?
2. How did not receiving ketamine treatment impact patients' pain?

3. What was the wider impact on patients during this period? How did patients cope with pain during this time? (Practical strategies, use of other medications, impact on wider system: family, friends, other health care professionals)
4. What did patients lose or gain during the period of time without having ketamine? (Were there any positive aspects of not going for appointments? Acquired new coping skills?)

2. Method

This study utilised a qualitative approach to explore the experience of chronic pain patients having their ketamine infusions stopped due to the COVID-19 pandemic at a PMC.

2.1 Joint working

This thesis is a joint project with Jenny Scott, who conducted a long-term follow-up comparing the long-term effects of ketamine and lidocaine on pain, mood, and cognitive functioning (Scott, in preparation). See Appendix 2.A for declaration on joint project. Moreover, this is the third iteration of a UCL Doctorate in Clinical Psychology project by trainees Catherine Trotman and Matt Knox in 2016, and Georgia Halls and Joe Kibble in 2020.

2.2 Ethics

Ethical approval for this project was obtained by the University College London (UCL) Research Ethics Committee and NHS ethics from South Central Berkshire NHS Research Ethics Committee (IRAS Project ID: 214864; see Appendix 2.B). An amendment was made to the original ethics which focused on face-to-face data collection. The amendment was intended to allow for a changed focus of the research questions in light of pandemic restrictions on face-to-face testing. The amendment allowed the impact of COVID-

19 on pain and pain management in the absence of ketamine treatment to be evaluated. (See Appendices 2.B for original ethics and 2.C for non-substantial ethics amendment).

2.3 Setting and Context

The setting of the research was within a specialist tertiary care PMC at a London hospital. Patients are referred into the service if they have persistent pain that has not been resolved with medication or pain management strategies at the primary or secondary care level, or if the pain is causing significant disability or distress. The PMC offer sub-anaesthetic ketamine infusions to patients with persistent pain that has been unresponsive to other pain medications. Usually, patients attend the PMC for ketamine infusions every 3-6 months, depending on an evaluation by the clinical team on the likely responsiveness and duration of previous ketamine treatments**.** Due to the COVID-19 pandemic and subsequent lockdown across the UK, the PMC was closed as the clinical team were redeployed to COVID-19 wards and the government commanded a halting to non-urgent healthcare procedures. As a result of the pandemic disruption some patients' ketamine treatment was delayed by 3-6 months.

2.4 Participants

A convenience sample was recruited from patients at the PMC. Participants were patients with chronic pain who received intravenous ketamine infusions as part of their treatment. The inclusion criteria were that patients had to have (i) received ketamine for chronic pain in the past, (ii) already have taken part in a previous phase of the research and (iii) experienced their infusions being halted as a consequence of the COVID-19 pandemic. Inclusion criteria were men and women between the ages of 18 – 70 who were fluent in English. Exclusion criteria were patients who had discontinued ketamine infusions for reasons other than through the restrictions brought about by the COVID-19 lockdown, a

record of traumatic or acquired brain injury, learning disability, pregnancy, or an inability to give informed consent.

2.5 Procedure

Participants were recruited via invitation emails sent to their personal email addresses (See Appendix 2.D). Participants that had taken part in the previous research projects had given their consent to be contacted again for future research.

Participants were provided with an information sheet (Appendix 2.E). Due to COVID-19 restrictions interviews were conducted via video conferencing or telephone. Participants were informed prior to their interviews that the interview would be audio-recorded and would last between 30 – 60 minutes. Participants were not renumerated for their participation in the study. All interviews were transcribed by the researcher. All personal identifiable information was removed at the point of transcription.

2.6 Data Collection

Semi-structured interviews were employed to collect data from the participants. In consultation with the research supervisor, the researcher designed a semi-structured interview schedule of four questions (see Appendix 2.G). The aims of the interview schedule were to explore how participants had experienced their ketamine infusions being paused due to the COVID-19 pandemic. The interview schedule was particularly focused on examining the impact halting infusions had on participants' subjective pain and emotions. Furthermore, any alternative coping strategies participants had used in the absence of ketamine infusions. To ascertain potential positive and negative aspects of not receiving infusions, participants were asked what they missed and did not miss about having ketamine.

The number of questions in the schedule was deliberately small in order to make the interviews less structured and more open-ended and explorative. The researcher gave

prompts, as appropriate, based on clinical judgement to open up answers and encourage participants to elaborate upon their responses. The interview schedule was piloted on one participant whose data was not included in the analysis. Thereafter a research supervisor with expertise in qualitative methods reviewed the interview transcript and made minimal alterations to the schedule. The interview schedule was reviewed and revised in consultation with the Consultant Anaesthesiologist at the pain management centre and one of the researcher's supervisors.

2.7 Data analysis procedures

Qualitative analysis methods were selected for this study as the aims were exploratory, focusing on patient's subjective experiences. Thematic analysis (TA) was selected on the basis of its flexibility and pervasive application across a broad range of qualitative research topics. Epistemologically, it allows the researcher freedom to explore meaning as it is devoid of constraints from pre-existing theoretical frameworks. TA is conducted in a transparent and systematic fashion yielding a rich description of the data (Braun & Clarke, 2006). As the aims of the research were to examine participant's thoughts, feelings and understandings about not receiving ketamine infusions during the pandemic a further benefit of employing TA was that it facilitated description of cognitive, affective and symbolic domains of the data (Joffe, 2011). TA is sometimes considered a generic method of qualitative analysis; however, it is also a distinct approach with specific methodological guidelines (Boyatzis, 1998; Braun & Clarke, 2006; Joffe, 2011).

For this study the researcher took an essentialist/realist approach focusing on experience and meaning within the data. The analytic approach was inductive and semantic in order to stay close to the words of the participants.

To uphold a systematic and rigorous TA the researcher chose to broadly follow TA as proposed by Braun & Clarke (2006) who offer 6 guidelines. Any deviations from the guidelines are justified within the discussion.

To start, the researcher familiarised themselves with the data by transcribing the audio-recorded interviews and immersing themselves in the data through multiple readings of the interview transcripts. Second, the researcher generated a list of preliminary ideas from the first readings of the interviews which resonated with the research questions. From there the researcher imported the transcripts into the qualitative research methods analysis software NVivo (QSR International, 2018). From here initial codes were devised and coded. An inductive approach was taken in that initial codes were data-driven and were not determined from researcher or theoretical assumptions. (Appendix 2.H shows an example of how initial codes were generated at this stage). Third, the researcher moved from codes to potential themes and sub-themes by way of an iterative process of re-reading codes and extracts. Where codes appeared sufficiently similar, they were merged or collapsed into other codes until there were few enough codes to start generating themes and sub-themes. Fourth, themes were reviewed by reading over extracts to confirm that they were internally homogenous and externally heterogeneous (Braun & Clarke, 2006; Patton, 1990). A thematic table was designed (See Table 2 for thematic table and Appendix 2.I for preliminary thematic table). Moreover, themes and sub-themes were corroborated against coded extracts and the complete dataset. Fifth, comprised the process of defining and naming themes. The final themes and composite names continued into the writing of the results to further enhance the coherence of the narrative. A summary of the themes was shared with participants who were invited to give feedback. Feedback from participants shaped and refined the final themes and names to honour their voices. Finally, the presentation of a written narrative in the results including supporting quotes from the interviews to expound upon the research questions.

2.8 Credibility Checks

To make the research process more systematic credibility checks were integrated into the data analysis (Guest et al., 2012). First, consensus checks were deployed at the coding phase of the analysis. The researcher recruited a peer to review codes for approximately 10-15% of the interview transcripts. The reviewer was given raw uncoded transcripts and asked to code as per the research questions to ascertain corroboration in coding between the reviewer and researcher. The process revealed a high level of coding corroboration. Discrepancies were discussed and amendments to coding were made were necessary. Second testimonial validity checks were performed after the preliminary themes and sub-themes had been devised. This came in the form of member checks (Seale, 1999). The researcher sent a summary of the themes and sub-themes to participants asking them to comment on whether themes made sense in relation to their experience and specify if any did not (see Appendix 2.J). Four out of 15 participants responded with comments.

2.9 Reflexive Statement

The researcher is a white British female from a middle-class family conducting research within the context of undertaking her Clinical Psychology Doctorate at University College London. Prior to studying Psychology, the researcher studied Theology and held an epistemological position that was more phenomenological or relativist. However, through clinical training the researcher's position has shifted to somewhere in the middle of the positivist– phenomenological continuum. Her interest in health psychology is influenced by her upbringing of having medical parents and also working in an operating theatre before pursuing a career in psychology. She is particularly attracted to the field of psychopharmacology which was influenced by Professor David Nutt in his research on the medical benefits of illicit substances which are obscured from research on account of their

illicit classification (Nutt, 2020). The researcher held *a priori* assumptions about the therapeutic advantages of illicit substances and holds progressive attitudes about use for medicinal purposes. The researcher sustained a shoulder injury which has resulted in some mild persistent pain which is controlled with self-management strategies. The researcher acknowledges that her own experience of pain could lead to over-identification with the research topic which could introduce bias into the results. The researcher holds another *a priori* assumption that self-management strategies are a more effective long-term solution to managing chronic pain than reliance on opioids. Within clinical work the researcher has a preference for integrative therapeutic approaches tailored to the needs of the client which also fit with her epistemological position. During the project the researcher received consultation from a supervisor with qualitative expertise and utilised a reflective research journal. The researcher conducted a bracketing interview with her supervisor to "bracket off" her assumptions and expectations pertaining to the topic to reduce researcher bias (Hill et al., 2005). The process of conducting and analysing the interviews challenged the researcher's *a priori* assumption around the precedence of self-management strategies over pharmacological treatment. Listening to the experience of intolerable pain levels depicted by participants made the researcher re-evaluate the crucial role of pharmacological methods of pain management. The researcher's supervisors were experts in psychopharmacology, chronic pain, health psychology, and neuropsychology.

3. Results

3.1 Participant characteristics

Of the 27 ketamine patients eligible to participate, 15 were included in the analysis. Table 5 presents participants demographic characteristics. Twelve participants were female, two were male and one was non-binary. Ages ranged between 35 and 66 years with a mean of 51.9 years. Participants were given a participant ID to ensure their anonymity in the study.

The majority of participants were white British and not working. The type of chronic pain condition or illness of participants has been omitted in order to protect anonymity.

3.2 Themes

Five higher order themes with 11 sub-themes were conceptualised. Table 6 displays a thematic table of themes with the prevalence (*n*) of participants who paid testament to the themes and sub-themes for greater transparency.

