EXPLORING THE OPIOID PRESCRIBING PRACTICES OF GENERAL PRACTITIONERS (GPs) IN WEST AND SOUTH ESSEX, UK

Dr. Edwin Ugoh, Consultant Psychiatrist, Essex Partnership University NHS Foundation Trust, England. Dr. Vincent Icheku, Senior Lecturer and Senior Fellow, London South Bank University, London, England.

Introduction:
The emerging evidence in recent studies shows that Opioid use and abuse have continued to grow at a significant rate, with fatal consequences. The evidence also indicates palpable apprehension and concern over the increasing opiate/opioid prescription numbers by General Practitioners (GPs). This present study aims to explore the opioid prescribing practices of General Practitioners (GPs) in West and South Essex. The objectives are to answer the following questions: Is an opiate prescription based on any available guideline? Is opioid prescribed primarily for pain management? How many times do the GPs prescribe opioids? How long are patients on pain prescription medications? Has the GPs attended training on the use of opioid for pain management? How many years has the GPs spent working as a practitioner? Finally, these researchers believe that answers to these question will add to the knowledge base towards improving the risk-benefit balance of prescribed opiates.

Methods:
A short self-questionnaire was sent to all GP practices in the South and West of Essex (n=25). There was a response rate of 80 per cent (20/25). Qualitative data from the questions were analysed using thematic analysis. In addition, nominal data were analysed using descriptive statistics to summarise the results.

Results:
The study found that most of the GPs who participated in the survey are experienced GPs, yet the majority are not complying with prescribing guideline and thus, overprescribes opioid for pain management.

Conclusion:
The overprescribing practices of opioids by GPs are affected by an absence of robust guideline on managing chronic pain. Thus, we recommend compliance with existing guideline and consultation on managing chronic pain over 16s to producea guideline on adult pain management.
Opioids can either be obtained synthetically or derived naturally from opium; the latter are opiates. Examples of opiates are Morphine, Codeine and Thebaine. Heroin (diacetylmorphine) is an ester of morphine, being more natural than semi-synthetic and still considered an opiate. Synthetic opioids include Tramadol, Methadone, Pethidine, Oxycodone and Fentanyl.\[3\]

Opioids are widely used and feared compounds linked to abuse, addiction, and the dire consequences of diversion. Yet, they are essential medications, the most effective drugs for relieving pain and suffering. [4] Thus, opioids play a unique role in ending pain and suffering in the whole world. However, in the United Kingdom, opioids have the potential to be a much bigger problem. Recent studies suggest that chronic opioid use is associated with regular A&E attendances, increased incidence of side effects and the risk of opioid abuse and diversion, overdose, and fatality. [5] Evidence abounds in literature, which shows that there are several known risk factors for drug-related deaths, and these include: being recently released from prison, recently discharged from hospital, recent heroin injector, declared misuse of alcohol and reported abuse of benzodiazepines, whereas receiving OST is protective. [6]

Higher opioid doses were associated with somewhat higher chronic pain and higher levels of patient-reported opioid-related psychosocial problems, control concerns and depression. [10] Chronic pain has a high prevalence globally. In America, for instance, the opioid epidemic is one of the most significant public health problems that the USA faces. A recent report by the Medical Journal Lancet shows that opioid overdose death rates have increased steadily for more than a decade and doubled in 2013–17. [11] In Europe, opioid abuse is a severe public health issue, with an estimated 1.3 million problem opioid users reported in 2012. The report added that the abuse of heroin and other illicit opioids, prescription opioid (“RxO”) abuse, also represents a component of the overall opioid abuse problem. Although RxOs are amongst the highest successful drugs for pain management, these medications also carry the risk of potential abuse and dependence. [12] In the United Kingdom, The House of Commons Home Affairs Committee has expressed concern concerning the lack of understanding and data collection surrounding prescription drug dependence. [13]

The UK Office of National Statistics (ONS) reported that 4,359 deaths resulted from drug poisoning in 2018. This is up 16 per cent from the previous year, which was the highest annual increase since records began in 1993. The ONS reported deaths amongst men increased from 89.6 per million in 2017 to 105.4 per million in 2018 - two-thirds of these were linked to the misuse of drugs. Opioids continue to be the most frequently mentioned substances on death certificates of individuals. [14] Given the role of doctors in opioid’s prescription, this study will review the literature to ascertain whether doctors’ prescribing practices helped fuel the opioid epidemic and the higher death rate due to opioid abuse. Thus, the literature review will be applied to this study to conduct a systematic search to find the relevant studies.

