

## **1.0 Introduction**

Management of chronic pain is a complex process, affected by the subjective nature of pain, physical and psychosocial comorbidities, the potential of medication abuse, as well as bias from those involved in the patient's care.

Women suffering chronic pain during pregnancy face many difficulties; one of the biggest questions pregnant women must answer is whether to continue their chronic pain medication during pregnancy. With limited research in this field, it is important to consider potential difficulties women may suffer to help guide future research as well as improve experiences for pregnant women with chronic pain.

## **2.0 Pain**

Pain is described as an “unpleasant sensory and emotional experience associated with actual or potential tissue damage”.(1) Pain is broadly classified as either acute or chronic, and can be neuropathic or nociceptive in nature. Nociceptive pain usually responds well to treatment with analgesics whereas neuropathic pain can be difficult to manage due to its poor response to conventional analgesics.(1)

## **2.1 Chronic pain**

Chronic pain is broadly defined as “pain that persists past the healing phase following an injury”.(1,2) The end of the healing phase can be difficult to ascertain,(2) so chronic pain is often defined as pain that persists past a fixed period following its initial onset. The National Institute for Health and Care Excellence (NICE) define chronic pain as pain persisting or recurring for more than three months.(1)

Pain affects many people; in the United Kingdom (UK), between one-third and one-half of the population is affected by chronic pain.(3) Pain, and chronic pain in particular, can have an impact on physical, psychological and societal aspects of peoples' lives. Pain contributes the most to disability measures, and two-thirds of those affected by chronic pain are unable to work outside their home.(3) Almost half of the people with chronic pain also have a diagnosis of depression.(3)

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Of those affected by chronic pain, it is not known how many need or wish to have treatment,(3) but different treatment options exist for those who request it.

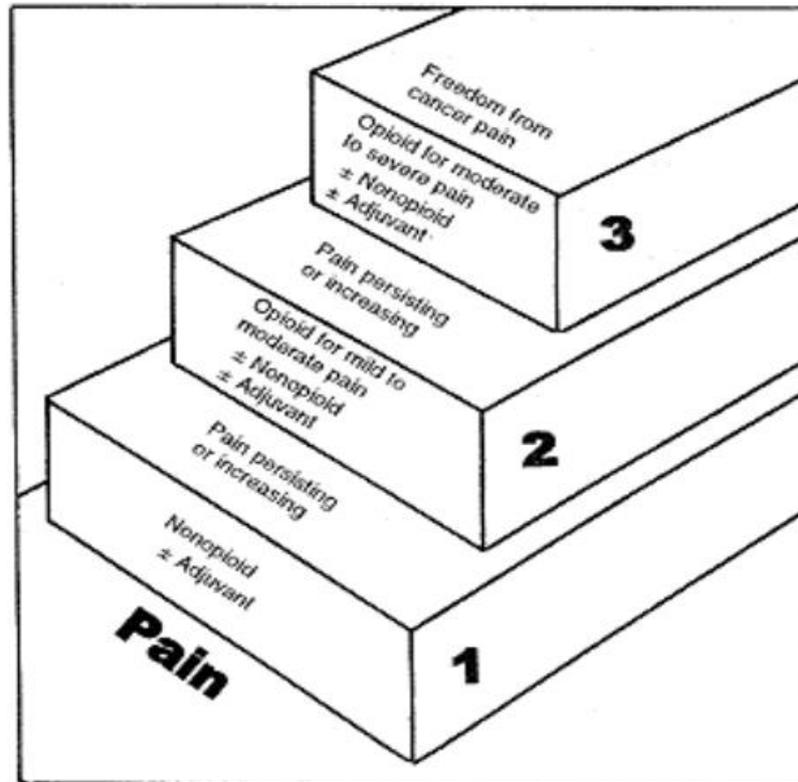
### **2.2. Management of chronic pain**

The aims of treating chronic pain is to “reduce the impact of chronic pain on quality of life, mood and function”(1). Both pharmacological and non-pharmacological treatment options exist for chronic pain, and NICE provide specific guidance on the management of chronic pain in osteoarthritis and soft tissue disorders, musculoskeletal conditions, and neuropathic pain.(1)

Non-pharmacological treatments may include exercise, transcutaneous electrical nerve stimulation, cognitive behavioural therapy, biofeedback, progressive relaxation as well as others.

