NICE Medicines and prescribing centre

DRAFT FOR CONSULTATION

Controlled drugs

Safe use and management

NICE guideline

Appendices

October 2015

Draft for consultation

National Institute for Health and Care Excellence

Disclaimer

This guideline represents the views of NICE and was arrived at after careful consideration of the evidence available. Those working in the NHS, local authorities, the wider public, voluntary and community sectors and the private sector should take it into account when carrying out their professional, managerial or voluntary duties.

Implementation of this guidance is the responsibility of local commissioners and/or providers. Commissioners and providers are reminded that it is their responsibility to implement the guidance, in their local context, in light of their duties to have due regard to the need to eliminate unlawful discrimination, advance equality of opportunity and foster good relations. Nothing in this guidance should be interpreted in a way that would be inconsistent with compliance with those duties.

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Appendices

Appendix A: Declarations of interest

A.1 Committee members

Dr Tessa Lewis (Chair)

GDG meeting	Declaration of interest	Action taken
Recruitment (10 October)	None	None
First committee meeting (9 February)		
Second committee meeting (15 May)	None	None
Third committee meeting (8 July)	None	None
Fourth committee meeting (14 August)	None	None

Dr Weeliat Chong (Vice-chair)

GDG meeting	Declaration of interest	Action taken
Recruitment (10 October)	None	None
First committee meeting (9 February)	None	None
Second committee meeting (15 May)	None	None
Third committee meeting (8 July 2015)	None	None
Fourth committee meeting (14 August)	None	None

Graham Brack

GDG meeting	Declaration of interest	Action taken
Recruitment (26 November)	I am a director in two community pharmacies operated by Michael Meagher Ltd and TMS Pharmacy Ltd. I have also received honoraria from Actavis UK Ltd in respect of an advisory board in October 2014 and Takeda Pharmaceuticals for presentations given in April and May 2014.	Noted and participate
First committee meeting (9 February)	None – same as recruitment	None
Second committee meeting (15 May)	None – same as recruitment	None
Third committee meeting (8 July 2015)	None	None
Fourth committee meeting (14 August)	None	None

Cathy Cooke

GDG meeting	Declaration of interest	Action taken
Recruitment (11 October)	Employed by Nestor Primecare (trading as Allied Healthcare) as Head of Medicines Management	Noted and participate
First committee meeting (9 February)	None	None
Second committee meeting (15 May)	None	None
Third committee meeting (8 July 2015)	None	None
Fourth committee meeting (14 August)	None	None

Sarah Dennison

GDG meeting	Declaration of interest	Action taken
Recruitment (4 November)	My post as the National Controlled Drugs Manager at the Care Quality Commission.	Noted and participate
First committee meeting (9 February)	My role at CQC is that of National Controlled Drugs Manager and as such I chair and attend a number of CD related meetings and policy groups and I am also the author of a number of reports and CD related information: Chair CQC led Controlled Drugs National Group and Cross Border Group Co-chair the Clinical Sub Group (with the Patient Safety team) – produce CD related safety information Member of NHS England national CD forum and support their training events Member of DH working group – hospices Member of CD related secure environment discussion groups Previously a member of the working group that produced PHE guidance on non-medical prescribing in the management of substance abuse Interviewed for input by Codemisused (codeine abuse project) Author of CQC controlled drugs annual reports Manage CD self-assessment tools on CQC website Member of the opioid prescribing resource steering	Noted and advised regards confidentiality. Participate at chair's discretion.

GDG meeting	Declaration of interest	Action taken
	group Author of the PMS CD myth-buster – on CQC website Oversee the CDAO register and associated process Represent CQC at CD LINs & associated learning events Answer CD related queries on behalf of CQC	
Second committee meeting (15 May)	Same as recruitment above	None
Third committee meeting (8 July 2015)	Same as recruitment	None
Fourth committee meeting (14 August)	Same as recruitment	None

Chris French

GDG meeting	Declaration of interest	Action taken
Recruitment (17 November)	None	None
First committee meeting (9 February)	None	None
Second committee meeting (15 May)	None	None
Third committee meeting (8 July 2015)	None	None
Fourth committee meeting (14 August)	None	None

Margaret Gibbs

GDG meeting	Declaration of interest	Action taken
Recruitment (28 November)	I am a committee member of the PCPN (Palliative Care Pharmacists Network) and our website and conference are sponsored by two pharmaceutical companies who make opioid-containing products. Membership of the PCPN (as above) Currently on a DH working party to monitor effects of new (Wholesaler dealer licensing) legislation	Noted and advised regards confidentiality. Participate at chair's discretion.
First committee meeting (9 February)	Committee member of the Palliative Care Pharmacists Network. Website sponsored by Napp pharmaceuticals (main sponsor) and Prostraken Member of the London Opioid Safety Group (LOSIG) based at Guys and St Thomas's Foundation Trust Member of a working party convened by the Department of Health looking at the impact of	Noted and advised regards confidentiality. Participate at chair's discretion.