The Aim and Objectives of this paper is to add to the knowledge of General practitioners in the United Kingdom who are essential stakeholders in the battle against prescription opioid abuse. Therefore, their knowledge and understanding of opioid abuse and diversion are crucial as this will go a long way in the quest for primary care evidence-based clinical interventions. This will help to reduce opioid-related morbidity and mortality. In Essex, prescription opiate dependency is on the increase, very much like the whole country, and the pressure is on the substance misuse services locally to help out as there is a lack of adequate pain management services available. This study explores the opioid prescribing practices of General Practitioners (GPs) in West and South Essex. The objectives are to ascertain:

1) whether the opiate prescription is based on any available guideline
2) whether the prescription of opioid is primarily for pain management
3) how many times the GPs prescribe opioids
4) how long are patients on pain prescription medications
5) whether the GPs attended training on the use of opioid for pain management
6) the number of years the GPs spent working as a practitioner.

Finally, the publication is expected to add to the knowledge base towards improving the risk-benefit balance of prescribed opiates.

Garrard (2016) stressed that a literature review is a survey of scholarly articles and any other appropriate source to a particular issue or study area. Doing so provides a description, summary, and critical evaluation of the studies under
review concerning a new research problem. A fundamental goal of literature reviewing is identifying knowledge gaps. A research gap refers to unknown or underexplored areas that have the potential for further research. [15] Also, an knowledge gap is has been described as a topic for which missing or insufficient information limits the ability of a reviewer to conclude a question. [16] In other words, when we identify a research gap, we find a direction for potentially new and exciting research. The term research problem is often used as a synonym for research gaps. A problem statement signifies a gap in the knowledge that, when scrutinised, results in a call for action or resolution.[16] [17] This literature review aims to fill the gap in the existing literature by generating new knowledge about the effect of beliefs and knowledge in primary care prescribed opioids in opiate dependents service users open to Tier 3 drug services in West and South Essex.

This literature review’s primary aim is to identify the gap in the literature that will inform the current study. To achieve these aim and objectives, these researchers needed systematically search databases. Parahoo (2006) recommends that a combination of databases leads to good search outcome. [18] The Cumulative Index to nursing and allied health Literature (CINAHL), which is recognised as a comprehensive and authoritative source for professional literature related to nursing, biomedicine, and allied health, was searched. In addition, the Elton and Stephens Co-host (EBSCoHost), Medline, and Elsevier database comprise a wide range of online nursing and allied healthcare academic articles that have been peer-reviewed was also searched.

Methods:-
The above databases were searched individually using identified search terms as General Practitioners (GP), management, prescription, patients, treatment, opiates and opioid. Further advanced search using Boolean operatives such, "AND", "OR" "GP" AND "prescription" AND "trend" AND "primary care" OR "Opioid" OR "dependent" were used in searching for relevant and up-to-date studies pertinent to the current research. Aveyard (2014) stressed that search terms combined with Boolean operators optimise the search process. Boolean operators organise and connect key search terms by narrowing down extracted articles using the various operator. [19] The Boolean's search terms and operators were used to limit and widen the search as appropriate and allow the literature relating to the prescription of opioid in primary care to be searched. These include search terms, which reference precisely to opiate dependents.

The database search using keywords and Boolean operatives generated so many studies, 260 to be precise. However, inclusion and exclusion criteria were carefully used to select relevant papers with full-text, scholarly (peer-reviewed) academic journal, articles written in English between 2011 to 2021. Some of the databases were also combined in searches removing duplication. For example, a Grey literature search found ten studies. Still, six were excluded because they were editorial consultation papers, primarily reports and policy documents that did not meet the inclusion and exclusion criteria. Thus, the search produced forty-five results; search limiters were used to narrow the results. Limiters consisted of the inclusion of full-text studies and studies published in the United Kingdom and primary healthcare. The limiters enable the screening out of duplicated studies, abstracts and founding of only six studies that met the inclusion and exclusion criteria.