Table 5: Demographic details of participants

Participant ID	Age	Sex	Ethnicity	Chronic pain condition
P1	62	Female	White British	McArdle's disease
P2	42	Female	White American	Multiple Sclerosis
P3	62	Female	White British	Unspecified
P4	55	Female	White	Morgellons's disease
P5	38	Female	White British	Unspecified
P6	39	Female	White British	Unspecified
P7	43	Non-binary	White British	Unspecified
P8	65	Male	White British	Unspecified
P9	55	Female	White British	Neuropathic pain
P10	58	Female	White British	Neuropathic pain
P11	51	Male	White British	Neuropathic pain
P12	51	Female	Black African	Unspecified
P13	56	Female	White British	Post-surgical pain
P14	35	Female	White British	Ehlers-Danlos syndrome
P15	66	Female	White British	Neuropathic pain

Table 6: Thematic table

Theme	Prevalence (*n*)
1.0 Pain increased without ketamine	14
1.1 Deterioration in quality of life	14
1.2 Missing the pain relief from ketamine	12
1.3 Gratitude for the pain clinic	9
2.0 Depression	10
2.1 Suicidal thoughts	5
3.0 Perceiving pain management as externally located	13
3.1 Abandonment and anger towards PMC and health system	6
3.2 Disruption to other services	7
3.3 Uncertainty about when next infusion will happen	10
3.4 Relying more on opiates	9
4.0 Adopting an internal locus of control	13
4.1 Pushing myself harder without ketamine	5
4.2 Resilience and self-compassion	7
4.3 Self-management strategies	13
5.0 Support from others	11

1. Pain increased without ketamine

All but one of the participants described their subjective pain increasing in the absence of ketamine. Participants talked about the pain being worse than their usual pain levels when they received ketamine more regularly. The increased pain was distressing and made it harder to function as normal.

Much more intense and much more frequent pain attacks that last for longer (P4).

The pain has come back badly; now it's pretty constant all the time. I used to have spells where it eases off and comes back, but it's pretty much there all the time (P11).

1.1 Deterioration in quality of life

Participants described how the experience of having their ketamine infusions paused led to a deterioration in their quality of life. Many noticed a decline in a number of areas including daily functioning, mobility, sleep, appetite, and self-care. Closely connected to this was an implicit description that they were existing as opposed to having pleasure in life.

I suppose, just the question that your whole life falls apart. You don't feel yourself. You eat bowls of cereal for days running. You don't look at your texts, you don't do emails, you don't even watch TV because it becomes so tiresome (P4).

Most participants were realistic about the limits that chronic pain placed upon them. Therefore, the absence of the relief produced by ketamine was felt strongly as it limited their lives even further than usual.

With the ketamine I feel I am back to normal, the usual aches and pain that go with my condition, I can cope with. Not having the infusion, I can't cope. I don't want to go back to knowing what it is like without ketamine (P10).

1.2 Missing the pain relief from ketamine

Overwhelmingly participants missed the analgesic effects of ketamine. Infusions made pain easier to cope with as it took a less central role in the participant's life. Many participants had gone through a long process trying a variety of other medications before ketamine.

I'm a huge fan of ketamine because I find it's been the most beneficial medication for me (P6).

I've missed the fact that I can take less morphine, I feel better about that (P4).

Participants relied upon ketamine to provide respite from pain. Participants focused on the date of their next infusion to get them through until their next instalment of pain relief.

I've missed knowing regularly if I can have it, the sense of security that I get, that despite everything that is happening…there was a constant, that was that I was going to get my treatment every three months (P4).

1.3 Gratitude for the clinic

Talking to other patients and staff at the clinic was something that participants valued about attending the PMC.

You can chat to other patients from bed, "have you tried this?" You know that opportunity to talk to others, even though they might not have the same disease as you, they are there because of their experience of pain. So, I have missed that (P1).

Some participants described feeling that they were held in mind by staff at the PMC and treated with kindness and dignity.

My experience at the pain clinic is that everybody I have encountered have been incredibly kind and treated me as if I am valued (P3).

Descriptions of barriers of travelling to the clinic co-occurred within the sub-theme of gratitude. There are very few specialist pain management services that offer ketamine infusions across the UK. Attending the PMC entails a long day with many having to travel significant distances to get there. Whilst travelling was cited as tedious, seven of the nine participants who talked about travel to the clinic said that the travel was made worthwhile by the benefits of ketamine.

I don't miss the journey. It's pretty much all day… But everything else it ticks all the boxes. With that said, even though it's hard work, it is worth that for the sake of three months of being out of pain... Ketamine is one of the most amazing treatments I have ever had. It has worked every time and it is instant… I am very lucky and fortunate. (P11).

2. Depression

Ten participants conveyed that they felt more depressed than usual without access to ketamine infusions.

Depression, this powerlessness feeds into a heighted depression and open-ended feeling of I don't know where we go from here (P4).

Participants described the interaction between depression and pain.

People just don't understand that once you are in that cycle of depression and pain, and the more pain and more depression and the isolation, they don't understand you can't get out of it (P14).

In conjunction with low affect, participants described self-hatred and negative thinking styles centring around defectiveness and weakness.

I thought "you need a grow a pair and deal with it" ... I thought, "everyone else copes but I must be really weak and pathetic because I can't cope" (P11).

3.1 Suicidal thinking

Five participants expressed that they experienced suicidal thoughts. The below excerpts demonstrate the point of desperation and hopelessness they reached.

I just rang up the surgery, and I said, "I'm just going to take my tablets and go to sleep. This is the last time you will hear from me, goodbye" (P14).

Despite these highly distressing thoughts none of the participants made any attempts on their lives. They described a variety of different protective factors including loved ones, support from care agencies and mental health teams, and hope that infusions would recommence.

The only thing that kept me strong was thinking about my grandkids, what would it do to my grandkids if I committed suicide. I was brought up to believe that suicide was selfish. (P10).

3. Perceiving pain management as externally located

This theme illustrates the concept of perceiving pain management as externally located. External locus of control is the belief that consequences in one's life are determined by external factors such as powerful others, fate or luck (Wallston et al., 1994). Thirteen participants believed their pain management was controlled by the PMC and wider NHS.

The way the whole system, and as a patient within the whole health system you have to be passive and just accept things…And I hate that, I hate the fact that I am dependent on other people (P4).

3.1 Abandonment and anger towards PMC and health system

Six participants described feeling abandoned. Closely linked to abandonment, five of the six participants also described feeling angry with the PMC and wider healthcare system.

It literally is abandonment…the NHS was okay about people like me falling off the end. We are the people with the most complex care, take up the most time, financially a burden (P1).

Whoever was head of the pain clinic should have said to whoever is head of the hospital, "look we can run this place without COVID, let's give it a go", "because these people are important patients" (P4).

Three participants explicitly reported "no one cares" about them at the PMC, although this was implicitly made reference to by other participants. Participants expressed difficulty in getting hold of the administration at the PMC which exacerbated their sense of abandonment.

I left so many messages for the pain management clinic, I lost count. And then all you got was "this inbox is full of messages". It was as if nobody cared. (P8).

Nobody cares, nobody gives a damn. My doctor wrote to the hospital nearly a month ago, she got a generated email saying they had received her correspondence and would reply in due course, she still hasn't heard anything from them (P13).

Participants were angry about the lack of consultation from the clinic about the closure. They were also angry towards the government for the perception that they were prioritising other health conditions over chronic pain. This intensified the sense of abandonment and powerlessness.

When I heard the health minister, say that he was delighted to say that invitro fertilisation services were going to resume…prioritising invitro fertilization so couples can have a baby, which I know is important, but they are not in pain, they're not dying (P8).

3.2 Disruption to other services

The closure of the PMC was not the only healthcare provider that participants could not access during lockdown. The cumulative implications of this heightened the uncertainty, abandonment and perceived lack of control over the situation.

I've got urology problems, gastro problems, they are getting worse and trying to sort out appointments related to them with lockdowns and COVID and everything was difficult, and a lot of stress (P5).

The pandemic caused disruptions to access to GPs and other primary care services. It left participants feeling as though they had been forgotten about and other services were too busy to deal with them.

It wasn't just the doctors it was the nurses; the district nurses, pharmacist, I mean they were so bogged down it was crazy…It was like they had gone underground; it was almost like they had a bloody holiday. (P13).

For most participants their pain management regimes were not served by infusions alone and relied on adjunct treatments and services. The closure of these types of services magnified the preclusion from the PMC leaving participants with scant pain management alternatives.

I would normally go for a massage to try and help the pain and I couldn't do that…I wasn't able to go to the physio (P7).

3.3 Uncertainty about when next infusion will happen

This sub-theme pertains to the uncertainty of how and when patients of the PMC would access their next ketamine infusion. During the first lockdown the UK government mandated the closure of non-urgent healthcare providers who could not operate remotely. Participants conveyed they attached significant importance on ketamine infusions for managing their pain. Often the date of the infusion was something they held onto to remind themselves that soon relief was coming.

When they first said that they're not doing any treatments, not knowing how long that was going to go on for, that for me was more anxiety provoking than actually the pain (P3).

The uncertainty about when infusions would recommence precipitated anxious thinking about how participants would cope with their pain without ketamine.

Very anxious, "what's going to happen to me?", "how am I going to manage my pain, it's bad enough", "how can they do this to me?" (P4).

The length of time without infusions led some participants to feel hopeless about whether they would receive an infusion again.

It leaves me with nothing. I don't know when they will contact me, I'm just worried, you know, just worry about it and because I'm already used to the infusions, so I'm always looking forward for that... I don't know what to do, I'm just hanging there (P12).

3.4 Relying more on opiates

In the absence of their ketamine infusions nine participants reported relying more on opiates to manage their pain. Infusions were often prescribed as opioids had limited analgesic effect or facilitated patients reducing the quantity of opiates they were taking.

I took more Morphine; I took more of everything in fact. I self-medicated on that a little (P4).

Difficulty getting opiates increased by GPs augmented participant's perceived lack of control. Due to deleterious long-term consequences, medical professionals are often reluctant to increase opiates.

You are treated like a drug addict. And you have to fight for your Oramorph to be increased to 10ml…I am not taking anything for any thought of getting high. It's so that I can function (P1).

Some of the participants were aware of the risks of relying too heavily on opiates. The hiatus from infusions left participants with a dilemma; to increase the opiates or live with much higher levels of pain.

I ended up having to up my Codeine so I will literally avoid it until I cannot move without wanting to scream... because I don't want to depend on painkillers. (P14).

4. Adopting an internal locus of control

This theme expounds adopting an internal locus of control to cope with pain. An internal locus of control is the extent to which a patient believes that their behaviour has control over their pain (Zuercher-Huerlimann et al, 2019). Participants were able to foster a sense of self-efficacy in the absence of external pain management. Thirteen participants spoke about adopting an internal locus of control.

4.1 Pushing myself harder without ketamine

Five participants described pushing themselves through the pain during the time they were not receiving infusions. Being without ketamine they "pushed" through the pain, locating control over their pain management within themselves.

You have a limit…and I push myself to that limit and more, but even so you do have a limit…You learn the hard way if you don't, because I am always pushing myself too much (P9).

For some, the responsibility to manage pain themselves was deeply engrained and they were reluctant to apportion duty upon the PMC. The below excerpts speak to a belief that one should not place high levels of control on the remedial effects of ketamine.

I imagine that there would be some people who would be really cross that they're not getting their ketamine…Whereas I'm the absolute opposite, thinking "you need to try harder; the fact that you are not getting your treatment is neither here nor there" (P3).