Analgesia for chronic pain consists of both non-opioids (e.g. paracetamol, NSAIDs) and opioids (e.g. codeine, oxycodone, tramadol, morphine). Although developed and validated for cancer pain,(1) the World Health Organisation (WHO) analgesic ladder offers a stepwise approach for the treatment of both acute and chronic pain, see figure one below.

There is little evidence supporting the use of the analgesic ladder in chronic pain, but it may provide a starting point for clinicians, especially non-specialists.



**Figure 1 – World Health Organisation (WHO) Analgesic ladder**

*(From The National Institute for Health and Care Excellence (NICE). Pain, Chronic).(3)*

It is recommended that patients are started on the lowest “step” of the analgesic ladder and increasing doses and stronger analgesics are offered if pain is not adequately managed.

Chronic pain can have many different causes and therefore pain management will vary for individuals. Even individual’s responses to analgesia vary considerably, both in terms of its efficacy and side effects. Chronic pain often manifests clinically with many tissue types involved, for example chronic back pain can consist of joint, muscle and nerve involvement, with varying involvements of tissue types in each individual patient,(2) complicating assessment and management in clinical practice. The subjective nature of pain, physical and psychosocial comorbidities, and the potential of abusing medications make managing chronic pain challenging.

### **3.0 Pain in pregnancy**

Pain is common during pregnancy(4,5); pregnancy causes many changes physiologically and can exacerbate prior non-obstetrical chronic pain conditions and/or cause both acute and chronic pain. The gravid uterus and relaxation of ligaments as well as weight gain, postural changes and pelvic floor dysfunction can cause back pain, an ailment affecting around two-thirds of pregnant women,(6) along with pelvic pain, ankle and leg pain, and migraines.

### **3.1 Chronic pain in pregnancy**

The overall prevalence of pregnant women with pre-existing chronic pain conditions is unknown (7) but smaller studies have reported chronic pain conditions prevalent in 28.2% of pregnant women.(8) The three most common conditions are chronic neck and back pain, and chronic headaches/migraines.(8–10) One study found that 95.5% of pregnant women with chronic pain were taking at least one analgesic, with nearly half taking paracetamol and/or opioids,(8) and only 20.5% were utilising non-pharmacological treatments.(8) The perinatal period is a particularly vulnerable period for women with chronic pain conditions, and women risk suffering severe pain during pregnancy without adequate support.

Achieving optimal pain management in chronic pain conditions is difficult, and this is further complicated by pregnancy because of the need to consider the risk-benefit ratio for both the mother and foetus, as well as the future neonate. But data supporting the prevalence, course, and management of chronic pain conditions in pregnancy are limited.(7)

Whilst some patients require secondary and tertiary care, most chronic pain patients will be managed in primary care.(11) Across the UK there is evidence of wide variation in the clinical practice and resource provision, with a general lack of knowledge about chronic pain and the management options that are available.(11) It is surprising that robust guidance is published on other aspects of antenatal care and pain management during labour, yet NICE does not provide specific guidelines on the treatment of pain or chronic pain in pregnancy. Evidence-based guidelines to assist both clinicians as well as mothers are lacking.(7)

Information provided to mothers about medication use in pregnancy on the National Health Service (NHS) website states “you should avoid taking medicines when you’re pregnant”; “get more advice from your midwife or GP”.(12)

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A study found that while 70.5% of pregnant women wanting information on medication during pregnancy approached a midwife or nurse and 49.4% a doctor, 44.4% approached pharmacy personnel for advice as well.(13) Pregnant women use a variety of sources and 49.6% would also first search the internet for advice.(13)

Doctors are already receiving inadequate pain management training, (7) and this highlights the need to not only provide better guidelines and training for doctors but to also include midwives, nurses and pharmacists. With increasing maternal age, treating chronic pain in pregnancy is going to become more common; it is vital that healthcare professionals have the best possible resources and support to manage their patients properly and know when to access appropriate specialist services when required.