All selected studies under review relate to opioid abuse, dependence, and societal costs of its prescription. The studies clearly presented their results and analysis, accompanied by wide-ranging arguments elaborating on their findings and acknowledging their limitations. Cicero and Ellis (2017) study show that the growth in opioid prescribing for long-term pain conditions led to more people taking opioids at higher doses. Long-term and high doses of opioids are associated with higher criminal justice costs and serious adverse events, including opioid dependence and opioid-related deaths. The study also found that the frequent prescription opioids comprise oxycodone, hydrocodone, and morphine. They also found that the common illegal opioids include fentanyl and heroin. While illegal opioids and not the focus of their study, it is essential to know that many addictions and overdose to these illicit opioids stem from prescription opioid.[20]

Ashaye et al. (2018) found that of the 703 trial participants with chronic musculoskeletal pain, 413 (59 per cent) patients were prescribed opioids. Among the participants that were prescribed an opioid, the total number of prescriptions of opioids issued per year fluctuates from 1 to 52. In total, 3319 opioid prescriptions were issued over the study period, of which 53 per cent were for potent opioids (tramadol, buprenorphine, morphine, oxycodone, fentanyl and tapentadol). One-quarter of the prescription was prescribed outside of National Institute for Health and Care Excellence (NICE) guidelines. They also found that over 1.5 million people with musculoskeletal problems receive opioids, and according to guidelines, 45 per cent over-prescribed, at a loss to the NHS of £100 million per
Krieger (2018) found that opioids are either prescribed by physicians as heavy strength painkillers for intense chronic or post-surgery pain or circulated illegally for their pain-relieving effect. [22] Bohnert et al. (2011) examined the association of maximum prescribed daily opioid dose with the risk of opioid overdose death among patients with cancer, chronic pain, acute pain, and substance use disorders. They found that for patients receiving opioid prescriptions for pain, higher opioid doses were associated with an increased risk of opioid overdose death. [23] In a cohort study, Dunn et al. (2009) examined the rates of opioid overdose and their association with the average prescribed daily opioid dose among patients receiving medically prescribed chronic opioid therapy. They found an increased risk of overdose among patients receiving medically prescribed opioids at higher dosage levels. Most opioid overdoses were medically severe, and 12 per cent were fatal. [24]

A recent study involving 1,968,742 new opioid users without cancer from primary care electronic health records across the UK found that between 2006 and 2017, codeine was the most commonly prescribed opioid. There was a 5-fold increase in codeine prescriptions, a 7-fold increase in tramadol prescriptions, and a 30-fold increase in oxycodone prescriptions for non-cancer pain. When individual patient factors were taken into consideration, Yorkshire, the Humber, the North West and South-West regions of England were linked with a considerable higher risk of long-term opioid use. The study also found that only 3.5 per cent of prescribers had significantly higher prescribing practices leading to long-term use after adjusting patient factors, where they did, rates were up to 3.5 times higher than the population average. [25]

In conclusion, this literature review has highlighted the association between higher prescribed opioid doses and the risk for overdose and overdose death. The finding supports the calls for action aimed at promoting the safe practice in opioid prescribing. The result is in line with the views of Dr William Shanahan, Medical Director and Clinical Director of Addictions, Priory Hospital Roehampton. He reported that opioid overdoses increased by 87 per cent to 12,000, and deaths increased by 41 per cent to 2,000 in the year. Dr Shanahan added that in 2020 50 million prescriptions for opioids were written, a 35 per cent increase over ten years. Of the 115,000 prescriptions written every day, five results in death. There are three times more deaths in the North East of the UK than in London, partly reflecting a more significant usage of opioids amongst the socially disadvantaged. Thus, these data call for an examination of practice in opioid prescribing. [26]

In terms of the Research Design, the chosen approach in this study is qualitative, which enable these researchers to collect in-depth data on live experience GPs prescribing opioid for opiate dependents service users open to Tier 3 drug services in West and South Essex. Phenomenology is one of the theories associated with a qualitative methodology. Many authors define phenomenology as "the lived experience", mainly seen in topics of this nature. [27] Phenomenology is the most suitable method for this study because it studies conscious human experiences in day-to-day life. [28] The interpretive, qualitative approach is chosen because these researchers want to focus on individual GPs perspective from a living experience perspective.