I tell these doctors that "I'm ok, I'm ok", and I'm not…I should be saying, "no I'm really struggling". But I'm not very good at saying that so I grit my teeth and say, "yeah I'm ok". I should ask for more help, but I don't want to be a burden and I have lots of feelings associated with that of guilt (P5).

4.2 Resilience and self-compassion

Seven of the participants depicted having resilience and self-compassion. Resilience featured strongly in accounts from participants as a means to endure the protracted period without infusions.

I just try to keep focused knowing that at some point ketamine will start again, that's kind of what's keeping me going... I just gotta stay strong and try to be positive and try to get through day by day, week by week (P11).

For some participants their health condition had bestowed resilience upon them, so it was easier to put these skills into practice during the lockdown.

I suppose I just look back, I have had my conditions for 19 years, and I've had so many bad days and I've come through them, anything can get chucked at me and I will find a way of getting through it (P5).

Participants posited the importance of thinking and behaving in a manner that was self-compassionate, kind, and realistic. Through this they minimised the extent to which they made unrealistic expectations of themselves.

I am very good at self-care, I always have that in mind when I am planning my week out, I need to be slower and gentler on myself and not push through (P7).

My mentality is… everyone has bad days. So, you take it for what it is. It's a bad day, but you don't let it become a bad week, a bad month (P14).

4.3 Self-management strategies

Thirteen participants expressed using more self-management strategies during lockdown. Four participants cited self-management skills they had learnt from pain management courses at the PMC. Six participants reported using meditation and relaxation techniques to help them deal with the pain.

Meditation in particular I really relied on heavily (P2).

Eight participants purported that movement and keeping active was a helpful strategy to manage pain.

I do a lot of stretching and very light exercises…Pilates, Yoga... And then I always try to go for a walk again to keep things moving (P6).

Whilst self-management strategies might not get rid of the pain, six participants noted that distraction techniques were useful in allowing them the ability to attend away from the pain.

My coping mechanism is quite genuinely either putting myself in a bath or going on a walk or something with an audiobook or classical music. And it's that distraction technique and it just gives me time outside the pain bubble (P14).

Participants highlighted the importance of slowing down and being realistic about what they are capable of doing, depending on pain levels. A crucial aspect of this referenced by six participants was resting and sleeping where required. Furthermore, pacing was evidenced by four participants.

Find your baseline and kind of go from that…how can I build more rest into my day? So rather than waiting for my week to be full or just making myself really busy. Can I build rest time into my schedule? (P7).

Four participants reported using cannabis or alcohol during the lockdown for pain relief. Participants were clear that they were not using substances to get high or drunk but to manage pain in the absence of ketamine.

I smoke cannabis in the evenings just before I go to bed and that helped my body relax and for my mind to relax... I found that I was smoking more because I was smoking so that I slept. (P10).

I'm not meant to drink with all this medication, but I did have the odd late-night drink… I don't enjoy it. I do it so that I can numb the pain pretty much. (P4).

5. Support from others

The final theme, support from others, was cited by 11 participants. This came in the form of support from friends and family and also support from other agencies. Family and friends were a source of both practical and emotional support.

Apart from the day to day helping with food, shopping, getting my prescriptions... And they know to just talk, if the stress of trying to sort out appointments... Having them, my partner there to give me a cuddle if I am struggling or just to be there to listen. (P5).

Chronic pain can be an isolating condition to live with for many. Having peer support from others with chronic pain offered the below participant with a sense of shared experience.

I have a group with some friends that I met on a pain course. We have a WhatsApp group... People who don't have chronic pain don't understand…If you've never been in that situation, you can never fully understand. It is just really beneficial having people to talk to, that are on your level and instantly know what you mean (P6).

As discussed previously, some participants were depressed. Talking to others allowed participants to ventilate their thoughts and feelings and feel that others cared about them. The below extracts testify that things could have been different if they did not have other people for support.

My best friend said, "if you don't phone me, I am coming to you", "I know you are depressed, ring me" …So I phoned her, and we had a good couple of hours on the phone. I cried and she cried with me, we talked, and I felt a lot better afterwards (P10).

My care agency gave me extra support. There have been times where I can sit and chat to a carer... I could release a lot of stuff that's been going around in my head and stuff that I've allowed to escalate without talking about it…I've been really gifted to have real professional good quality carers who have turned the corner for me (P11).

4. Discussion

4.1 Summary of main findings

This study explored the experience of chronic pain patients having their ketamine infusions paused during the COVID-19 pandemic. The study sought to answer the following research questions: (1) How not receiving ketamine treatment impact participants emotionally; (2) How not receiving ketamine treatment impacted pain; (3) How participants

coped with their pain during this time and (4) What participants lost and gained from not having ketamine.

Emotionally participants described feeling more depressed, helpless, anxious and abandoned as a result of not receiving their ketamine infusions. They described increased pain, decreased pain coping and a marked deterioration in quality of life. Without ketamine participants broadly coped with pain by increasing opiates, self-management strategies and via social support from others in their system. Participants missed the analgesic properties of ketamine, relief from pain, having a date for their next infusion to focus on and being able to do more. They did not miss the travel to the clinic but noted that this was worth it for the pain relief from ketamine.

Using a thematic analysis 5 higher-order themes were devised. First, *Pain increased without ketamine* pertained to the subjective experience of deterioration in pain and quality of life, missing the pain relief from ketamine and participants gratitude for provision of infusions during normal operation of the PMC.

Second, *Depression* was experienced by some participants from no longer having access to their usual pain management and the interaction with increased pain. Some discussed experiencing thoughts of suicide.

Third, *Perceiving pain management as externally located* examined the feelings of loss of control and the wider loss of agency brought about by the COVID-19 pandemic. The theme examined abandonment and anger towards the clinic and broader healthcare system, disruption to other services and uncertainty about when they would receive their next infusion. In the absence of ketamine participants cited increased reliance on opioid medications.

Fourth, *Adopting an internal locus of control* attested to the use of personal agency and self-efficacy in the face of infusions being terminated. It explored how participants

pushed themselves harder, how they tried to uphold resilience and self-compassion and increased use of self-management strategies.

Fifth, *Support from others* described how participants made use of others within their system such as friends, family and other agencies to cope with pain whilst without ketamine.

4.2 Results in the context of other studies

It is unsurprising that participants experienced increased pain without their ketamine infusions. This is consistent with the literature that ketamine reduces pain in persons with complex regional pain syndrome (Keifer et al, 2008). Moreover, the efficacy of ketamine for pain reduction was evidenced from a single intravenous ketamine infusion in patients with peripheral nervous system disease (Backonja et al., 1994).

The literature posits that there is a correlation between decreased quality of life and chronic pain (Duenas, 2016; Philips, 2009; Tuzun, 2007). Quality of life is multifactorial comprising biological, psychological and social factors (Hunfield et al., 2001). The limiting interaction of these factors can lead patients to experience a decline in quality of life especially when making comparisons to their premorbid level of functioning (Savvakis & Kolokouras, 2019). There is some emerging literature suggesting that chronic pain patients experienced a deterioration in quality of life during lockdown (Zambelli et al., 2021).

Cognitive and affective distress brought about by an intolerance of uncertainty is well documented in the literature (Buhr & Dugas, 2002; Dugas et al., 2004). The government mandated closure of non-urgent healthcare services brought about uncertainty for chronic pain patients. The theme of uncertainty within this study reflects contemporaneous research indicating that uncertainty distress during the pandemic was prevalent and, in some instances, could lead to anxiety and depression (Del Valle et al., 2020; Freeston et al., 2020). Moreover, this was augmented by the disruption to wider services which is similar to the findings of

another study which found that cancelled healthcare appointments were associated with higher levels of anxiety and depression (Consonni et al., 2020).

There is an interaction between pain and depression with the two often co-occurring (Gerrits et al., 2015). Research suggests that ketamine has dual efficacy for treating pain and depression (Kryst et al., 2020; Nourozi et al., 2010). However, studies have found that the antidepressant effects of single dose ketamine reduce quickly and are negligible after 1 – 2 weeks (Corriger & Pickering, 2019). Given patients at the PMC normally receive infusions every three months it seems improbable that depression was solely attributable to having a longer period of time without ketamine. One could hypothesise that the interplay between increased pain and uncertainty about when infusions would recommence might have augmented depression. Higher levels of depression were associated with difficulty managing pain and dependency on others during the pandemic (Consonni et al., 2020). Being in a vulnerable group and social isolation were found to contribute to increased suicidality (Hai et al., 2020). Whilst there is no direct evidence on prevalence of suicidal ideation in chronic pain patients during the pandemic, increased pain, depression, isolation and preclusion from services could offer a tentative explanation of these findings.

Participants perceiving pain management as externally located, namely to "powerful others" at the PMC, is also supported by the extant literature. Patients with pain associated with lower limb ulcerations were more inclined to attribute control over pain to powerful others and perceive themselves as helpless in managing pain (Cwajda-Bialasik et al., 2012; Herber et al., 2007). The additional level of context of the pandemic may well have amplified external locus of control attributions leaving participants feeling impotent and passive in the decision to close the PMC. Linked to this, the finding that some participants relied more heavily on opioids is consistent with other research that "powerful others" locus of control

was associated with greater pain distress and increased the likelihood of opioid use by 60% in an older adult population (Musich et al., 2020).

The feelings of abandonment described by participants reflects their attachment relationship to the PMC and its clinicians. Some patients had been going to the clinic for years and relied heavily on them for support. Fearful attachment style was associated with greater levels of depression and pain catastrophising, and preoccupied attachment style was associated with more than weekly pain-related visits (Ciechanowski et al., 2003). Treatment abandonment was reported in paediatric cancer care during the pandemic (Graetz et al., 2021). To date, there is no published research on abandonment in chronic pain patients, but one could surmise that the closure of the PMC could have been experienced as being highly abandoning, particularly for patients with insecure attachment styles.

Higher internal locus of control is predictive of better pain outcomes (Keedy et al., 2014; Lester et al., 2007; Zuercher-Huerlimann et al., 2019). Closely associated with this, increased pain self-efficacy is linked to a reduction in pain disability outcomes (Gandy et al., 2018; Karasawa et al., 2019).

The findings that some participants demonstrated resilience and self-compassion has been evidenced in other pain studies. In the context of chronic pain, resilience is understood to be a multimodal construct which comprises a greater belief in control over pain, awareness of emotional states, optimism, and pain acceptance (Sturgeon & Zautra, 2010). In contrast, lower levels of resilience and self-efficacy are correlated with higher levels of pain distress (Ahmed et al., 2019). Self-compassion pertains to having kindness, humanity and a mindful awareness towards oneself (Neff, 2003). Specifically related to chronic pain, self-compassion is linked to higher resilience, coping and pain acceptance and lower pain disability, depression and catastrophising (Costa & Pinto-Gouveia, 2011, 2013; Edwards et al., 2019).

Self-efficacy and self-management strategies coalesce and provide internal controls over pain management. Whilst most participants discussed employing self-management strategies during the pandemic it is important to note that these did not diminish the loss of having their regular infusions. Locus of control is dynamic; participants depicted vacillating between internal and external attributions which is reflective of the uncertain circumstances they found themselves in. Barriers to self-management strategies include distress from ongoing pain, difficulty in motivating self-management and unsupportive relationships with clinicians (Devan et al., 2018), all of which are factors participants reported contending with during the pandemic.