GDG meeting	Declaration of interest	Action taken
	new MHRA licensing requirements and the need for a Home Office Controlled Drugs licence on the supply of medicines to hospices and other bodies Deputy Accountable Officer for St Christopher's Hospice	
Second committee meeting 15 May	Same as recruitment	None
Third committee meeting (8 July 2015)	Same as recruitment	None
Fourth committee meeting (14 August)	Same as recruitment	None

Devina Halsall

GDG meeting	Declaration of interest	Action taken
Recruitment (24 November)	None	None
First committee meeting (9 February)	Employed by NHS England and University of Manchester. Research funding from Pharmacy Research UK	Noted and participate
Second committee meeting (15 May)	Same as recruitment	
Third committee meeting (8 July 2015)	Same as recruitment	
Fourth committee meeting (14 August)	Same as recruitment	

Roger Knaggs

GDG meeting	Declaration of interest	Action taken
Recruitment (25 November)	Honoraria from Napp Pharmaceuticals (November 2013) for attendance at an advisory board regarding an educational internet resource on opioids and Pfizer for a presentation at a local GP education meeting on neuropathic pain but no discussion of controlled drugs (May 14). No further personal financial interests are anticipated during the course of the development of this practice guideline. Research funding from Grűnenthal Ltd investigating trends in opioid prescribing and associated outcomes. Member, British Pain Society Council, Chair, Pain Management Group, United Kingdom Clinical Pharmacy Association,	Noted and advised regards confidentiality. Participate at chair's discretion.

GDG meeting	Declaration of interest	Action taken
	Member, Clinical subgroup for controlled drugs, Care Quality Commission and NHS England, Joint editor, Opioid Prescribing Resource, Faculty of Pain Medicine, Member, Working group developing pain prison formulary, Public Health England and NHS England	
First committee meeting (9 February)	None	None
Second committee meeting (15 May)	Research funding from MundiPharma Research on prescription opioid abuse European League Against Rheumatism June 2015 - The global use and abuse of opioids European Pain Federation September 2015 - Update on prescription opiod related harms and analysis of emerging data on misuse of gabapentin and pregabalin	Noted and advised regards confidentiality. Participate at chair's discretion.
Third committee meeting (8 July 2015)	None	None
Fourth committee meeting (14 August)	BBC1 Panorama (forthcoming programme on use of opioids in UK) Presentation Clinical Pharmacy Congress (April 2015): optimising medicines for pain	Noted and advised regards confidentiality. Participate at chair's discretion.

Lehane Ryland

GDG meeting	Declaration of interest	Action taken
Recruitment (28 November)	None	None
First committee meeting (9 February)	None	None
Second committee meeting (15 May 2015)	The National Substance Misuse Non-Medical Prescribers Forum - Steering group member and Wales lead. (appointed May 2015)	Noted and advised regards confidentiality. Participate at chair's discretion.
Third committee meeting (8 July 2015)	None	None
Fourth committee meeting (14 August)	None	None

Cathy Stannard

GDG meeting	Declaration of interest	Action taken
Recruitment (23 November)	I am co-ordinator and chair of a national group collating an Opioid Prescribing Resource that will be widely disseminated to prescribers to support informed clinical decision making when prescribing opioid medicines for pain.	Noted and advised regards confidentiality. Participate at chair's discretion.
First committee meeting (9 February)	Chair: Opioid Prescribing Resource Project (collaboration of clinicians and policymakers collating resource to promote safe opioid prescribing) Member: ACMD committee on misuse and illicit supply of medicines Member: CQC Controlled Drugs Clinical subgroup Lectures in past year: Royal Marsden Opioid Conference: Opioids for non-cancer pain Faculty of Pain Medicine: Update on opioids for non-cancer pain Pain Management in the addicted patient British Pain Society: update on the opioid prescribing resource ACMD committee on misuse and diversion of medicines: Diversion and illicit supply of medicines: a pain perspective Society for the Study of Addiction: Pain and problematic use of opioids Clinical Pharmacy Congress: optimising medicines for pain Neuropathic Pain International Meeting: proposer in debate Opioids have no role in neuropathic pain (May 2015) Papers Gaskell H, Moore RA, Derry S, and **Stannard C** Oxycodone for neuropathic pain and fibromyalgia in adults Cochrane Database Syst Rev. 2014 Jun 23;6:CD010692. doi: 10.1002/14651858.CD010692.pub2. Weisberg, Becker, Fiellin and Stannard Prescription opioid misuse in the United States and the United Kingdom: cautionary lessons	Noted and advised regards confidentiality. Participate at chair's discretion.

GDG meeting	Declaration of interest	Action taken
	Int J Drug Pol 2014;25; 1124-1130 Media BBC R4 Inside Health: opioids and pain BBC R4 Inside Health: impact of Drug Driving legislation for patients on painkillers BBC1 Panorama (currently filming programme on use of opioids in UK) features my high dose opioid service	
Second committee meeting (15 May)	Apologies	None
Third committee meeting (8 July)	None	None
Fourth committee meeting (14 August)	Apologies	None

Duncan Williams (recruited from 8 July 2015)

GDG meeting	Declaration of interest	Action taken
Recruitment (November 14)	NA	
First committee meeting (9 February)	NA	
Second committee meeting (15 May)	NA	
Third committee meeting (8 July 2015)	I am a practicing GP and Clinical Director of PSALT – a substance misuse provider to the NHS in Wales. I have advising roles to the Health Boards as a GP lead and substance misuse advice.	Noted and advised regards confidentiality. Participate at chair's discretion.
Fourth committee meeting (14 August)	Apologies	None

Colin Wilkinson

GDG meeting	Declaration of interest	Action taken
Recruitment (November 14)	None	None
First committee meeting (9 February)	None	None
Second committee meeting (15 May)	None	None
Third committee meeting (8 July 2015)	None	None
Fourth committee meeting (14 August)	None	None