Inconsistent and dangerous guidance for patients from web-based resources on which medications are safe during pregnancy (14) further highlights the inadequate evidence base and inconsistent guidance, and the need for a more comprehensive resource for both the layman and professional to access reliable information. Lack of clear recommendations makes decisions concerning medication use during pregnancy difficult.

### **3.2 Effects of pharmacological management of chronic pain on the foetus**

Treatment for chronic pain during the perinatal period include both pharmacological and non-pharmacological options, however, uncertainties around treatment impact both the patient's and the healthcare professional's decision-making regarding treatment.

The Royal College of Obstetricians recommends that non-pharmacological interventions should be considered first line,(5) such as acupuncture, aromatherapy, exercise, physiotherapy, rest, hot/cold compresses or massage. But as the use of analgesics for pain becomes more common in pregnancy,(15) it is necessary for healthcare professionals to be knowledgeable on their safe use to manage pain in pregnancy. Prior to administration in pregnant women, all medicines should be assessed for risk versus benefit, and be used sparingly to try to minimise adverse effects on the developing foetus.(5)

Safety data for analgesic use in pregnancy is mostly limited to animal studies or observational studies in humans, due to ethical concerns,(16) and is thus prone to selection bias, and exposure or outcome misclassification.(17,18) Many studies in pregnancy also suffer from low recruitment rates, inadequate sample sizes affecting their statistical power and external

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validity,(19,20) as well as falsely increased risk estimates due to less than ideal study designs.(18) The impact of polypharmacy on perinatal outcomes is understudied, and data derived from studies investigating outcomes from opioid exposure in utero are often from addiction studies and may not be directly applicable to chronic pain in pregnancy.(21) Safety data should therefore be interpreted carefully, which can be difficult for busy healthcare professionals.

So which analgesics are suitable for use in pregnancy?

Table 1 (see next page) summarises some of the recommended advice around pharmacological agents in the management of chronic pain during pregnancy. Further research is needed; there is very little safety data for many agents, inconsistent results across various studies, and there is little literature on the long-term neonatal consequences of in utero exposure in pregnancy.(5)

Many women discontinue analgesics upon knowledge of conception and/or avoid the use of analgesics during pregnancy due to concerns over foetal safety.(13) 72.8% of women reported deliberately avoiding medicines during pregnancy due to fear of harming the foetus (19.5%) , and 6.3% of women reported they would rather suffer as long as possible before having to take any medication.(13) Studies however shows that women overestimate the risks of taking over the counter and prescribed medicines during pregnancy.(22) Even paracetamol, which is deemed safe during pregnancy,(23–25) is perceived as a risky medication by pregnant women and a large number of women would avoid it during their pregnancy.(13) Professionals may need to counsel patients of overall risks (3% for major congenital abnormalities and 15% for miscarriage)(26) regardless of taking medications. More work needs to be done to explore these concerns with pregnant women at the outset in order to address their beliefs and concerns regarding medicines, and explain the risks and benefits of each pharmacological option,(4) however this can only be achieved once the healthcare professional's knowledge is improved.

It is worth noting, that as up to one in two pregnancies are unplanned, women may go through pregnancy on pain medication that is contraindicated in pregnancy. Interestingly, studies have shown that less than a quarter of reproductive-aged women with long-term opioid prescriptions pick up their contraceptive prescriptions regularly,(8) suggesting an opportunity for a public health intervention.