This explores the opioid prescribing practices of General Practitioners (GPs) in West and South Essex. Essex Specialist Treatment and Recovery Service (Essex STaRS) is a specialised substance misuse service set within Essex Partnership University NHS Foundation Trust (EPUT). It provides a detailed assessment of clients with opioid and other addictions in the community referred by Open Road, a partnership agency that offers psychosocial support. Part of the role by Essex Stars is to provide substitute prescribing for opioids to achieve stabilisation and detoxification, as well as hepatitis B vaccination and Hepatitis C testing and referral to treatment, motivational interviewing and so on. Essex STaRS covers Essex, including Basildon, Harlow, Colchester and Chelmsford, and surrounding areas. In the South and West of Essex, Essex Stars offers assessments in Basildon and Harlow, respectively. Essex Stars and Open Road clients engage with regular reviews and ongoing monitoring and support through close liaison with the general practitioner.

The West and South Essex, as of August 2020, has a total of 92 General Practices, from which 20 participants were randomly selected. The semi-structured interview technique was most appropriate for this study. However, all participating GPs were sent a pre-prepared self-questionnaire due to the UK Government's non-contact policy of COVID 19. For the GP who completed and returned the survey, the data from the questionnaire was then extracted.
and put onto the computer software package Microsoft Excel using pre-prepared spreadsheets. All data was anonymised. Practices not wishing to participate could opt-out. Data were analysed using Microsoft Excel and then displayed using tables and graphs. For example, table one shows that the data collection conforms to the ethical requirement.

**Results:**
There were 20 participant GPs; of these, 12 were from the South of Essex and eight from the North of Essex. Please see Table 1 for demographic details of GP practices.

### Table 1: Summary of demographics of South and West GP practices.

| Gender   | Number |
|----------|--------|
| Male     | 13     |
| Female   | 7      |
| Age      |        |
| 31 – 49  | 11     |
| 50+      | 9      |
| Ethnicity|        |
| White    | 9      |
| Mixed    | 0      |
| Asian    | 9      |
| Black    | 2      |
| Chinese or Other | 0  |
| Born in the UK. |      |
| Yes      | 9      |
| No       | 11     |
| Years Working as a GP. |      |
| 5 or less| 7      |
| 6 to 15  | 5      |
| 15 or more| 8   |
| Area     |        |
| City     | 2      |
| Town     | 14     |
| Village  | 4      |

### Table 2: Analysis and summary of participants' responses.

| Questions/Statements | Participant Answers | Emerging Themes |
|----------------------|---------------------|-----------------|
| Is your opiate prescribing based on any available guideline? | N=3 Strongly agree Agree N=2 Unsure N=6 Disagree N=4 Strongly disagree | N=5 The majority are not complying with prescribing guideline |
| You prescribe opioid primarily for pain management. | N=8 Strongly agree Agree N=0 Unsure N=4 Disagree N=2 Strongly disagree | N=6 Prescribes mostly for pain management |
| In a typical month, how many times have you prescribed opioids? | N=4 between 1-10 N=5 between 10-20 N=7 between 20-30 N=4 between 30 and over | Overprescribing |
| You often keep patients on pain prescription medications for too long | N=2 Strongly agree Agree | N=9 Patients remain on pain prescription medications for too long |
The six questions in table 2 and subsequent themes are illustrated further in figure 1 to 6 below. The use of the charts is intended to condense the same information in table 2 into easy-to-understand formats that clearly and effectively communicate the findings of this study.

**Figure 1**: Is your opiate prescribing base on any available guideline?
**Figure 2:** Do you prescribe opioid primarily for pain management?