Mark Woolcock

GDG meeting	Declaration of interest	Action taken

GDG meeting	Declaration of interest	Action taken
Recruitment (24 November)	None	None
First committee meeting (9 February)	None	None
Second committee meeting (15 May)	None	None
Third committee meeting (8 July 2015)	Apologies	None
Fourth committee meeting (14 August)	Apologies	None

A.2 NICE guideline development team and additional committee meeting attendees

Emma Aaron

GDG meeting	Declaration of interest	Action taken
Recruitment/First committee meeting (9 February)	None	None
Second committee meeting (15 May)	None	None
Third committee meeting (8 July 2015)	None	None
Fourth committee meeting (14 August)	None	None

Sarah Glover

GDG meeting	Declaration of interest	Action taken
Recruitment/First committee meeting (9 February)	None	None
Second committee meeting (15 May)	Did not attend	None
Third committee meeting (8 July 2015)	Did not attend	None
Fourth committee meeting (14 August)	Did not attend	None

Johanna Hulme

GDG meeting	Declaration of interest	Action taken
Recruitment/First committee meeting (9 February)	Member of the CQC Controlled drugs national group	Noted and participate
Second committee meeting (15 May)	None	None
Third committee meeting (8 July 2015)	None	None
Fourth committee meeting (14 August)	None	None

Ian Pye

GDG meeting	Declaration of interest	Action taken

GDG meeting	Declaration of interest	Action taken
Recruitment/First committee meeting (9 February)	None	None
Second committee meeting (15 May)	None	None
Third committee meeting (8 July 2015)	None	None
Fourth committee meeting (14 August)	None	None

Louise Shires

GDG meeting	Declaration of interest	Action taken
Recruitment/First committee meeting (9 February)	None	None
Second committee meeting (15 May)	Apologies	None
Third committee meeting (8 July 2015)	Apologies	None
Fourth committee meeting (14 August)	None	None

Appendix B: Scope

1.1 Topic

Through the medicines practice guideline topic selection process, the safe use and management of controlled drugs was identified as a priority area for guidance development.

1.2 Who the guideline is for

The guideline should be of value to a wide range of health and social care practitioners who encounter controlled drugs and those who are part of any processes involving controlled drugs.

Who should take action:

- Health professionals.
- Social care practitioners.
- Staff who have responsibility for security around controlled drugs.
- Providers of services where controlled drugs are used.
- Commissioners of care services using controlled drugs.
- Local authorities.

It may also be relevant for:

- People using services, families and carers and the public.
- Individual people and organisations delivering non-publicly funded services.
- Health and social care regulators.
- Secure environments.
- Police.
- Armed forces.
- Some voluntary services using controlled drugs.

NICE guidelines cover health and care in England. Decisions on how they apply in other UK countries are made by ministers in the Welsh Government, Scottish Government, and Northern Ireland Executive.

Equality considerations

NICE will carry out an equality impact assessment during scoping. The assessment will:

- list equality issues identified, and how they have been addressed
- explain why any groups are excluded from the scope, if this was done.

1 What the guideline is about

1.1 Who is the focus?

1.2.1 Groups that will be covered

- All health and social care practitioners.
- Organisations commissioning (for example clinical commissioning groups or local authorities), providing or supporting the provision of NHS and other publicly funded services using controlled drugs.
- Adults, young people and children (including neonates) using or taking controlled drugs, or those caring for these groups.

1.2 Settings

1.2.2 Settings that will be covered

- All settings, including people's own homes, where publicly funded health and social care[a] is delivered (see also section 'who the guideline is for').

1.2.3 Settings that will not be covered

- Care homes (this is covered by Managing medicines in care homes [2014] NICE guideline SC1).

1.3 Activities, services or aspects of care

1.2.4 Key areas that will be covered

1 Systems and processes that involve the use and management of scheduled 2, 3, 4 and 5 controlled drugs in the following areas:

   – Security

a This includes, but is not limited to: people's own homes; schools; Ministry of Defence; and ambulance services.

- Prescribing (including monitoring and advising patients on the safe use of controlled drugs)
- Supply (including dispensing, obtaining)
- Possession
- Storage (safe custody)
- Administration
- Recording
- Monitoring controlled drugs use
- Processes for sharing information between practitioners in different care settings
- Reporting, investigating and learning
- Destruction and disposal
- Transportation
- Diversion
- Managing controlled drugs in specific settings (for example prisons).

1.2.5 Areas that will not be covered

1 Schedule 1 of the Misuse of Drugs Regulations 2001 as they have no recognised medicinal use.

2 Treatment of specific clinical conditions.

3 Unlicensed and 'off label' use of controlled drugs.

4 Medicines specific shared care arrangements for controlled drug use across primary and secondary care.

5 Education and training of health and social care practitioners which falls under the remit of Health Education England.

6 Needle exchange services (this is covered by Needle and syringe programmes [2014] NICE guideline PH52).

7 Home care (this is covered by Home care NICE guideline in development, publication expected July 2015). This covers general personal care and practical support to people living in their own homes.

1.4 Economic aspects

Developers will take into account both clinical and cost effectiveness when making recommendations involving a choice between alternative interventions. A review of the economic evidence will be conducted and analyses will be carried out when

appropriate. The Committee developing the guideline will take into account resource implications when making recommendations for good practice. Further detail on the methods can be found in developing NICE guidelines: the manual.

1.5 Key issues and questions

For the safe use and management of controlled drugs for people, robust systems and processes are needed. The main key areas relating to controlled drug use include: prescribing, obtaining and supplying, administering, handling, recording and monitoring use. Recording information in relation to controlled drugs will be addressed throughout the guideline where relevant.