Social support is a protective factor for pain management behaviours. Social support has been found to moderate the effects of stress on depression (Wang et al., 2014). McMurtry and colleagues (2020) posit that it is the role of pain management practitioners to identify facilitators and barriers to greater quantity and quality of social support for patients. Quality and quantity of social support varied considerably across participants in the present study. One could conjecture participants who reported depression were more likely to have reduced quality and quantity of social support during their time without infusions.

4.3 Strengths and limitations

This is a novel piece of research exploring the experiences of the termination of ketamine infusions for chronic pain patients during lockdown. The qualitative approach provided scope for a rich exploration of the data and facilitated deeper interpretations than could be offered from quantitative research methods.

The researcher's decision to deploy TA allowed for flexibility in the interpretation of the data. The researcher sought to be transparent and rigorous in the analytic methods, adhering closely to the tenets of TA and avoiding common pitfalls of this method as outlined by Braun and Clarke (2006; 2020). The researcher wished to honour the voices of

participants so approached analysis from an inductive and semantic position. The researcher chose to numerically display the prevalence of themes and sub-themes to convey their representativeness within the study. Themes were endorsed by between nine and 14 of the 15 participants. This suggests that despite variability in the experiences of individual patients, there was considerable shared experience. Whilst this may be more closely aligned to content analysis (Forman & Damschroder, 2008) than TA, the researcher made this decision to demonstrate greater clarity.

The researcher spent time developing the interview schedule and thinking about emotional posture with their supervisor. This set the scene for good rapport during interviews which gave forth to a deeper emotional tone and enhanced the richness of the data. At the beginning of interviews, the researcher explicitly positioned themselves as outside the PMC to demarcate themselves from the system and avoid socially desirable responses.

The use of consensus and testimonial validity checks added weight to the quality and credibility of the qualitative analysis (Guest et al., 2012). As this study is within the sphere of applied research, it provides a level of "qualitative pragmatism" to the findings (Ritchie & Spencer, 1994). However, only four of the 15 participants responded to invitations to participate in the testimonial validity checks. The use of email invitations might have meant that some participants overlooked or missed the email. Further, given that participants gave a significant amount of time interviewing they may have not wished to spare more time, especially if they were still contending with high levels of pain. It is important to highlight that this is a slight deviation from the guidelines for TA (Braun & Clarke, 2020). Ultimately, this was a trade-off decision between fidelity to the TA guidelines and a desire to enhance the coherence and validity of the findings.

Sixteen of the 27 eligible participants at the PMC agreed to be interviewed. This is an acceptable number of participants for a qualitative analysis. The reasons for the 11

participants who did not conduct interviews included: feeling unable to commit to the interview due to pain levels, personal issues, unable to contact, feeling angry with the PMC. Those that declined based on feeling angry could have introduced some bias into the results as participants who agreed to participate might have held more favourable views towards the PMC. However, *abandonment and anger from the PMC and healthcare system* was a sub-theme endorsed by six participants which indicates that the sample was still able to capture those with more negative attitudes towards the PMC.

There are a number of limitations of the present study. Whilst in theory the researcher sought to bracket their assumptions and preconceptions through a bracketing interview, in practice this is impossible to do entirely. The researcher acknowledges that they hold biases and cannot operate in a "theoretical vacuum" (Braun & Clarke, 2006, 2020). The researchers' preliminary reading, clinical training, and *a priori* assumptions may have influenced the decision-making process in the conception of codes and themes.

Given the specificity of this sample population, one ought to be cautious about generalising the findings to other chronic pain populations. The setting was a national centre for pain management and the provision of ketamine infusions is not a standard form of treatment across UK pain management clinics.

The majority of participants within this sample were female and white. It is understood that women are more likely to access pain management than males (Unruh, 1996). Further, pain related outcomes have been shown to differ across ethnicities (Campbell & Edwards, 2012). Whilst the researcher was bound by methodological restrictions, the findings offer limited representation for ethnic minority and male patients with chronic pain.

The aetiology, chronicity, intensity and site of pain were heterogenous across participants. Similarly, there will have been variation in the type and dose of opioids and other analgesics that patients were prescribed. Participants' descriptions of their subjective

experience are to be taken within the context of the heterogeneity of the sample**.** However, it is interesting that there was such consistency in prevalence of themes despite this heterogeneity.

Due to data collection restrictions brought about by COVID-19 most interviews were conducted over video call. There was a small number of participants who did not have stable internet connection or who were unfamiliar with video conferencing, so they asked to do interviews over the telephone. Not being able to see participants may have limited the quality of these interviews as non-verbal cues could not be observed by the researcher.

4.4 Clinical and policy implications

The increased pain, external locus of control and abandonment highlighted by our findings suggest that more can be done to facilitate patients feeling connected with services during these unprecedented times. The introduction of telemedicine and eHealth interventions for pain management could keep patients in touch with pain specialists and administration staff, even if they cannot receive infusions. Online and web-based psychologically informed self-management programmes are relatively low-cost which could not only support self-management but also ameliorate the emotional distress brought about by the pandemic (Eccleston et al., 2020).

Redeploying staff onto COVID-19 wards led to increased waiting lists and backlog of patients in chronic pain settings (Karos et al., 2020). Moreover, chronic pain patients experienced poorer wellbeing during lockdown compared to pre-lockdown (Zambelli et al., 2021). It would be of mutual benefit to patients and staff if services remained partially open, offering a skeleton service for those most in need whilst adhering to pandemic precautions. With the possibility of future pandemics, the government and healthcare providers need to amend policy and create future plans for how pain services can continue to operate in light of what has been learned from COVID-19.

This pandemic was unforeseen but there are important lessons learnt from the experience that can be taken up by stakeholders when they think about reconfiguring services post-pandemic. The increased provision of online and telemedicine remains at the fore of how service delivery can be better adapted to those with chronic pain, offering remote medical consultation and remote self-management courses. The implementation of Quality and Improvement and co-production projects in consultation with patients would help to carve out new ideas about how pain management services can be run in a post-COVID-19 healthcare system.

4.5 Future research

This study demonstrates that disruption to pain management services during the pandemic had a range of deleterious consequences for patients. More widespread research on the impact of the pandemic on other pain clinics, particularly those offering ketamine infusions, would help to make the findings of this study more generalisable. Moreover, the application of mixed methods research to incorporate pain, quality of life, and self-efficacy outcome measures would cement the generalisability of findings.

It is unclear whether the gratitude expressed by participants for the provision of infusions was pre-existent to or came as a consequence of the COVID-19 lockdown. Future research could examine whether the experience of going without ketamine instilled a renewed gratitude for infusions that may have been amplified by the protracted period of increased pain.

Treatment abandonment during the pandemic could be an interesting area for future research. Examining attachment styles and relationships to pain services and the impact closure of services had upon patients who often place a strong emphasis on their relationship with their clinical team would be of benefit to research. Further research on the association between self-management strategies and adopting an internal locus of control during the

pandemic could explore whether closure of services might have increased internal locus of control attributions and enhanced positive pain coping strategies compared to pre-pandemic levels. Quantitative research would be useful to examine the interaction between closure of services, chronic pain, depression, and limited social support during the pandemic. Finally, closer consideration of patient demographics that are under-represented in chronic pain research such as ethnic minorities and male patients would broaden the generalisability of pain research.

5. Conclusion

To the best of the knowledge of the author, this was a novel piece of research examining the experiences of chronic pain patients having their ketamine infusions halted during the pandemic. The researcher adopted TA to analyse the interviews and devised five themes: (1) *Pain increased without ketamine,* (2) *Depression*, (3) *Perceiving pain management as externally located*, (4) *Adopting an internal locus of control*, and (5) *Support from others*. The themes emphasise the negative impact on pain, emotion and agency experienced by participants without their regular infusions. That withstanding, it is promising that at times most participants in our study were able to adopt an internal locus of control and utilise self-management strategies. Our study contributes to the nascent body of research on the impact of COVID-19 on chronic pain patients. More research will emerge on this phenomenon which would benefit from combining mixed methods analyses to examine the experiences of going without ketamine infusions in other pain clinics to broaden the generalisability of the findings of this study.

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Part 3: Critical appraisal

1.0 Introduction

The critical appraisal comprises reflections on the empirical paper starting with my background preceding the project and what initially attracted me to the topic. It presents my reflections on the impact of COVID-19 on the project and changes that were made to comply with COVID-19 guidelines on data collection. I reflect on managing my own biases before and during the research process and the use of a bracketing interview and reflective research journal to aid this process. I discuss my experience of conducting interviews and analysing the data as well as obstacles during these stages and how I overcame them. Finally, I offer some personal reflections on the experience of conducting the research project.

1.1 Background and initial interest in topic

My initial interest in the project came from my pre-training reading of Professor David Nutt's book *Drugs Without the Hot Air* (Nutt, 2020). Professor Nutt lays out how illicit drugs are negatively viewed by society and governments and how clinical research is made extremely difficult. There is increasing evidence of the therapeutic and medical benefits of illicit substances for treating depression, PTSD and alcohol dependence (Nutt, 2020). When I met with my supervisors Professor Val Curran and Professor Sunjeev Kamboj I was excited by the prospect of adding to research in an area in which I was politically and academically fascinated. Further, I was thrilled to find out that Professor Curran had conducted a vast amount of research with Professor Nutt and had similar research interests. At the outset of the project, I was fairly unfamiliar with ketamine's medicinal properties, but knew that it was used in accident and emergency settings as an analgesic (Holloway et al., 2000). I was very unfamiliar with research on chronic pain but was curious to find out more about ketamine's utility in this area.

Furthermore, coming from the North of England and training in London I was struck by how health services in the South of England appeared to have more extensive provision than in the North. Professor Curran informed me before we started the project that many patients travelled far to receive ketamine infusions at the PMC as they are not a standard treatment offered by all pain services. I was struck by the inequity of how it appeared to be a postcode lottery for who might receive ketamine infusions; those who lived further away had to travel long distances to get treatment. I felt a political desire to contribute to research that might help to improve the geographical parity of ketamine infusions for chronic pain patients across the UK.

I was also keen to conduct a joint project with another trainee as the prospect of working alone for over 2 years on research felt daunting. Knowing that I would have another trainee alongside me in the process who I could confer with as we progressed through each step of the project was another important factor in my decision to choose this project. I have been hugely grateful to have had Jenny as a project partner during this period, especially during COVID-19 when we had to change our project. The process would have felt so much more challenging without her.

1.2 Impact of COVID-19

COVID-19 restrictions on face-to-face data collection in March 2020 meant that our original research project had to be overhauled in a hurry. Originally the research would have been conducted face-to-face at the pain management centre whilst patients were receiving their ketamine infusions. My aspect of the project was going to focus on quantitative pain and depression outcome measures and Jenny's on cognitive measures. Initially when the restrictions were announced we had no idea how we could make the project work remotely.