**Figure 3:** Do you often keep patients on pain prescription medications for too long?
**Figure 4**: In a typical month, how many times have you prescribed opioids?

**Figure 5**: Have you been in any kind of training on the use of opioid for pain management?
Discussion:
The literature review in this study is organised to critically analyse existing studies publications on compliance of primary care physicians (GPs) with existing opioid management guidelines, the GPs level of training in opiate prescriptions opioid prescription, the disturbing emerging trend of opiate overprescribing. Thus, this qualitative study explores the opioid prescribing practices of General Practitioners (GPs) in West and South Essex. The objectives are to examine compliance with opiate prescribing protocol and guideline; explore the extent to which opiate is prescribed for pain management; investigate the preponderance of opiate prescription; investigate how long patients are kept on opiate prescription; determine whether or the GPs attain training on the use of opioid for pain management and consider the practice experience of the opiate prescribing doctors.

The complaint of pain is a frequent presence at GP practices. General Practitioners see many people of various ages and backgrounds. Without clear opioid prescribing guidelines, they are faced with the difficulty of balancing managing patients with pain presentations who may be at increased risk of experiencing uncontrolled pain to those with possibly drug-seeking behaviours. Chronic primary pain cannot be accounted for by another diagnosis or where it is not the symptom of an underlying condition (this is known as chronic secondary pain). It manifests with considerable functional disability and emotional distress. Examples include widespread chronic pain and chronic musculoskeletal pain and conditions such as chronic pelvic pain. All GPs prescribed opioids for acute and chronic pain in our study, but none of the GPs prescribed opioid substitution therapy such as methadone or buprenorphine. This is, of course, a specialist prescribing, and most GPs are uncomfortable initiating the controlled drugs without specialist input and ongoing support. Keeping with some other studies looking at the prescribing patterns, the GPS had expressed concerns about their ability to prescribe opioids safely. However, just over half of the cohort of GPs in this survey felt they had good knowledge of opioid prescribing; however, 4 out of 10 GPs that responded did not have an adequate understanding of prescribing opiate management.

Similar to other studies, several of the GPs in this present study expressed concern with the adequacy of training they had received. There were 10 (50 per cent) GPs that reported the only training on pain management and use of...
opioids was in medical school. There was a consensus that further training was needed to increase the confidence in prescribing opioids amongst GPs. Other studies looking at the prescribing patterns of opioids by GPs have commented on the belief in the appropriateness of opioids within certain constraints. To a lesser extent, the age of the GP influences prescribing practices. In our study age of the prescriber was not a significant factor in prescribing opioids. As with other studies, there is a concern with the risk and abuse of opioids. Besides the lack of dissatisfaction with their training on pain, 50% of GPs surveyed admitted a lack of clarity on guidelines might have influenced their overprescribing. Just eight out 20 strongly agreed that their prescribing is based on available guidelines, and out of that 8, only 3 GPs strongly agreed that they prescribed within the confines of available guidelines; however, 60 per cent of GP surveyed either were not sure or disagreed that they do not prescribe base on guidelines. This is disturbing proportions of GPs, and if this is a trend locally, this highlights the importance of further training of identified GPs. Even more striking is the fact that 30% admitted they are prescribing opiates but not for pain management, giving the risks of dependency, morbidity and mortality from patients on long term opiate use; this needs to urgently address through a more comprehensive national guidelines and more training for GPs at both primary care network level and maybe countywide level.

The frequency of prescribing and the length of time patients are left on their opiate prescriptions is also a source of concern identified during this survey. 60 per cent of GPs surveyed agreed or strongly agree that they leave patients on their opiate prescriptions for too long, and 55% of GPs surveyed admitted to prescribing opiates more than 20 times in a month. One obvious factor influencing overprescribing is the length of time spent working as GPs, 65 per cent of GPs surveyed have worked as GPs for 10 years or less, this iterates the need for more available workshops, courses and training for these newly qualified GPs, and possibly a requirement for their GP trainees to do a special interest or at least one workplace assessments in either an addiction service or a pain management service.