While writing this scope, we have identified the following key questions:

1 In line with legislation and regulation for scheduled 2, 3, 4 and 5 controlled drugs, what interventions, systems and processes are effective for **secure prescribing** to reduce controlled drugs related incidents, including patient-safety incidents?

2 In line with legislation and regulation for scheduled 2, 3, 4 and 5 controlled drugs, what interventions, systems and processes are effective for **obtaining and supplying** (including dispensing and requisitions) controlled drugs to reduce controlled drugs related incidents, including patient-safety incidents?

3 In line with legislation and regulation for scheduled 2, 3, 4 and 5 controlled drugs, what interventions, systems and processes are effective for **administering** controlled drugs to reduce controlled drugs related incidents, including patient-safety incidents?

4 In line with legislation and regulation for scheduled 2, 3, 4 and 5 controlled drugs, what interventions, systems and processes are effective for **handling** (including, storing, transporting, possessing, disposing and destroying) of controlled drugs to reduce controlled drugs related incidents, including patient-safety incidents?

5 In line with legislation and regulation for scheduled 2, 3, 4 and 5 controlled drugs, what interventions, systems and processes are effective for **monitoring**[b]

[b] Monitoring includes analysing, reporting incidents, recording harms, sharing information, sharing learning, addressing concerns and feedback.

of the use of controlled drugs to reduce controlled drugs related incidents, including patient-safety incidents?

1.6 Main outcomes

The main outcomes that will be considered when searching for and assessing the evidence are:

1 Controlled drug related **patient-safety incidents**[c], including but not limited to:
- potentially avoidable controlled drugs-related hospital admissions and readmissions
- prescribing errors
- inadequate review or follow-up of the person taking the controlled drug
- dispensing errors
- administration errors
- recording errors
- potentially avoidable adverse events
- missed doses of medicines
- near misses (a prevented medicines related patient safety incident which could have led to patient harm)
- misuse
- fatalities and serious harm.

2 Patient and carer reported outcomes such as shared decision making, quality of life, patient experience, patient satisfaction and medicines adherence, concordance and compliance.

3 Health and social care practitioner reported outcomes such as satisfaction and collaborative working.

4 Process measures as reported in the study or guidance, for example time taken to investigate controlled drugs related incident.

5 Controlled drug related incidents as reported in the study or guidance, including but not limited to:
- diversion (obtaining controlled drugs to sell on and theft)
- health and social care practitioner misuse

[c] Unintended or unexpected incidents that were specifically related to medicines use, which could have, or did, lead to patient harm.

- inadequate storage
- stock discrepancies
- record keeping
- monitoring use
- controlled stationery for example, prescriptions used to prescribe controlled drugs.

6 Compliance with legislation, regulation and national policy.

2 Links with other NICE guidance and NICE Pathways

2.1 NICE guidance

1.2.6 NICE guidance about the experience of people using NHS services

NICE has produced the following guidance on the experience of people using the NHS. This guideline will not include additional recommendations on these topics unless there are specific issues relating to the safe use and management of controlled drugs:

- Patient experience in adult NHS services (2012) NICE guideline CG138
- Service user experience in adult mental health (2011) NICE guideline CG136

1.2.7 NICE guidance in development that is closely related to this guideline

NICE is currently developing the following guidance that is closely related to this guideline:

- Medicines optimisation. NICE guideline. Publication expected March 2015.

2.2 NICE Pathways

When this guideline is published, the recommendations will be added to NICE Pathways. NICE Pathways bring together all related NICE guidance and associated products on a topic in an interactive topic-based flow chart.

3 Context

3.1 Key facts and figures

The key responsibilities for patient safety developed by the National Patient Safety Agency (NPSA)[d] transferred to NHS England in 2012. The system for reporting medicines related incidents in England and Wales is the National Reporting and Learning System (NRLS). Healthcare organisations report all patient safety incidents (including controlled drugs related patient safety incidents) to the NRLS. These incident reports are analysed to identify common risks to patients and opportunities to improve patient safety. Resources are developed to disseminate actionable learning from patient safety incident reports.

There were a number of reports of deaths and harm due to the administration of high dose (30mg or greater) diamorphine or morphine injections to patients who had not previously received doses of opioids. In response to this in May 2006, the NPSA issued a Safer Practice Notice Ensuring safer practice with high dose ampoules of diamorphine and morphine, which aimed to ensure that look-alike packages of morphine or diamorphine were not misselected.

Up to June 2008 the NRLS had received reports of 5 deaths and over 4,200 dose-related patient safety incidents concerning opioid medicines. A rapid response report was disseminated to healthcare organisations to review local medicines and prescribing policies, including standard operating procedures, to reduce dosing errors with opioid medicines.

There were 498 patient safety incidents between November 2004 and November 2008 reported to the NRLS where the dose of midazolam injections prescribed or administered to the patient was inappropriate. Three of these incidents resulted in death. A rapid response report was issued providing healthcare organisations with guidance to prevent future patient safety incidents.

[d] In June 2012, the key functions and expertise for patient safety developed by the National Patient Safety Agency (NPSA) transferred to NHS England.