My experience before Psychology is firmly rooted in the Humanities. At undergraduate I studied Theology and Religion and undertook semi-structured interviews

with Jehovah's Witnesses. I am more comfortable with the narrative accounts of people's experiences and was glad when Sunjeev suggested that one of us could design a qualitative study of the experience of ketamine patients having their infusions paused during the pandemic. Whilst having to change the project was stressful for a short period of time, I was pleased that I would be able to perform research methods I was more competent in and felt intrigued and galvanised by the prospect of what I would find out.

It was important that the changes to the project were aligned with the stakeholders within the service and reflected an area of research that would be of clinical relevance to the PMC. Our research team consulted with staff at the PMC, including the Consultant Anaesthesiologist Dr Dmitry Kruglov, to ascertain if the proposed direction would be viable and clinically useful. The outcome of our consultation was affirmative which bestowed in me a sense that I was contributing to a valuable and unchartered area of research that would be of relevance to both patients and the service. Val and Sunjeev were extremely helpful in thinking with us about how we could alter the existing ethical approval for the project to enable us to address important questions related to pain management using ketamine in the context of COVID-19.

1.3 Managing researcher bias and assumptions

Once we had ethical approval, we brought in the support of Dr Kathy White to consult with me on setting up the interview schedule and discerning the type of qualitative research method I would employ. Kathy encouraged me to start a reflective research journal to assist me in reflecting on my biases and assumptions about the topic as well as reflecting on my emotional responses to participants at interview. This was immensely helpful as I had not realised until this point that I had a number of *a priori* assumptions about the topic that I had not yet consciously acknowledged. Being unaware of one's assumptions and "pre-understandings" of a particular area or topic is seen as inevitable (Andersen, 1995).

Qualitative researchers are advised to think carefully about implicit assumptions they might bring to the research field and try to make those assumptions more explicit by "bracketing" them off (Hill et al., 2005). I conducted a bracketing interview with Kathy which revealed that I held more assumptions about chronic pain than expected. At the end of my first year of training I developed mild persistent pain in my left shoulder. There was no clear cause to the pain and my GP and physiotherapist proposed that a combination of stress and poor posture sitting at a computer could have been contributing factors. I remember feeling very frustrated by the pain not having a clear origin such as from injury in an accident. I also noticed how others talked to me about my shoulder pain appearing to take it less seriously when I could not provide a clear aetiology. From my experience, I wondered if there was an implicit assumption held by some that chronic pain is less credible than diseases that have a more defined epidemiology and aetiology. Having experienced preclusion from physiotherapy during the pandemic myself, I wondered how others with persistent pain felt about the closure of pain services and whether they might have felt abandoned and forgotten about during the pandemic. I became aware that my lived experience may have mirrored (in a milder form) those of participants and that this could have biased my approach to questioning and analysis. I held a sense that my pain was not as severe and enduring as those that I would be interviewing and did not want to diminish their experience by ascribing the same problem to myself. I was also aware that I could have assumptions and blind spots about how pain could be managed in light of my own pain and wanted to try as best as possible to 'bracket off' my own assumptions.

This led me onto consideration of another assumption I held around agency and responsibility to self-manage chronic pain. Due to my own experiences with persistent pain and my psychological training, I held assumptions about the place of self-management strategies over heavy reliance on pharmacological treatments. Whilst I uphold that ketamine

is vastly important for managing chronic pain, to rely on this alone leaves someone with an incomplete programme of pain management as the effects of medications wear off and there are limits to how much you can take. Self-management strategies encourage a level of acceptance that chronic pain is a disease that may never go away. My training biases me to the benefits of psychological approaches to pain management such as CBT and ACT, which promote a level of psychological flexibility and adjustment to radical acceptance of pain. At the same time, I acknowledge that I do not know what it is like to live with severe chronic pain, and I did not want to make assumptions that my own beliefs and personal values around autonomy and agency could apply to participants in the study. Being able to discuss these tensions with Kathy during the bracketing interview and noting any thoughts or feelings down after interviews helped me to be more aware of my assumptions and enabled me to attempt, within the realms of possibility, to bracket off my assumptions more readily during the analysis phase. Braun and Clarke (2020) note that the pursuit of total avoidance of bias contravenes the tenets of reflexive thematic analysis (TA) and is "ultimately meaningless". Instead, they propose that bias should be acknowledged and reframed as a vital resource to the researcher to guide and cultivate the analysis.

1.4 Conducting interviews

Given the context of COVID-19 and the PMC closing I was uncertain whether we would have difficulties recruiting participants. My initial hunch was that some participants may be angry with the PMC for closing and therefore may not want to take part in the research. Similarly, I wondered whether patients might feel let down by the PMC and not want to give their valuable time to a project associated with a service that was not providing them access to care. Jenny and I were surprised to discover that participants were largely very willing to take part in the project and noted that they are always willing to offer assistance for further research into chronic pain. Many participants told me that they were very pleased I

was doing the research, and some noted that they hoped that their perspectives and accounts would be listened to by the PMC should the UK have to go through another pandemic. I was immensely grateful to all the participants that took part, but it did leave me with a sense of responsibility for honouring their voices and perspectives and wondering how I could best capture their experiences and stay true to what they described.

On reflection I wonder whether the restrictions on face-to-face data collection and conducting interviews remotely might have made it easier for participants to be involved. As participants were at home due to government mandate the context of COVID-19 might have served as a facilitator to recruitment over and above if it required travel for in-person data collection.

Prior to interviews taking place I spent time with Kathy thinking carefully about how I would position myself in relation to the PMC to participants. We determined that an explicit statement at the beginning of the interview noting that I was located outside of the PMC system, working as an independent researcher psychologist for UCL would denote my impartiality and reduce the likelihood of socially desirable responses. At the same time, I held a level of professional loyalty to the PMC and their staff for facilitating the research and allowing us access to their patients. Whilst this tension existed internally, I wanted to externally portray a degree of separateness from the system to participants in order to foster a more honest discussion about their experiences. As far as I am able to deduce this appeared to enhance rapport in the interviews and seemingly enabled participants to be candid about the more negative aspects and emotions of being without ketamine. Of course, I cannot fully know if participants moderated or censored their responses but, on the whole, it felt as though participants were able to be open and transparent.

After Kathy had read a transcript of my pilot interview, we discussed methods and techniques to enhance the richness of the description offered by participants and ways to

bolster the emotional content and quality of the interviews. Whilst the interview asked explicitly about the emotional impact of going without ketamine infusions, Kathy encouraged me to ask participants to expand upon their remarks about the emotional aspects of the experience. She reminded me of my clinical interviewing skills developed during training and encouraged me to tap into the skills that I used in therapeutic sessions to open up the emotional experiences of participants. As one might expect, this was easier with some participants than others. Some participants were able to access the emotional quality of their experiences with ease, whereas others needed significant probing or rephrasing of questions to access emotional dimensions. I wondered whether talking about their feelings in a chronic pain setting might feel unfamiliar to some, and whether they were more used to talking about the more tangible physical aspects of chronic pain. I also wondered whether the system of the PMC and medical consultations might have set a precedent for talking more about the physical and medical components. It has been found that when chronic pain patients present to GPs psychosocial cues can be missed by practitioners and interpreted as a desire for greater understanding of physical symptoms (Salmon et al., 2004). I wondered whether participants had preordained scripts about their pain orientated around physical symptoms that I was asking them to deconstruct and talk about in different ways.

I discussed with Kathy the broadly systemic tenets of sticking close to participant's words and language and adopting a position of un-knowing (Burnham, 1999), which also aligned with the approach of inductive and semantic TA that I intended to adopt. I was conscious of not wanting to bias the interviews by leading participants in my questioning or taking things in a direction that I thought we should go. During interviews I was mindful when I asked follow-up questions to use their language and not make assumptions about what they meant. If I was uncertain what they meant I asked tentative clarification questions as opposed to making interpretations of their descriptions.

1.5 Analysing the data

Before and during interviews I talked with Kathy about my epistemological position of opting for an inductive and semantic approach to analysis of the data. This decision was made in order to honour the voices of the participants in an attempt for the analysis to be data-driven and not determined from researcher or theoretical assumptions. Whilst in theory this was my approach, I was aware that as codes moved to preliminary themes, I was starting to cluster together units of codes which were informed somewhat by my knowledge of the literature and understanding of psychological approaches. I felt a tension between remaining wholly data-driven whilst needing to make decisions about how codes could become themes and seeing clear domains that could cluster together to make themes. Uncertain if I was deviating from TA, I looked to the literature on TA for answers. I was relieved to find that Braun and Clarke stress that it is impossible to operate in a "theoretical vacuum" (Braun & Clarke, 2020) and that whilst one can make efforts to reduce researcher bias the philosophy of qualitative methods is such that researcher interpretation is unavoidable and indeed necessary.

Another area of debate in the analysis was the distinction between a theme and a topic. I sought clarification from Braun and Clarke who noted a common pitfall of TA is when researchers mistake topics for themes (Braun & Clarke, 2020). Themes are united patterns of shared meaning whereas topics are summaries of shared domains within the dataset (Braun & Clarke, 2020). I queried whether the themes of "*Depression*" and *"Support from others*" were topics as opposed to themes. I wondered whether "*Depression*" could be a sub-theme of "*Perceiving pain management as externally located*" but felt that it was better positioned as a theme in its own right as there was such a high prevalence of participants who talked about depression, and it also mapped on well to my research questions. In a similar vein "*Support from others*" felt like it could have been a topic, but I was also struck by how it

captured an important aspect of coping without infusions which would have felt like an omission not to include. Ultimately, I feel that I made the right decision as the subjectivity of qualitative methods mean that researchers will vary in how they interpret the data and make decisions in the analysis. I defer to the expertise of Braun and Clarke who emphasise that analysis could go on *ad infinitum* and eventually the researcher has to make an executive decision to stop (Braun & Clarke, 2006). I feel that not including these as higher order themes would have detracted from the descriptions of the participants and also deviated from my epistemological decision to be more data-driven.

1.6 Personal reflections

I was not prepared for how emotionally evocative some of the interviews with participants would turn out to be. Whilst I had hunches participants might experience increased pain and depression, I wasn't prepared for the pervasive impact going without ketamine would have upon their daily lives. I was struck by the feelings of powerlessness and helplessness expressed by many participants and their anger and abandonment at the pain clinic being closed. Prior to interviewing participants, I felt I had some understanding of the life-limiting aspects of chronic pain. However, my eyes were opened to the extent to which pharmacological treatments like ketamine felt like a small glimmer of relief, hope and agency to be able to do basic aspects of daily living. I have concerns about the most recent "anti-medication" NICE guidance as valuable treatments like ketamine which enhance quality of life could be precluded from patients in favour of solely non-pharmacological management (NICE, 2021). I was saddened by the narrowing of one's life and world and how one participant described how living with chronic pain was like "being in my own lockdown" well before COVID-19 emerged.

In tandem I felt deference and admiration towards participants for their strength, resilience and self-efficacy to manage in spite of the absence of ketamine. Whilst the

experience was unequivocally despairing, in their own way all participants demonstrated incredible resourcefulness and determination to try their best to cope without ketamine. The sheer level of use of self-management strategies utilised by participants paid homage to their ability to adopt an internal locus on control and take some ownership of a highly distressing and challenging situation.