NHS ethics approval is not required as this is a service evaluation and will not generate transferable data. Service evaluation seeks to assess how well a service is achieving its intended aims. It is undertaken to benefit the people using a particular healthcare service and is designed and conducted with the sole purpose of defining or judging the current service. [29]

Data have been stored and will be used in compliance with GDPR 2018. None of the data is identity revealing. Data usage is compliant with the initial purpose for which it was gathered, that is, to evaluate an intensive care course. The results of this service evaluation and recommendations made will be shared with the local primary care physicians through their primary care network (PCN) or their Clinical Commissioning Groups (CCG). It will also be available to local commissioners who commission both Public Health England and seven different CCG clinical services in Essex County.

Conclusions:-
The literature review in this study was organised to critically analyse existing studies on opioid prescription, which provides an overview of the knowledge available. The review found that doctors are overprescribing driven mainly by a lack of knowledge or usage of existing guidelines on managing chronic pain.

This survey has highlighted the emerging trend of overprescribing by local GPs in the West and South Essex GP Practices, much in keeping with observed trends nationally and possibly globally. This overprescribing is driven by a lack of knowledge or usage of available guidelines on managing chronic pain. Ashaye et al. (2018) pointed out 59 per cent in their trial of 703 participants were prescribed opioids for their chronic musculoskeletal pain, with a total of 3319 opioid prescriptions issued within the study period and 25 per cent of these prescribed outside NICE guidelines and with the study concluding that the long-term prescribing of opioids for chronic musculoskeletal pain is common in primary care. [21] There is a clear correlation between overprescribing of opiates by primary care physicians and the increasing morbidity and mortality from opiates oversedation and respiratory depression. Bohnert et al. (2011) found out that for patients receiving opioid prescriptions for pain, higher opioid doses were associated with an increased risk of opioid overdose death. [23] In their cohort study, Dunn et al. (2009) found an increased risk of overdose among patients receiving medically prescribed opioids at higher dosage levels. Most opioid overdoses were medically severe, and 12 per cent were fatal. [24]

Most people with chronic pain understandably expect a precise diagnosis and effective treatment plan; however, the complexity of their clinical presentations and the fact that GPs and specialists alike find chronic pain very challenging to manage is often not possible. This mismatch between patient expectations and treatment outcomes
can affect the therapeutic relationship between healthcare professionals and patients. The potential negative consequence of this is the prescribing of ineffective but harmful drugs.

Rose et al. (2019) qualitative literature review exploring the drivers influencing over-prescribing by GPs in primary care and recommendations to reduce unnecessary prescribing [30] had similar findings with our studies. The main themes and drivers of overprescribing were GP attitudes and feelings and anxiety/fear concerning prescribing; external factors such as pressures from time, patient demands and expectation and more importantly, lack of education as the primary drivers affecting GP over-prescribing.

The King's Fund Inquiry into the Quality of General Practice specifically focused on England published was in 2011. This highlighted the need to prescribe against safety indicators developed by the Royal College of General Practitioners (GP); it further said these indicators could be as evidence of further discussions during appraisal and also as a prompt for auditing significant events. Also, it recommended that GPs adhere to their Quality and Outcomes Framework that stipulates careful assessment of medication reviews to determine if they are of high quality. [31]The authors of this study agree with all of these recommendations, and we also recommend the following:

Training of GPs in the use of local and national guidelines, these training and workshops can be at the primary care network, CCG or local practice level. GPS should have workshops in adhering to the use of the soon to be published National Institute for Health and Clinical Excellence (NICE) Guideline on managing chronic pain in the over 16s. The National Institute for Health and Clinical Excellence (NICE) has now published in April 2021 the new guideline NG 193 ‘Chronic pain (primary and secondary) in over 16s: assessment and management of all types of chronic pain’. In this guideline, the preferred approach in patient-centred management is the non-pharmacological management of chronic primary pain and the use of existing guidelines to manage chronic secondary pain. The GPs are now advised not to prescribe opiates in the management of new cases of chronic primary pain and consider the benefit/risk approach in their clinical judgments on patients already on existing opiates or opioids. The authors strongly advise GPs to use this new guideline and other existing guidelines in their opioid prescribing practice. GPs should also be aware of Local and other National Clinical guidelines in managing chronic secondary pain. These guidelines and the above recommendations would minimise overprescribing and reduce morbidity and mortality. The authors believe this new guideline will go a long way in giving much-needed clarity to the needless use of opioids in chronic primary pain and the importance of GPs in discussing with patients evidence-based non-pharmacological approaches.