A 7 year review[e] of medicines-related safety incidents concerning controlled drugs reported to the NRLS found the risk of death with controlled drug incidents was significantly greater than with medication incidents generally. Incidents involving overdose of controlled drugs accounted for 89 (69.5%) of the 128 incidents reporting of serious harm (death and severe harm). Five commonly used controlled drugs were responsible for 113 incidents (88.4%) leading to serious harm. A detailed review of the 128 incident reports associated with serious harm found that only 1 incident had been referred to the Controlled Drug Accountable Officer (CD AO).

The Care Quality Commission (CQC) has a statutory duty to oversee the safe management arrangements for controlled drugs in England. In addition to ensuring that the regulations are implemented, the CQC produce annual reports describing developments for managing the risks associated with handling and using controlled drugs. The most recent report The safer management of controlled drugs, Annual report 2013 outlines national trends on the safe use and management of controlled drugs. This report shows that the number of controlled drugs dispensed in primary care was similar to the number in 2012 but the costs increased by 10%.

The NHS Business Services Authority (NHS BSA) provides information on costs and trends in prescribing in England and Wales. The NHS BSA produces 2 sets of reports for controlled drug monitoring:

- comparator charts available for the last 2 quarters' prescribing data
- analysis reports that can be accessed via the information services portal (username and password required).

These reports monitor the prescribing of schedule 2 and 3 controlled drugs allowing CD AOs 'to highlight potential causes for concern within the prescribing of CDs through: demonstrating variance in the prescribing of controlled drugs between organisations, and by identifying prescribers or organisations exhibiting unusual prescribing behaviour'. The Health and Social Care Information Centre (HSCIC) also produces an annual report showing prescribing trends for dentists which includes controlled drugs.

[e] Cousins D, Gerrett D, Warner B (2013) A review of Controlled Drug incidents reported to the NRLS over seven years. Pharmaceutical Journal Vol 291

New regulations governing the safe use and management of controlled drugs came into force in April 2013 to ensure consistency with the new structure of the NHS. As a result of the implementation of the new regulations, all Local Intelligence Networks (LINs) have undergone changes to their core membership, processes and reporting arrangements which are currently being re-established.

There has been significant activity to help ensure the safe use and management of controlled drugs at a local and national level. However, ongoing activity and vigilance is required to sustain the positive developments that have been achieved since the change in the NHS structure. This guideline is needed to consider the following: changes to legislation and NHS structure; national polices; controlled drug related patient safety incidents; and evidence for effective interventions, to provide further clarity and good practice recommendations for the safe use and management of controlled drugs across all NHS settings. This guideline will support organisations to minimise harms associated with the use and management of controlled drugs by having robust systems and processes in place.

3.2 Current practice

Arrangements have been established to encourage good practice in the management of controlled drugs, as well as helping to detect unusual or poor clinical practice, systems criminal activity or risk to patients. Organisations have variable systems and processes in place for obtaining, storing, supplying, recording, monitoring, disposing of and destroying safely of controlled drugs, while at the same time helping to ensure appropriate and convenient access for those patients that require controlled drugs.

NHS England[f] CD AOs have a critical role in the management and safe use of controlled drugs, minimising harm to patients and feeding back local intelligence through LINs.

All health professionals who prescribe, dispense or administer controlled drugs are required to work within the legal and their professional frameworks to ensure safe use of controlled drugs.

[f] The NHS Commissioning Board was established in legislation in the Health and Social Care Act 2012 but is now known as NHS England.

New NHS governance structures are in place to support the safe reporting of medicines-related patient safety incidents through the NRLS, NHS England and Medicines and Healthcare products Regulatory Agency (MHRA). This network discusses potential and recognised safety issues and identifies trends and actions to improve the safe use of medicines.

3.3 Policy, legislation, regulation and commissioning

1.2.8 Legislation, regulation and guidance

Since the Shipman Inquiry's Fourth Report in 2004, there have been significant legislative changes to the Misuse of Drugs Act 1971 introduced by the Government to strengthen the governance arrangements for controlled drugs.

Controlled drugs are defined and governed by the Misuse of Drugs Act 1971 and associated regulations. The Home Office is in charge of government policy on security-related issues including activities related to the Misuse of Drugs Act 1971. The Home Office controlled drugs list which includes the most commonly encountered drugs currently controlled under the misuse of drugs legislation and shows their respective classifications under both the Misuse of Drugs Act 1971 and the Misuse of Drugs Regulations 2001.

The Misuse of Drugs Regulations 2001 and subsequent amendments set out who is authorised to supply and possess controlled drugs. Robust arrangements for the management and use of controlled drugs are required to minimise patient harm, misuse and criminality.

The Health Act 2006 and its associated regulations – principally the Controlled Drugs (Supervision of Management and Use) Regulations 2006 - required that all designated bodies (for example NHS trusts) appointed a CD AO to govern the use and management of controlled drugs and to share intelligence on controlled drug issues.

The Health and Social Care Act 2012 abolished Primary Care Trusts (PCTs) from April 2013. This had a direct impact on the role of CD AOs and on PCT CD AOs who, in particular, had responsibility for leading controlled drug LIN meetings.

The Controlled Drugs (Supervision of Management and Use) Regulations 2013 carried forward the main provisions of the 2006 regulations and introduced new provisions to reflect the changes made to the structure of the NHS in England as a result of the Health and Social Care Act 2012. The responsibility for leading controlled drug LIN meetings now lies with NHS England CD AOs.

The Department of Health's information about the Controlled Drugs (Supervision of management and use) Regulations (2013) provides support and additional information about the changes made to the regulations which came into effect on 1 April 2013. The supporting information continues to promote good governance concerning the safe management and use of controlled drugs in England and Scotland. Wales and Northern Ireland have their own equivalent but separate regulations which are unaffected by these changes.