Through my bracketing interview and research log I thought about assumptions that participants might make about me. To uphold rigor and consistency in the interviews I did not disclose any personal information about myself to participants, however I wondered what they might surmise about me based on my appearance, voice, and how I conducted myself. They were aware I was a Trainee Clinical Psychologist, and I pondered over what assumptions they may make about me based on this. At the end of some interviews, participants told me that they had found talking to me helpful and made them feel listened to and understood. Whilst the interviews were for research purposes, and I was conscious of not slipping into "therapy mode", it was unavoidable not to think about participants psychologically. I felt an internal tension between maintaining fidelity to the research approach versus noticing an opportunity that offering something more therapeutically aligned might be of help. This tension was particularly pronounced when some participants talked about experiencing suicidal thoughts. I made a decision to continue the interviews and at the end check in with them about their risk. After the interviews I obtained their consent to inform the PMC about the risk concerns so that they could contact them. Whilst we had agreed a risk protocol in advance of the interviews with the PMC staff, I still felt a little guilty that I was not able to do more, despite being very aware that as a researcher I did not hold clinical responsibility for participants. I discussed these feelings with my supervisors, and we talked about how it was challenging to be operating out of two different positions:

that of researcher and that of Trainee Clinical Psychologist. At times these distinct positions coalesced but at others were dichotomous.

I was aware when I was curating the thematic narrative within the results section of the paper that certain participants felt more memorable than others. Whilst I was conscious to not privilege select voices, I was drawn more to certain participants' language than others. In part this may have been that some participants were more expressive and provided a richer account of their experiences than others, but perhaps there was an element of me also feeling greater congruence and empathy towards them. I found looking back at my reflective research log a helpful tool for making sense of this, often finding that I had written more in my post-interview reflections for those which were more memorable to me. Ultimately, I feel that I gave equal parity to the voices of all participants however it was something that I thought important to reflect upon.

1.7 Conclusion

Whilst I came into the project with prior interest in the area of psychopharmacology, I was surprised to find out how fascinated I have become with the field of chronic pain. Changing the project to qualitative research methods due to COVID-19 was a blessing in disguise and I thoroughly enjoyed the experience of researching in this paradigm. It was a privilege to interview participants, and I am grateful to them for being so candid about their experiences. The richness of the data is a testament to their openness and, despite hundreds of hours transcribing and analysing the data, it was a pleasure to undertake. Whilst the project is imperfect and there are things that could have been done differently, I feel far more experienced and competent in qualitative research methods and would revel at the opportunity to do further research in this area after I qualify.

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Appendices

Appendices: Literature review

Appendix 1.A: Risk of bias rating Buhrman et al.

Buhrman et al. (2011) (ITT)

No	Domain	Response option
1.1	Randomisation	Y
1.2		Y
1.3		N
1.4		**Low**
2.1	Assignment	Y
2.2		Y
2.3		N
2.4		
2.5		
2.6		
2.7		
2.8		**Low**
3.1	Missing outcomes	N
3.2		PY
3.3		
3.4		
3.5		**Low**
4.1	Measurement of outcome	N
4.2		**N**
4.3		Y
4.4		PN
4.5		PN
4.6		**Low**
5.1	Reported result	Y
5.2		N
5.3		N
5.4		**Low**
6	**Overall risk of bias**	**Low**

Appendix 1.B: Risk of bias Chiauzzi et al.

Chiauzzi et al. (2010) (ITT)

No	Domain	Response option
1.1	Randomisation	Y
1.2		Y
1.3		N
1.4		**Low**
2.1	Assignment	Y
2.2		Y
2.3		N
2.4		
2.5		
2.6		
2.7		
2.8		**Low**
3.1	Missing outcomes	N
3.2		PN
3.3		NI
3.4		NI
3.5		**Some concerns**
4.1	Measurement of outcome	N
4.2		**N**
4.3		Y
4.4		PN
4.5		PN
4.6		**Low**
5.1	Reported result	Y
5.2		N
5.3		N
5.4		**Low**
6	**Overall risk of bias**	**Some concerns**

Appendix 1.C: Risk of bias Irvine et al.

Irvine et al. (2015) (ITT)

No	Domain	Response option
1.1	Randomisation	Y
1.2		Y
1.3		N
1.4		**Low**
2.1	Assignment	PN
2.2		Y
2.3		N
2.4		
2.5		
2.6		
2.7		
2.8		**Low**
3.1	Missing outcomes	N
3.2		Y
3.3		
3.4		
3.5		**Low**
4.1	Measurement of outcome	N
4.2		**N**
4.3		PN
4.4		
4.5		
4.6		**Low**
5.1	Reported result	Y
5.2		N
5.3		N
5.4		**Low**
6	**Overall risk of bias**	**Low**

Appendix 1.D: Risk of bias Petrozzi et al.

Petrozzi et al. (2019) (ITT)

No	Domain	Response option
1.1	Randomisation	Y
1.2		Y
1.3		N
1.4		**Low**
2.1	Assignment	PN
2.2		N
2.3		
2.4		
2.5		
2.6		
2.7		
2.8		**Low**
3.1	Missing outcomes	N
3.2		Y
3.3		
3.4		
3.5		**Low**
4.1	Measurement of outcome	N
4.2		N
4.3		N
4.4		
4.5		
4.6		**Low**
5.1	Reported result	Y
5.2		N
5.3		N
5.4		**Low**
6	**Overall risk of bias**	**Low**

Appendix 1.E: Risk of bias Sander et al.
Sander et al. (2020) (ITT)

No	Domain	Response option
1.1	Randomisation	Y
1.2		Y
1.3		N
1.4		**Low**
2.1	Assignment	Y
2.2		Y
2.3		N
2.4		
2.5		
2.6		
2.7		
2.8		**Low**
3.1	Missing outcomes	N
3.2		N
3.3		PY
3.4		PN
3.5		**Some concerns**
4.1	Measurement of outcome	N
4.2		**N**
4.3		Y
4.4		PN
4.5		PN
4.6		**Low**
5.1	Reported result	Y
5.2		N
5.3		N
5.4		**Low**
6	**Overall risk of bias**	**Some concerns**

Appendix 1.F: Risk of bias Schlicker et al.

Schlicker et al. (2020) (ITT)

No	Domain	Response option
1.1	Randomisation	Y
1.2		Y
1.3		N
1.4		**Low**
2.1	Assignment	Y
2.2		Y
2.3		N
2.4		
2.5		
2.6		
2.7		
2.8		**Low**
3.1	Missing outcomes	N
3.2		N
3.3		PY
3.4		PN
3.5		**Some concerns**
4.1	Measurement of outcome	N
4.2		**N**
4.3		Y
4.4		PN
4.5		PN
4.6		**Low**
5.1	Reported result	Y
5.2		N
5.3		N
5.4		**Low**
6	**Overall risk of bias**	**Some concerns**

Appendix 1.G: Risk of bias Strom et al.

Strom et al. (2019) (ITT)

No	Domain	Response option
1.1	Randomisation	Y
1.2		Y
1.3		Y
1.4		**Some concerns**
2.1	Assignment	Y
2.2		Y
2.3		N
2.4		
2.5		
2.6		
2.7		
2.8		**Low**
3.1	Missing outcomes	N
3.2		N
3.3		PY
3.4		PN
3.5		**Some concerns**
4.1	Measurement of outcome	N
4.2		**N**
4.3		Y
4.4		PN
4.5		PN
4.6		**Low**
5.1	Reported result	Y
5.2		N
5.3		N
5.4		**Low**
6	**Overall risk of bias**	**Some concerns**

Appendix 1.H: Risk of bias Buhrman et al.
Buhrman et al. (2004) (PP)

No	Domain	Response option
1.1	Randomisation	Y
1.2		PY
1.3		N
1.4		**Low**
2.1	Assignment	Y
2.2		Y
2.3		Y
2.4		**N**
2.5		**N**
2.6		
2.7		
2.8		**Low**
3.1	Missing outcomes	N
3.2		Y
3.3		
3.4		
3.5		**Low**
4.1	Measurement of outcome	N
4.2		**N**
4.3		Y
4.4		PN
4.5		PN
4.6		**Low**
5.1	Reported result	Y
5.2		N
5.3		N
5.4		**Low**
6	**Overall risk of bias**	**Low**

Appendix 1.I: Risk of bias Carpenter et al.

Carpenter et al. (2012) (PP)

No	Domain	Response option
1.1	Randomisation	Y
1.2		Y
1.3		N
1.4		**Low**
2.1	Assignment	Y
2.2		Y
2.3		Y
2.4		**N**
2.5		**N**
2.6		
2.7		
2.8		**Low**
3.1	Missing outcomes	N
3.2		N
3.3		PY
3.4		PN
3.5		**Some concerns**
4.1	Measurement of outcome	N
4.2		**N**
4.3		Y
4.4		PN
4.5		PN
4.6		**Low**
5.1	Reported result	Y
5.2		N
5.3		N
5.4		**Low**
6	**Overall risk of bias**	**Some concerns**

Appendices: Empirical paper

Appendix 2.A: Joint project statement

This thesis is a joint project with Jenny Scott, who investigated long-term follow-up comparing the long-term effects of ketamine and lidocaine on pain, mood, and cognitive functioning. Research proposals were submitted independently. Jenny recruited from the same ketamine sample but used an independent sample of lidocaine patients which were not included in this thesis.

Recruitment of the ketamine sample was split equally between both researchers. Data collection was conducted independently as Jenny's aspect focused on quantitative data collection and mine comprised qualitative interviews. Analysis and writing of the systematic review, empirical paper and critical appraisal were undertaken independently by each researcher.

Appendix 2.B: Original NHS Ethics Approval

NHS
Health Research Authority
South Central - Berkshire Research Ethics Committee
Bristol REC Centre
Whitefriars
Level 3, Block B
Lewins Mead
Bristol
BS1 2NT

Telephone: 020 7104 8057

Please note: This is the favourable opinion of the REC only and does not allow you to start your study at NHS sites in England until you receive HRA Approval

06 December 2017

Prof Valerie Curran
UCL
Gower Street
London
WC1E 6BT

Dear Prof Curran,

Study title:	**Comparing the Effects of Ketamine and Lidocaine on Cognition, Pain and Mood**
REC reference:	**17/SC/0567**
Protocol number:	**N/A**
IRAS project ID:	**214864**

Thank you for your letter of 1st December 2017 responding to the Proportionate Review Sub-Committee's request for changes to the documentation for the above study.

The revised documentation has been reviewed and approved by the sub-committee.

We plan to publish your research summary wording for the above study on the HRA website, together with your contact details. Publication will be no earlier than three months from the date of this favourable opinion letter. The expectation is that this information will be published for all studies that receive an ethical opinion but should you wish to provide a substitute contact point, wish to make a request to defer, or require further information, please contact please contact hra.studyregistration@nhs.net outlining the reasons for your request.

Under very limited circumstances (e.g. for student research which has received an unfavourable opinion), it may be possible to grant an exemption to the publication of the study.