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<b>Drug</b>	<b>1<sup>st</sup> Trimester</b>	<b>2<sup>nd</sup> Trimester</b>	<b>3<sup>rd</sup> Trimester</b>	<b>Recommendations</b>
<b>Paracetamol</b>	Generally safe	Generally safe	Generally safe	Use in all trimesters (23–25) Does not increase risk of major birth defects.(24) Some studies have shown an increased incidence of childhood asthma, behavioural problems, delay in gross motor and communication development with long term use, but studies all shown to have limitations in study design. Some studies found an increased risk of undescended testicles.(27,28)
<b>Aspirin</b>	Increased risk of gastroschisis. Increased risk of bleeding at analgesic doses.	Increased risk of bleeding at analgesic doses.	Increased risk of bleeding at analgesic doses.	Avoid analgesic doses. Use low dose aspirin if needed for obstetrical reasons.
<b>Ibuprofen and other NSAIDs</b>	Generally safe	Generally safe	Avoid	No increased risk of miscarriage.(29,30) Use in third trimester can lead to neonatal pulmonary hypertension and premature closure of ductus arteriosus,(31–33) reduced foetal renal blood and reduced amniotic fluid.(31,34) Does not increase risk of major birth defects – naproxen only increases risk of cardiovascular defects.(35)
<b>Codeine</b>	Possible increased risk for cardiac defects(36)	Generally safe	Generally safe	Generally safe.(37,38) Use with caution in women at risk of unintended pregnancy and in first trimester due to increased risk for cardiac defects. Increased risk of neonatal withdrawal syndrome (NAS) with long-term opioid use or use in last trimester.(34,39) Increased risk of NAS with codeine over other opioid analgesics.(37,40,41) For all opioids reduce dose if possible closer to delivery due to risk of neonatal respiratory depression.*
<b>Fentanyl</b>				No significant safety information available.
<b>Hydrocodone</b>				No significant safety information available, although widely used in pregnancy.
<b>Morphine</b>				Most affected by pregnancy with increased clearance rate, decreased half-life and rapid placental transport.(38)
<b>Oxycodone</b>				No significant safety information available.
<b>Tramadol</b>				Increased risk of NAS. Increased risk for cardiac septum defects and pes equinovarus with tramadol.(42)

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<b>Buprenorphine</b>				Risk of NAS higher than with opioids, but less than that of methadone. Not well studied in pregnancy.(43)
<b>Methadone</b>				Increased risk of NAS in many well designed studies; as high as 70%.(43)
<b>Gabapentin</b>				Does not increase risk of birth defects. (15)

**Table 1 – Pharmacological management of chronic pain in pregnancy recommendations**

*(Adapted from Pritham UA, Mckay L. Safe Management of Chronic Pain in Pregnancy in an Era of Opioid Misuse and Abuse. JOGNN - J Obstet Gynecol Neonatal Nurs. 2014 Sep 1;43(5):554–67) (15)*

Table shows common drugs used in the management of chronic pain and recommendations and considerations for their use within pregnancy.

\* Opioids in general showed no strong teratogenic effects.(18,47) – further large prospective studies are needed. Neonatal withdrawal syndrome (NAS) – higher risk with long-term opioid use and use in the last trimester. Study found a 2.2-fold increase in risk in neural tube defects prevalent in periconceptional opioid use (5.9 per 10,000 live births).(48)

### **3.3 Effects of pharmacological management of chronic pain on the mother**

If not well managed, chronic pain can lead to maternal stress and anxiety, depression, sleep deprivation and hypertension, which can in turn impact on both the physical and psychological wellbeing of both the mother and foetus.(5,15) This can impact a woman's ability to care for their child, cause women to be unable to continue working or being an integrated member of society, which can cause a further downward spiral.

So why are healthcare professionals reluctant to prescribe analgesics in pregnancy?

Pain, especially lower back pain, is often dismissed by doctors and justified as being a “normal feature of pregnancy”.(7) One study found that in pregnant women with low back pain, only 32% discussed their pain symptoms with their healthcare professional, and 75% of healthcare professionals did not make any recommendations to manage the patients' pain symptoms.(44) Women are left feeling dismissed and unsupported.

Online forums such as Mumsnet, the UK's most popular website for parents and a midwife approved chat thread, reports women receiving comments from their GP's such as “women with chronic pain are irresponsible wanting to start a family”, “stop all the drugs or deal with the horrible guilt”, and GP's telling pregnant women to stop all pain medications immediately. Sudden termination of analgesics has been shown to cause adverse effects on the foetus as well as leaving women with poorly managed chronic pain. Poorly managed pain can lead to women using inappropriate choices of over-the-counter medications or herbal remedies, as well as overusing of over the counter medications.(5) This highlights the need for healthcare professionals to be aware of their unconscious biases that may affect their clinical decision making, better awareness of opioid management in pregnancy, and how to best support pregnant women with their choice of pain management in pregnancy.