The GPs should make the best use of other Information sources currently available to support prescribing in general practice, including General Medical Council Good Medical Practice. This is freely available from the GMC website, and printed pamphlets are sent to all doctors through the post. In addition, the British National Formulary (BNF) is freely available to all prescribers in the NHS through a website and a printed book delivered to most GP practices regularly.

Finally, we must emphasise at this juncture that the findings of this study are limited to a small sample of primary care practices and patients in Essex. Further studies with a larger sample size are required to increase the reliability and validity of the results and additional training and support for GPs in applying the evidence in practice and how to support their patients appropriately.

References:-
1. Bedson J, Belcher J, Martino OI, et al. (2013) The effectiveness of national guidance in changing analgesic prescribing in primary care from 2002 to 2009: an observational database study. Eur J Pain 2013;17:434–43.
2. Stannard C. (2013) Opioids in the U.K.: what's the problem? British Medical Journal 2013;347:f5108. doi:10.1136/bmj.f5108
3. Chou R, Turner JA, Devine EB, et al. (2015) The effectiveness and risks of long-term opioid therapy for chronic pain: a systematic review for a National Institutes of Health Pathways to Prevention Workshop. Ann Intern Med 2015;162:276–86
4. Gilson, A.M., Ryan, K.M., Joranson, D.E., Dahl, J.L. (2004). A reassessment of trends in the medical use and abuse of opioid analgesics and implications for diversion control: 1997–2002. J Pain Symptom Management 28, 176–188.
5. Okie, S. (2010). A flood of opioids, a rising tide of deaths. N Engl J Med 363, 1981–1985. g- Gureje O, von Korff M, Simon GE, Gater R. Persistent pain and well-being: a World Health Organization Study in Primary Care. JAMA 1998; 280: 147–151.
6. Merrall, E.L.C., Bird, SM, & Hutchinson, S.J. (2013). A record linkage study of drug-related death and suicide after hospital discharge among drug-treatment clients in Scotland, 1996–2006. Addiction, 108, 377–384.
7. Degenhardt, L., Randall, D., Hall, W., Law, M., Butler, T., & Burns, L. (2009). Mortality clients of a state-wide opioid pharmacotherapy program over 20 years: Risk factors and lives saved. Drug and Alcohol Dependence, 105, 9–15.
8. Bird, SM, & Hutchinson, S.J. (2003). Male drug-related deaths in the fortnight after release from prison: Scotland, 1996–1999. Addiction, 98, 185–190.
9. Pierce, M., Bird, S.M., Hickman, M., & Millar, T. (2014). National record-linkage study of mortality for a large cohort of opiate users ascertained by drug treatment or criminal justice sources, 2005–2009. Drug and Alcohol Dependence, in press.
10. Joseph O. Merrill, Michael Von Korff, Caleb J. Banta-Green, Mark D. Sullivan, Kathleen W. Saunders, Cynthia I. Campbell, (2012) Constance Weisner. Prescribed opioid difficulties, depression and opioid dose among chronic opioid therapy patients, General Hospital Psychiatry, Volume 34, Issue 6, 6.
11. Hodder, s. L., Feinberg, J., Strathdee, S. A., Shoptaw, S., Altice, F. L., Ortenzio, L., Beyrer, C. (2021) The opioid crisis and HIV in the USA: deadly synergies, The Lancet (IF 60.392) Pub Date: 2021-02-19, DOI: 10.1016/s0140-6736(21)00391-3
12. European Monitoring Centre for Drugs and Drug Addiction. European Drug Report 2014: Trends and Developments. Luxembourg: Publications Office of the European Union; 2014.
13. House of Commons Home Affairs Committee. Drugs: New Psychoactive Substances and Prescription Drugs. London: The Stationery Office Limited; 2013. August 7, 2014, www.publications.parliament.uk/pa/cm201314/cmselect/cmhaff/819/819.pdf