Confirmation of ethical opinion

On behalf of the Committee, I am pleased to confirm a favourable ethical opinion for the above research on the basis described in the application form, protocol and supporting documentation as revised.

Conditions of the favourable opinion

The REC favourable opinion is subject to the following conditions being met prior to the start of the study.

Management permission must be obtained from each host organisation prior to the start of the study at the site concerned.

Management permission should be sought from all NHS organisations involved in the study in accordance with NHS research governance arrangements. Each NHS organisation must confirm through the signing of agreements and/or other documents that it has given permission for the research to proceed (except where explicitly specified otherwise).

Guidance on applying for HRA Approval (England)/ NHS permission for research is available in the Integrated Research Application System, www.hra.nhs.uk or at http://www.rdforum.nhs.uk.

Where a NHS organisation's role in the study is limited to identifying and referring potential participants to research sites ("participant identification centre"), guidance should be sought from the R&D office on the information it requires to give permission for this activity.

For non-NHS sites, site management permission should be obtained in accordance with the procedures of the relevant host organisation.

Sponsors are not required to notify the Committee of management permissions from host organisations.

Registration of Clinical Trials

All clinical trials (defined as the first four categories on the IRAS filter page) must be registered on a publically accessible database. This should be before the first participant is recruited but no later than 6 weeks after recruitment of the first participant.

There is no requirement to separately notify the REC but you should do so at the earliest opportunity e.g. when submitting an amendment. We will audit the registration details as part of the annual progress reporting process.

To ensure transparency in research, we strongly recommend that all research is registered but for non-clinical trials this is not currently mandatory.

If a sponsor wishes to request a deferral for study registration within the required timeframe, they should contact hra.studyregistration@nhs.net. The expectation is that all clinical trials will be registered, however, in exceptional circumstances non registration may be permissible with prior agreement from the HRA. Guidance on where to register is provided on the HRA website.

It is the responsibility of the sponsor to ensure that all the conditions are complied with

before the start of the study or its initiation at a particular site (as applicable).

Ethical review of research sites

The favourable opinion applies to all NHS sites taking part in the study, subject to management permission being obtained from the NHS/HSC R&D office prior to the start of the study (see "Conditions of the favourable opinion" above).

Approved documents

The documents reviewed and approved by the Committee are:

Document	*Version*	*Date*
Evidence of Sponsor insurance or indemnity (non NHS Sponsors only) [Insurance Proof]	1	04 October 2017
IRAS Application Form [IRAS_Form_25102017]		25 October 2017
IRAS Application Form XML file [IRAS_Form_25102017]		25 October 2017
IRAS Checklist XML [Checklist_01122017]		01 December 2017
Letter from sponsor [HRA cover letter]	1	04 October 2017
Non-validated questionnaire [Depression VAI]	1	22 April 2017
Other [Hayling Sentence Completion Task]	1	13 October 2017
Other [Spot the Word Test]	1	13 October 2017
Other [Trail Making Task]	1	13 October 2017
Other [Prose Recall Task]	1	13 October 2017
Other [Cognitive Measure N-Back]	1	13 October 2017
Other [Study Insurance Certificate]	2	14 November 2017
Other [REC Response Email]	1	20 November 2017
Participant consent form [Consent Form]	3	12 November 2017
Participant information sheet (PIS) [Participant Info]	4	12 November 2017
Research protocol or project proposal [Protocol]	1	21 June 2017
Summary CV for Chief Investigator (CI) [CI CV]	1	05 October 2017
Summary CV for student [CT CV]		04 October 2017
Summary CV for student [MK CV]		04 October 2017
Summary CV for supervisor (student research) [CV]	1	05 October 2017
Validated questionnaire [BDI]		
Validated questionnaire [PHQ-9]		
Validated questionnaire [Pain]		
Validated questionnaire [Drug Effects Questionnaire]		

Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

After ethical review

Reporting requirements

The attached document "After ethical review – guidance for researchers" gives detailed guidance on reporting requirements for studies with a favourable opinion, including:

- Notifying substantial amendments
- Adding new sites and investigators
- Notification of serious breaches of the protocol
- Progress and safety reports
- Notifying the end of the study

The HRA website also provides guidance on these topics, which is updated in the light of changes in reporting requirements or procedures.

Feedback

You are invited to give your view of the service that you have received from the Research Ethics Service and the application procedure. If you wish to make your views known please use the feedback form available on the HRA website:
http://www.hra.nhs.uk/about-the-hra/governance/quality-assurance

We are pleased to welcome researchers and R & D staff at our RES Committee members' training days – see details at http://www.hra.nhs.uk/hra-training/

17/SC/0567	**Please quote this number on all correspondence**

With the Committee's best wishes for the success of this project.

Yours sincerely

[redacted]

Mr David Carpenter
Chair

Email: nrescommittee.southcentral-berkshire@nhs.net

Enclosures: *"After ethical review – guidance for researchers" [SL-AR2]*

Copy to: *Ms Nikkayla Dixon*

Mr Joe Mirza, UCLH NHS Foundation Trust

Appendix 2.C: NHS Ethics non-substantial amendment approval

Dear Dr Dmitry,

Project ID: 17/0139 (Please quote in all correspondence)
IRAS ID: 214864
REC Ref: 17/SC/0567
Title: Comparing the Effects of Ketamine and Lidocaine
Amendment: NSA1

Confirmation of Amendment Capacity & Capability

The [REDACTED]/UCL Joint Research Office (JRO) acknowledges receipt of the above non-substantial amendment.

We have reviewed the amendment and the HRA Approval email dated 03/08/2020.

The JRO has no objections to this amendment and the study may continue at [REDACTED]

If applicable, you must ensure that you localise all patient facing documentation prior to consenting participants; this will be subject to random audit checks.

Please forward this email on to all relevant parties involved with this study at [REDACTED].

Please insert a copy of this email in your site file.

Best wishes with your research.

Kind regards,

Eyoanwan Simon-Modebe (EYO)
JRO Amendments Officer
Joint Research Office
Suite B, First Floor, Maple House, 149 Tottenham Court Road, London W1T 7DN
We are committed to delivering
top-quality patient care, excellent
education and world class research
safety kindness teamwork improving

****Please note we will NOT be issuing a separate hard copy/electronic R&D Acknowledgment letter; please accept this email as confirmation of amendment implementation at [REDACTED]**

Appendix 2.D: Recruitment email

Dear patient of the pain management Centre,

The Pain Management Centre (PMC) at [REDACTED] is working alongside University College London (UCL) to carry out research into the effects of pain medication on mood, thinking and pain. We are the two researchers: Jenny Scott and Laura Marks.

We are contacting you as you previously participated in a study comparing the effects of ketamine and lidocaine infusions on mood, thinking and pain. We would love for you to continue your involvement in this research and let us hear your story.

Would you be willing to take part in a follow-up study exploring the impact of the Covid-19 pandemic on patients who were treated at the PMC? We hope that this study will help the PMC provide patients like yourself with the safest and most effective treatments.

This study consists of three parts. You may choose to take part in as many (or as few) parts as you want. If you choose to complete more than one part, these can either be done at the same time or spread out across different days – whatever you prefer.

Part 1 – A telephone call where you will be asked the same questions that you were asked on the day of your infusion. These questions ask you about how you are feeling and there are also some brief tests of memory and language that you did before at the PMC (20 minutes).
Part 2 – A telephone call to answer a brief questionnaire about the impact the Covid-19 pandemic has had on you (5 minutes).
Part 3 – An interview with a researcher (over telephone or Microsoft Teams) to hear the story of your experiences of managing chronic pain during the Covid-19 pandemic in more depth (up to 60 minutes).

We have included an information sheet which provides more details about the study and what will happen if you take part. **Please note that your decision whether or not to take part in this research will not affect your treatment at the PMC in any way**. Information about your decision to participate will be completely confidential and not shared with your medical team. All data collected will be anonymised (not have you name or date of birth) and stored securely.

If you are interested in any part of this research, please select "reply all" to email Laura [REDACTED] and **Jenny** [REDACTED] We will then be in contact to arrange a convenient time when we could speak with you.

If we don’t hear from you in the next week, we hope you don’t mind if we give you a call to see if you are interested in participating. If you would prefer us not to call you, please let us know.

If you have any questions in the meantime, please do not hesitate to contact us by email [REDACTED].

Appendix 2.E: Participant information sheet

Comparing the Effects of Ketamine and Lidocaine on Cognition, Pain and Mood

Participant Information Sheet

(Version 7: 09/04/2020) IRAS ID: 214864

We would like to invite you to take part in our research study which is a student research project that will contribute to a clinical psychology doctorate. Before you decide, we would like you to understand why the research is taking place and what it would involve for you. Please take the time to read the following information carefully, and discuss it with family, friends and your GP if you wish.

Part 1 tells you about the purpose of this study and what will happen if you take part.

Part 2 gives you more detailed information about the conduct of the study, please keep the information in case you wish to refer to it later.

This study has been reviewed by Dr Amanda C de C Williams and Dr Miriam Fornells-Ambrojo and is sponsored by UCL as part of the Doctorate in Clinical Psychology. The ethics application has been reviewed by the South Central Berkshire Research Committee.

Part 1

What is the purpose of the study?

The purpose of this study, which has been running since 2018, is to investigate the psychological effects of ketamine in people with chronic pain. In particular, we are interested in how ketamine affects thinking, pain and mood. We will compare the effects of ketamine with the effects of the control condition lidocaine. Previous studies have shown both medications to be effective treatments for the management of chronic pain and we hope to add to this body of evidence by investigating their broader psychological effects.

In light of the COVID-19 outbreak, our usual methods of data collection have been paused. However, we are still very keen to hear about your experience of chronic pain and how this may have been impacted by COVID-19.

Why have I been invited?

You are being invited because you have been treated for chronic pain with an infusion of either ketamine or lidocaine.

Do I have to take part?
No. It is entirely up to you to decide whether or not to take part in the study. If you do agree to take part, we will then ask you to sign a consent form. However, you are free to withdraw at any time, without giving a reason.

What are the possible benefits of taking part?
Taking part in the study will not benefit you directly, but everyone who decides to participate will contribute to scientific knowledge about chronic pain. Your participation will also contribute to the continual development of best clinical practice for the treatment of chronic pain.

Expenses and payments
No expenses or payments can be issued to participants of the study who will be receiving their normal clinical care.

What will happen if I take part and what will I have to do?
A researcher will call you to go through what is involved, answer questions, and make sure you are able to take part in the study.

The study involves completing some questionnaires either online or over the phone These will ask you to rate your pain, your mood, and other experiences linked to chronic pain and your medication. If you have participated in the study before, these will be the same questionnaires that you completed on the day of your infusion.

In addition, some participants will be invited to participate in a brief telephone interview about the impact of COVID-19 on your chronic pain. For example, whether it has affected your ability to access your usual NHS treatment and altered your strategies for managing pain. We anticipate that it will take no longer than 1 hour to complete the questionnaires and interview.

What are the possible disadvantages or risks of taking part?
The study includes a questionnaire about your mental health. You might like to talk to someone about any issues it raises. Researchers would be able to discuss this with you and make appropriate recommendations. You may also find some of the questionnaires tedious. However, we endeavour to make participation in the research as engaging as possible.