Women on pain medication worry about judgement from healthcare providers for putting their child at risk, but surprisingly studies have shown doctors concerns are focussed more on drug abuse and addiction rather than foetal toxicity, with doctors reporting feeling less compassion for pregnant women on opioids and referring many patients to addiction services.(45) A study investigated management of pregnant women with chronic lower back pain managed by opioids and found that over 50% of obstetrical healthcare providers would suspect that not only is a women requesting an increase of her opioid prescription during pregnancy exaggerating her pain, but also suspect her of having ulterior motives.(45) Interestingly this study also found that the top concern for healthcare professionals about prescribing an opioid medication for

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black patients was foetal harm, whereas opioid abuse was the primary concern for white patients.(45)

Only 29% of physicians in this study were willing to re-prescribe the same opioid the patient is already taking.(45) Physicians are likely to swap a patient from opioid medication onto a non-opioid medication, despite studies cautioning against triggering opioid withdrawal during pregnancy due to adverse foetal outcomes such as foetal growth retardation, preterm labour, foetal distress and even foetal demise as well as long-term behavioural consequences such as attention disorders and learning difficulties.(15)

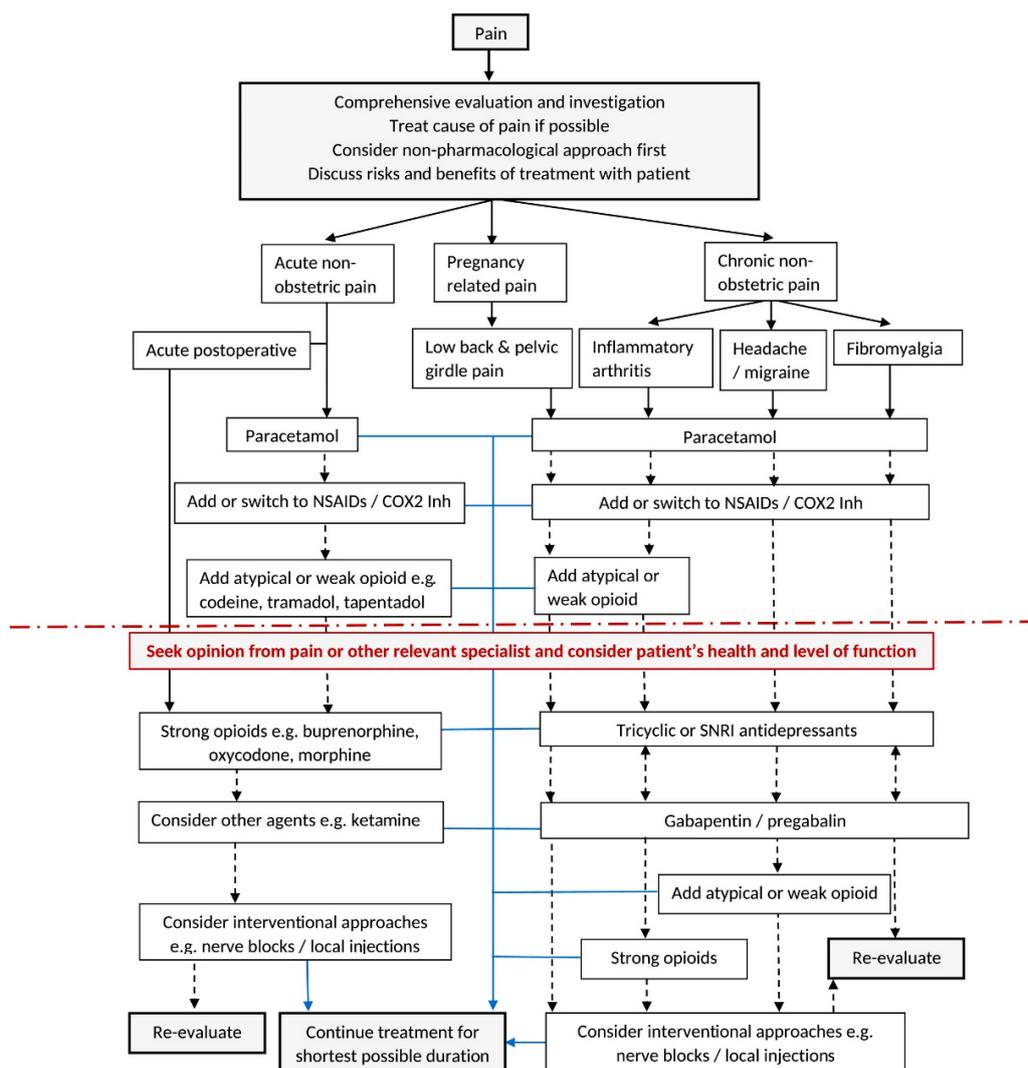
Studies have shown that pain thresholds in healthy women without chronic pain increase throughout pregnancy, reaching a peak just prior to delivery, (46) but women with chronic pain often have decreased pain thresholds at baseline.(7) Women with chronic pain are going to have an increased need for pain management in pregnancy, and opioid requirements for patients on chronic opioid therapy tend to increase during the course of pregnancy,(15) yet many healthcare professionals are resistant to increase doses or even refusing to prescribe any analgesia at all.(45)