NHS England guidance The Controlled Drugs (Supervision of management and use) regulations 2013 Single Operating Model supports NHS England area teams in establishing their statutory responsibility in relation to the Controlled Drugs (Supervision of management and use) Regulations 2013.

NHS protect has a national responsibility for tackling criminal activities. This may include activities that involve controlled drugs. Their main aim is to ensure the safe and proper use of NHS resources and to protect NHS staff from activities that may affect the way in which care is delivered.

Professional and regulatory bodies have good practice guidance to ensure those using controlled drugs work within the legal framework and ensure safe use and management.

Significant legislative changes that have been introduced over the years and the key documents outlined above will be used to inform this guideline. In addition, evidence will be used to identify robust systems and processes for the safe use and management of controlled drugs to develop good practice. This guideline will provide good practice recommendations that are in line with legislation and regulations, and that support health and social care practitioners to improve the safe use and management of controlled drugs.

4 Further information

This is the final scope. The consultation dates were 3 November to 1 December 2014.

The guideline is expected to be published in March 2016.

You can follow progress of the guideline.

Our website has information about how NICE guidelines are developed.

Appendix C: How this guideline was developed

C.1 Search strategies for the guideline

C.1.1 Scoping searches

Scoping searches were undertaken on the following websites and databases (listed in alphabetical order) in August 2014 to provide information for scope development and project planning. Browsing or simple search strategies were employed.

- Advisory Council on the Misuse of Drugs
- BNF (2014)
- Canadian Medical Association Infobase
- Care Quality Commission
- CDSR
- Clinical Knowledge Summaries
- COMET (Core Outcome Measures in Effectiveness Trials)
- DARE
- Department of Health
- DUETS (UK Database of Uncertainties about the Effects of Treatments)
- Guidelines International Network (GIN)
- Healthtalk Online
- HEED
- HM Government
- HTA Database
- Joint Royal Colleges Ambulance Liaison Committee
- Map of Medicine
- Midwives
- Ministry of Health NZ
- National Health and Medical Research Council (Australia)
- National Institute for Health Research (NIHR) Health Technology Assessment Programme
- National prescribing centre (NPC)
- NHS Choices
- NHS EED

- NHS England
- NHS England clinical policies and statements for specialised services commissioning
- NICE Evidence Services
- NICE Guidance
- Nursing and Midwifery Council
- Patient UK
- Pharmaceutical Services Negotiating Committee Dispensing controlled drugs
- Professional bodies/associations/societies (include patient information)
- Prospero
- Royal College of Anaesthetists
- Royal College of GPs
- Royal College of Nursing
- Royal College of Obstetricians and Gynaecologists
- Royal College of Physicians
- Royal College of Psychiatrists
- Royal College of Surgeons
- SIGN
- The Home Office
- Trip database
- TRIP Database
- US National Guideline Clearinghouse
- YouthHealthTalk.

C.1.2 Main searches

Sources searched for the guideline

- Cochrane including CDSR, CENTRAL, DARE and HTA
- Embase
- Medline
- Medline in Process
- PsycINFO
- PubMed

Identification of evidence for clinical questions

The searches were conducted between February 2015 and April 2015.The aim of the searches was to identify evidence for each of the clinical questions. The MEDLINE search strategies and details of sources searched for each question are presented below. They were translated for use in all other databases.

C.1.2.1 Review question 1

In line with legislation and regulation for scheduled 2, 3, 4 and 5 controlled drugs, what interventions, systems and processes are effective and cost effective for the **prescribing process** to reduce **controlled drugs related incidents**, including **patient-safety incidents?**

C.1.2.2 Review question 2

In line with legislation and regulation for scheduled 2, 3, 4 and 5 controlled drugs, what interventions, systems and processes are effective and cost effective for **obtaining and supplying** (including dispensing and requisitions) controlled drugs to reduce **controlled drugs-related incidents**, including **patient-safety incidents**?Insert search strategy

C.1.2.3 Review question 3

In line with legislation and regulation for scheduled 2, 3, 4 and 5 controlled drugs, what interventions, systems and processes are effective and cost effective for administering controlled drugs to reduce controlled drugs related incidents, including patient-safety incidents?

C.1.2.4 Review question 4

In line with legislation and regulation for scheduled 2, 3, 4 and 5 controlled drugs, what interventions, systems and processes are effective and cost effective for handling (including, storing, transporting, possessing, disposing and destroying) of controlled drugs to reduce controlled drugs related incidents, including patient-safety incidents?

C.1.2.5 Review question 5

In line with legislation and regulation for scheduled 2, 3, 4 and 5 controlled drugs, what interventions, systems and processes are effective and cost effectiveness for monitoring use (including, analysing, identifying and reporting incidents, recording harms, sharing information, sharing learning, addressing concerns, feedback) of controlled drugs to reduce controlled drugs related incidents, including patient-safety incidents?

C.1.2.6 Search strategies

Two strategies were developed to answer all the review questions. The Medline versions can be found here:

MEDLINE strategy 1:

Database: Ovid MEDLINE(R) <1946 to February Week 1 2015>

Search Strategy:

1 "Drug and Narcotic Control"/

2 Controlled Substances/

3 controlled drug*.tw.

4 controlled substanc*.tw.

5 controlled medicine*.tw.

6 controlled narcotic*.tw.