14. Office of National Statistics (2019): Deaths related to drug poisoning in England and Wales: 2018 registrations, https://www.ons.gov.uk/peoplepopulationandcommunity/birthsdeathsandmarriages/deaths/bulletins/deathsrelatedtodrugpoisoninginenglandandwales/2018registrations
15. Garrard, J., 2016. Health sciences literature review made easy. London: Jones & Bartlett Learning.
16. Robinson, K. A., Saldanha, I. J., and McKoy, N. A. 2011. "Development of a Framework to Identify Research Gaps from Systematic Reviews," Journal of Clinical Epidemiology (64:12), pp. 1325–1330.
17. Jacobs, R. L. 2011. "Developing a Research Problem and Purpose Statement", in The Handbook of Scholarly Writing and Publishing, T. S. Rocco and T. Hatcher (eds.), San Francisco: Jossey-Bass, pp. 125–141.
18. Parahoo, K. (2006). Nursing Research: Principles, Process and Issues. (2nd edition).London: Macmillan Press Ltd.
19. Aveyard, H. (2014). Doing a literature review in health and social care: A practical guide. London: McGraw-Hill Education (UK).
20. Cicero, Theodore J., and Matthew S. Ellis. (2017) "Understanding the Demand Side of the prescription Opioid Epidemic: Does the Initial Source of Opioids Matter?" Drug & Alcohol Dependence, vol. 173, Apr. 2017, pp. s4–s10. EBSCOhost.
21. Ashaye et al. (2018) Opioid prescribing for chronic musculoskeletal pain in UK Primary Care: Results from a cohort analysis of the COPERS Trial. BMJ Open 2018;8:e019491
22. Krieger, Carrie. (2018) "What Are Opioids and Why Are They Dangerous?" Mayo Clinic, Mayo Foundation for Medical Education and Research, 21 Mar. 2018, www.mayoclinic.org/diseases-conditions/prescription-drug-abuse/expert-answers/what-are-opioids-faq-20381270.
23. Bohnert AS, Valenstein M, Bair MJ, Ganoczy D, McCarthy JF, Ilgen MA, Blow FC. Association between opioid prescribing patterns and opioid overdose-related deaths. JAMA. 2011;305:1315–1321. [PubMed] [Google Scholar]
24. Dunn KM, Saunders KW, Rutter CM, Banta-Green CJ, Merrill JO, Sullivan MD, Weisner CM, Silverberg MJ, Campbell CI, Psaty BM, Von Korff M. (2009) Opioid prescriptions for chronic pain and overdose: a cohort study. Ann Intern Med. 2009;152:85–92. [PMC free article] [PubMed] [Google Scholar]
25. Jani et al., (2020) Time trends and prescribing patterns of opioid drugs in UK primary care patients with non-cancer pain: A retrospective cohort study, https://journals.plos.org/plosmedicine/article?id=10.1371/journal.pmed.1003270
26. Shanahan, W. (2021) Opioids: understanding the current state in the UK,https://www.priorygroup.com/blog/opioids-understanding-the-current-state-in-the-uk
27. Silverman D. [2005]. Doing Qualitative Research: A Practical Handbook. London, UK: Sage; [Google Scholar]
28. Bowling A. (2002). Research Methods in Health. Investigating Health and Health Services, Berkshire, UK: Open University Press;

29. National Research Ethics Service (NRES) (2013) Defining research. 2013. http://www.nres.nhs.uk/EasySiteWeb/GatewayLink.aspx?alId=355 (accessed 22 Apr 2014).

30. Rose, et al. (2021) qualitative literature review exploring the drivers influencing antibiotic over-prescribing by GPs in primary care and recommendations to reduce unnecessary prescribing. https://pubmed.ncbi.nlm.nih.gov/31633458/

31. Goodwin, et al. (2011) Improving the quality of care in general practice: Report of an independent inquiry commissioned by The King's Fund, https://www.kingsfund.org.uk/sites/default/files/improving-quality-of-care-general-practice-independent-inquiry-report-kings-fund-march-2011_0.pdf.