Doctors expressed concerns about increasing opioid abuse and following rules and regulations regarding opioid prescribing.(45) With rising rates of neonatal abstinence syndrome (NAS) in new-borns, increased media attention has resulted in increased scrutiny around prescribing of pain medication and opioids in pregnancy.(45)

If GPs and obstetricians are reluctant to prescribe opioids, then why are very few women being referred to pain management clinics? Obstetricians are assumed “de facto” experts in all conditions during pregnancy,(15) when pain clinics could provide more expert knowledge. Unfortunately, pregnancy is often an exclusion criteria for chronic pain programmes,(7,15) and limited funding and coverage means waiting lists for pain clinics can be over six months long in the UK. Doctors are left unsure of who should be managing these women’s pain and women can end up with inadequate pain control or any management plan at all.(15)

One Australian study formulated an algorithm (4) (see figure 2 below) that can assist clinicians to follow their recommendations for analgesia use in pregnancy. Easy to follow and quick reference guides like these should be made readily available for healthcare professionals, especially GPs with very limited time to manage a broad range of conditions.

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**Figure 2** – Flowchart guideline for the management of pain in pregnancy

(Adapted from Black E, Khor KE, Kennedy D, Chutatape A, Sharma S, Vancaillie T, et al. Medication Use and Pain Management in Pregnancy: A Critical Review. Pain Pract. 2019 Nov 13;19(8):875–99.) (4)

Easy to read, quick reference chart suggesting appropriate use of pharmacological agents to manage pain in pregnancy.

Objective guidelines for chronic pain management in pregnancy by NICE would make decision making regarding suitable and adequate pain management quicker and easier, and might mean that more women have access to adequate pharmacological pain management during pregnancy, by reducing physician bias and easing physician uncertainty over the safety of pharmacological agents. These reference guides should be kept up to date as new scientific evidence regarding foetal effects comes to light, and include guidance on who should manage pregnant women's pain and who to refer to for further advice or escalation of pain medication is also needed.

#### **4.0 Conclusion**

With studies investigating the risks of common chronic pain medications and their usage in pregnancy showing inconsistent results, and poor training being provided for healthcare professionals, pregnant women are left with confusing and conflicting advice. Women who request pain medication during pregnancy are being judged for exaggerating their pain, and are being suspected of ulterior motives and concerns over drug abuse and addiction. Women are being treated with less compassion, and healthcare professionals are being reluctant, or outright refusing, to increase doses or even prescribe pain medication in pregnancy. Women are receiving inadequate and even harmful treatment in the antenatal setting, leading to increased maternal and foetal complications during pregnancy and beyond.

More research is needed into chronic pain in pregnancy, and reference guides for chronic pain management need to become more available. Better training is required for healthcare professionals, in terms of up to date guidance regarding medication safety, opioid management and withdrawal in pregnancy, as well as clarification of who manages patients' pain, and awareness of potential biases affecting clinical decision making.

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