7 or/1-6

8 animals/ not humans/

9 7 not 8

10 limit 9 to english language

11 limit 10 to (letter or news or newspaper article)

12 10 not 11

MEDLINE strategy 2:

Database: Ovid MEDLINE(R) <1946 to March Week 1 2015>

Search Strategy:

---

1 Benzodiazepines/

2 benzodiazepine*.tw.

3 "Hypnotics and Sedatives"/

4 (sedative* or hypnotic*).tw.

5 Analgesics, Opioid/

6 (opioid* or opiat*).tw.

7 Central Nervous System Stimulants/

8 analeptic*.tw.

9 (central adj1 stimulant*).tw.

10 (central adj1 nervous adj1 stimulant*).tw.

11 (CNS adj1 stimulant*).tw.

12 Barbiturates/

13 barbiturate*.tw.

14 Narcotics/

15 narcotic*.tw.

16 or/1-15

17 exp Prescriptions/

18 Drug Prescriptions/

19 Prescription Drugs/

20 (e-prescript* or e prescript* or eprescript* or e-prescrib* or e prescrib* or eprescrib*).tw.

21 (electronic* adj1 (prescrib* or prescript*)).tw.

22 Point-of-care systems/

23 (point-of-care adj1 system*).tw.

24 Physician's practice patterns/

25 Dentist's practice patterns/

26 ((prescrib* or prescript*) adj1 (process* or system* or intervention* or procedure* or method* or over or inappropriate or anticipat*)).tw.

27 Inappropriate Prescribing/

28 Prescription Drug Diversion/

29 (diversion adj4 (incident* or prescript* or prescrib* or drug* or medication* or medicin* or abus* or opioid* or misus* or non-prescript* or non-prescrib* or addict* or illicit* or illegal*)).tw.

30 Prescription Drug Misuse/

31 nmupd.tw.

32 Drug Dosage Calculations/

33 ((drug* or medication* or medicin* or pharmaceutical) adj1 (calculat* or arithmetic*)).tw.

34 (out of hours or out-of-hours or after-hours or after hours).tw.

35 (unsocia* adj1 hour*).tw.

36 (point of sale* or point-of-sale*).tw.

37 refill*.tw.

38 exp Drug Utilization/ or "Drug Utilization Review"/

39 ((drug* or medicin*) adj1 (utilis* or utiliz*)).tw.

40 ((medication* or medicin* or drug* or dos*) adj2 (review* or assess*)).tw.

41 Polypharmacy/

42 polypharmacy.tw.

43 Medication Reconciliation/

44 Reconciliation*.tw.

45 or/17-44

46 pharmaceutical services/ or community pharmacy services/ or pharmacy service, hospital/ or Pharmacies/ or Pharmacists/

47 (pharmac* adj1 (service* or care* or communit* or hospital*)).tw.

48 requisition*.tw.

49 (dispense* or dispensing).tw.

50 Pharmaceutical Preparations/sd [Supply & Distribution]

51 ((medicin* or medication* or drug* or opioid* or dos* or prescrib* or prescript* or days or disrupt* or emergenc* or stock*) adj4 (supply* or supplie*)).tw.

52 wholesale*.tw.

53 exp Fraud/

54 (fraud* or falsif* or forger* or forged or forges or deceive* or deception* or dishonest*).tw.

55 ((take* or mail* or send or sent) adj1 back).tw.

56 (stock* adj1 (maintain* or control* or balance* or level* or expire* or expiry or return*)).tw.

57 exp Medication Systems/

58 ((medication* or hospital* or pharmac*) adj1 system*).tw.

59 (drug adj1 distribution adj1 system*).tw.

60 "Forms and Records Control"/

61 Dosage forms/

62 ((manag* or control* or drug* or medication* or medicin* or dos*) adj1 (record* or form*)).tw.

63 (record* adj1 keep*).tw.

64 ((medication* or medicin*e) adj1 complian*).tw.

65 or/46-64

66 Pharmaceutical Preparations/ad [Administration & Dosage]

67 Directly Observed Therapy/

68 (direct* adj1 observ*).tw.

69 ((witness* or oversee*) adj1 (ingest* or inject* or transdermal* or patch* or intravenous* or oral* or dos* or admin* or treatment* or consumption)).tw.

70 ((supervised or unsupervised) adj1 (consumption or treatment* or dos* or ingest* or inject* or transdermal* or patch* or intravenous* or oral* or syringe* or pump*)).tw.

71 ((single* or double* or cross*) adj1 check*).tw.

72 "Attitude of Health Personnel"/

73 Clinical Competence/

74 (unused or leftover* or left-over* or recycl* or re-us*).tw.

75 (spilled or spills or spillage).tw.

76 Risk assessment/ or Risk Management/

77 Medication errors/

78 Medical errors/

79 ((medication or drug* or medical or medicin*) adj2 (error* or mistake* or incident* or harm* or near-miss* or near miss* or untoward)).tw.

80 exp Professional Role/

81 ((professional* or nurse* or physician* or doctor*) adj1 (role* or standard*)).tw.

82 Patient care team/ or patient care planning/

83 Physician-patient relations/

84 Health Knowledge, Attitudes, Practice/

85 Patient education as topic/

86 Patient education handout/

87 Pamphlets/

88 Patient medication knowledge/

89 Needs Assessment/

90 Information Centers/

91 Information Services/

92 Health Education/

93 Counseling/

94 Social Support/

95 Self-Help Groups/

96 Self Care/

97 ((patient* or parent* or famil* or relative* or carer* or caregiver* or care-giver* or spous* or husband* or wife* or wive* or partner*) adj6 (educat* or informat* or communicat* or pamphlet* or handout* or hand-out* or hand out* or booklet* or leaflet* or support* or need* or advice* or advis*)).ti.