What if there is a problem?
Any complaint about the way you have been dealt with during the study or any possible harm you might suffer will be addressed. Detailed information about these processes is given in Part 2.

Will my taking part in the study be kept confidential?
Yes. We will follow ethical and legal practice and all information about you will be handled in confidence.
The details are included in Part 2.

Part 2 – Further Details

What will happen if I don’t want to carry on with the study?

You are free to withdraw from the study at any time on the day that you participate simply by telling the researcher that you wish to do so. Your further treatment would not be affected in any way by withdrawing from the study. Once your data has been entered into the study database, it will be anonymised and thus it would not be possible to identify your specific data.

What if there is a problem?
If you have a concern about any aspect of this study, you should ask to speak to the researchers who will do their best to answer your questions. You can contact them by ringing on the numbers given below. If you remain unhappy and wish to complain formally you can do this by contacting the Patient Advice and Liaison service at [REDACTED].

Will my taking part in the study be kept confidential?
All information which is collected about you during the course of the research will be kept confidential. If you take part in the study you will be assigned a code number that will be used to identify you on all computerised and written data. Your name, and any other identifying information, will not be attached to the information obtained from the study. All personal data will be kept securely in locked filing cabinet with access available only to members of the research team. Electronic anonymised data will be kept in password protected files and will be stored securely. Data will be kept for no more than 20 years and will then be destroyed.

What will happen to the results of the research study?
The results of this study will be reported in scientific journals and are likely to be published after the whole study finishes in 2021. You can obtain a copy of the published results by contacting us at address on the bottom of this sheet after the study has finished. You will not be identified in any report or publication resulting from this study.

Further Information
If during the course of the trial you have questions about the nature of the research, your rights as a patient, or you believe you have sustained a research related injury, or you are concerned about any aspects of the study, please contact:

Thank you for taking the time to read this information sheet

Contacts

Primary Researchers: Professor Valerie Curran [REDACTED], Professor Sunjeev Kamboj [REDACTED] Laura Marks [REDACTED], [REDEACTED] Address: UCL, Gower Street, London, WC1E 6BT

Consultant Anaesthesiologists: Dr Dmitry Kruglov, Dr Roman Cregg: Address [REDEACTED].

Appendix 2.F: Consent form

IRAS ID: 214864
Version 6 (09/04/2020)

Participant Identification Number for this trial:

CONSENT FORM

Title of Project: Comparing the Effects of Ketamine and Lidocaine on Cognition, Pain and Mood

Name of Researchers: Laura Marks and Jenny Scott

	Please initial box
1. I confirm that I have read the information sheet for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily.	☐
2. I understand that my participation is voluntary and that I am free to withdraw at any time without giving any reason, without my medical care or legal rights being affected.	☐
3. I understand that the information collected about me will be used to support other research in the future which I may be contacted about, and may be shared anonymously with other researchers.	☐
4. If during the course of the research, suicidal thoughts or depression are discussed this information will be passed on to your consultant to inform your care.	☐
5. I agree to take part in the above study.	☐

_____	_____	_____
Name of Participant	Date	Signature
_____	_____	_____
Name of Researcher	Date	Signature

Appendix 2.G: Interview schedule

1. How did not receiving your ketamine treatment during the pandemic impact your pain?
2. How has not receiving your ketamine treatment impacted you emotionally during the pandemic?
3. How have you been coping with your pain during this time? (*prompt practical strategies, use of other medications, impact on wider system- family, friends, other health care professionals)*
4. What have you missed and not missed about having ketamine? (*prompt have there been any positive aspects of not going for appointments? Acquired new coping skills?)*

Appendix 2.H: Transcript Excerpt with initial codes

R = Researcher
P = Participant

Transcript	Initial codes
R: how did not receiving your ketamine treatment during the pandemic impact your pain?	
P: I was in really really severe pain because I didn't have it for a very long time and I was so much in pain, it was unbearable.	Pain increased. Unbearable pain.
And all medication and strong painkillers were not really working because I didn't have the injection so it is really really taking it out on me because I couldn't go to the hospital, they couldn't give me appointment to come in, so it was really really bad.	Painkillers not working
R: You mentioned that the pain was unbearable?	
P: yeah its unbearable.	Pain increased
R: could you say a bit more about that? Could you say a little bit more about it being unbearable?	
P: it's just I was so much in pain, all my bones too much, I couldn't even stand on my feet properly. I keep falling the legs keep giving way. I keeping falling around the house and the pain was so much it was unbearable. If I had the injection it help reduce pain. If it take the strong painkiller it helps, but without having the injection for quite some time the pain is very very severe.	Pain increased without ketamine. Decreased mobility Ketamine helps to reduce pain. Painkillers not working as well
R: Was it worse than it would be if you were having the infusions regularly?	
P: I'm having the pain again and my medication is not working on the pain. I've not received any letter from them, I tried to call to see when my next visit would be, I left a message nobody get back to me.	Other pain relief not working Not able to get hold of staff at PMC. Abandonment
R: how does that make you feel?	
P: it makes me feel so bad, I just, I don't know when I will go again, I don't know.	Not knowing when next infusion will be
R: what's it like not knowing when you will have your next infusion?	

P: Yeah because normally whenever I go for the appointment they always give the next appointment date but this one they didn't give me anything because, I don't know, when I'm going again. I know people were complaining about it.	Not knowing when next infusion will be. Not hearing from PMC.
R: yeah, so at the moment I guess during the time of the pandemic the not knowing when your next appointment would be, what was that like for you?	
P: err, I do not know, I'm just, I'm just seeing, I don't know what to do. I don't know when my next appointment will be. Not hearing from them, no appointment, not even phone call, not even text message no letter, so I don't know.	Helpless. Poor communication. Not able to speak to anyone. Uncertainty when infusion will happen. Abandonment
R: And the not hearing from them where does that leave you?	
P: it leaves me with nothing. With nothing like I don't know when they will contact me, I'm just worried, you know, just worry about it and because I'm already used to the infusions, so I'm always looking forward for that and this reduce my pain, for me a bit, but for this pandemic time it leave me with nothing. I don't know what to do, I'm just hanging there.	Abandonment. Stuck. Helpless. Worry and anxiety Missing pain relief from ketamine Stuck. Helpless. Abandoned
R: just hanging there?	
P: yes until I hear from them.	Waiting to hear from clinic
R: What does it feel like just hanging there?	
P: it feels, I just feel nothing, I just feel I'm just tired about everything that is going around for now. I don't know, you know. It's so much that is going on with me, you know, I have diabetes, this pain, and everything is just too much for me, for now.	Numb. Exhausted. Harder to cope Other health problems Too much
R: yeah I can really hear in your voice that it feels too much	
P: yes	
R: and I wondered what the emotional impact of not receiving the ketamine has had on you?	
P: errr, I don't know everything is just too emotional, everything is just, because 3 days ago I was with my sister in the shopping mall and I use a walking stick and all of a sudden my leg just give way, I couldn't, when it give way like that, I cannot hold myself, I just fell l completely all over the floor. And my sister came over to me, so people had to come in and help. I couldn't even and move my leg, I was so much in pain, so they have to	Emotional distress Mobility reduced Falling Increased pain

get the chair and let me sit down on the chair for a while until I can be able to stand up again. I was so much in pain, my legs keep on giving way like that, the bone is getting weaker and weaker and the pain getting too much for me. So that is what I'm feeling about not having this infusion on time.

Weaker. Pain increased without ketamine.

R: that sounds really difficult. In terms of the emotional impact what have you noticed? The impact that not having the ketamine has made on you emotionally, if at all.

P: mmm, I don't know, it's just, I feel, I'm so weak, you know. Very weak. I just want to hear from them give me an injection. I tried to call them like, I think called yesterday but nobody was there to answer the call so I left a message but not hear back from them again. Because I am just anxious I just want to know my next appointment will be.

Weak.

Wanting to hear from PMC

Abandonment
Anxiety and uncertainty about when next infusion will be

Appendix 2.I: Preliminary thematic table

Theme/ Sub-Theme
1.0 Abandonment
1.1 Anger towards clinic and healthcare system
1.2 No one cares
1.3 Poor communication
2.0 Depression
2.1 Suicidal
3.0 Increasing opiates
3.1 Above prescribed dose
3.2 Difficulty increasing
4.0 Internal locus of control
4.1 Pushing myself
4.2 Try harder
4.3 Positive outlook
4.4 Positive affirmations
4.5 Resilience
4.6 Self-compassion
4.7 Acceptance of pain
5.0 Self-management strategies
5.1 Distraction
5.2 Heat
5.3 Meditation and relaxation
5.4 Movement and keeping active
5.5 Rest and sleep
5.6 Pacing
5.7 Resisting opiates
6.0 Gratitude for clinic
6.1 Clinical staff appreciation
7.0 Missing the pain relief from ketamine
7.1 Relief from pain
7.2 Nothing else works
7.3 Better quality of life
7.4 Not realising the effects of ketamine
7.5 Benefits of ketamine
7.6 Taking fewer medications
8.0 Pain increased
8.1 Deterioration in quality of life
8.3 Going back to pain levels before infusion
9.0 Harder to cope
9.1 Decreased mobility
9.2 Sleep disturbance
9.3 Other health problems
10.0 Support from others
10.1 Befriending

10.2 Care agency
10.3 Charities
10.4 Support from friends and family
10.5 Therapy
10.6 Shared experience
11.0 Uncertainty
11.1 Anxiety and worry
11.2 Desperation
11.3 Not knowing when next infusion will be
11.4 When will covid end?
11.5 Disruption to other services
12.0 Travel to clinic
12.1 Long day
12.2 Early starts

Appendix 2.J: Member checks email sent to participants

Dear XXXX,

I would like to thank you for taking part in the research interview (part 3) of the ketamine study regarding your experiences of not receiving ketamine during the pandemic. Your participation was invaluable, and I believe will be of much interest to the PMC and also increasing the body of literature on chronic pain research.

I have analysed the interviews (15) and I have generated 6 provisional themes and sub-themes from the data. I would like to share these themes with you and invite you to comment on them, if you wish, however this is of course voluntary.

1) **External locus of control**
i) Abandonment
ii) Increasing opiates

2) **Depression**
i) Suicidal

3) **Internal locus of control**
i) Pushing myself
ii) Resilience and self-compassion
iii) Self-management strategies

4) **Pain increased without ketamine**
i) Deterioration in quality of life
ii) Missing the pain relief from ketamine
iii) Gratitude for the clinic offering ketamine
iv) Not missing the travel and long journey to the clinic

5) **Uncertainty brought about by covid**
i) Anxiety and worry
ii) Not knowing when next infusion will be
iii) Disruption to other services

6) **Support from others**
i) Support from friends and family
ii) Support from other agencies

In your experience, do these six themes make sense?
Please specify which themes make the most sense to you.
Please note any that do not make sense to you.

Many thanks for giving your views on the results. Your views are very important to the research and to future pain clinic patients

Warm wishes,

Laura Marks - **Researcher**