98 ((patient* or parent* or famil* or relative* or carer* or caregiver* or care-giver* or spous* or husband* or wife* or wive* or partner*) adj6 (counsel* or selfhelp* or self-help* or self help* or selfcar* or self-car* or self car*)).ti.

99 Consumer Health Information/

100 patient* diar*.tw.

101 Telemedicine/

102 (telemedicine or mhealth*).tw.

103 (mobile adj1 health).tw.

104 or/66-103

105 Drug Storage/

106 ((handl* or manufactur* or distribut* or import or imports or importing or imported or export* or ship*) adj1 (drug* or medicin* or medication* or dos* or stock* or supplie or supply)).tw.

107 ((tamper* or abus*) adj4 (deter* or resist*)).tw.

108 (store* or stora* or storing).tw.

109 Drug Packaging/ or Drug labeling/

110 ((Drug* or medicin* or medication* or substance*) adj1 (packag* or container* or closure*)).tw.

111 (safe* adj4 custody).tw.

112 exp Safety Management/

113 ((safe* or hazard*) adj1 (control* or manage*)).tw.

114 (hazard* adj1 surveill*).tw.

115 Security Measures/

116 secur*.tw.

117 Theft/ [prevention and control]

118 exp Transportation/

119 ((transport or transports or transportation) adj1 (drug* or medicin* or medication* or dos* or stock* or supplie* or supply)).tw.

120 Travel/

121 ((travel* or distribut*) adj1 (drug* or medicin* or medication* or dos* or stock* or supplie* or supply)).tw.

122 Controlled Substances/sd [Supply & Distribution]

123 Medical Waste Disposal/

124 Dental Waste/

125 Refuse Disposal/

126 Waste disposal, fluid/

127 ((destruction* or destroy* or dispose or disposal*) adj4 (safe* or needle* or syring* or medication* or dos* or drug* or medicin* or substance* or option* or program* or proper* or unused)).tw.

128 ((unauthori* or illicit* or illegal* or unlawful* or unofficial*) adj1 (staff or personnel or access*)).tw.

129 or/105-128

130 (Local adj1 Intelligence adj1 Network*).tw.

131 LINs.tw.

132 (controlled adj1 drug* adj1 accountable* adj1 officer*).tw.

133 CDAO*.tw.

134 exp Medical records, computerized/

135 ((health or medical or drug* or medication* or medicin*) adj4 (information adj4 exchange*)).tw.

136 Datasets as topic/

137 Information Dissemination/

138 ((information or data or intelligence or learning or audit or barrier or incident) adj1 (shar* or distribut* or disseminat* or collect* or record* or system* or process* or report*)).tw.

139 Drug Monitoring/

140 ((drug* or substance* or medicin* or medication*) adj1 (monitor* or report*)).tw.

141 Mandatory Reporting/

142 (report* adj1 (mandat* or misus* or abus*)).tw.

143 Databases as Topic/

144 Databases, Factual/ or databases pharmaceutical/ or medication systems, hospital/

145 Documentation/

146 (data* adj1 (entry or entries or enter* or access*)).tw.

147 Clinical Pharmacy Information Systems/ or Hospital Information Systems/ or Medication systems, hospital/ or Medical order entry systems/

148 Pharmacy Administration/

149 ((anaesthesi* or anesthesi*) adj1 (information adj1 manag* adj1 system*)).tw.

150 Drug information services/

151 Adverse drug reaction reporting system/

152 Quality improvement/

153 (quality adj1 improv*).tw.

154 (implement* adj2 (learn* or improv*)).tw.

155 or/130-154

156 45 or 65 or 104 or 129 or 155

157 16 and 156

158 animals/ not humans/

159 157 not 158

160 limit 159 to english language

161 limit 160 to (letter or news or newspaper article)

162 160 not 161

163 "Drug and Narcotic Control"/

164 Controlled Substances/

165 controlled drug*.tw.

166 controlled substanc*.tw.

167 controlled medicine*.tw.

168 controlled narcotic*.tw.

169 or/163-168

170 animals/ not humans/

171 169 not 170

172 limit 171 to english language

173 limit 172 to (letter or news or newspaper article)

174 172 not 173

175 162 not 174

C.1.2.7 Study design filters

No study design filters were applied to the searches

C.1.2.8 Citation searches

Sources searched:

- Google Scholar
- Web of Science

In June and July 2015 searches were conducted using papers that were selected to inform the recommendations to see if the papers which cited them were also relevant.

C.1.2.9 Additional website searches

In March 2015 the following websites were searched, browsing or simple search strategies were employed:

- Audit Commission
- Care Quality Commission
- Guidelines and Audit Implementation Network
- Health and Social Care Information Centre
- MHRA
- National Audit Office
- National Clinical Audit and Patient Outcomes Programme
- Public Health England
- The General Dental Council
- The General Medical Council
- The General Pharmaceutical Council
- The Health and Care Professions Council
- The Nursing and Midwifery Council
- UK Data Service

C.1.3 Economic evaluations and quality of life data

Sources searched to identify economic evaluations

- DARE
- Embase
- MEDLINE
- MEDLINE in-Process
- NHS EED

Health economics studies

Economic searches were undertaken for all review questions. Filters were applied to the clinical search strategy. The searches were carried out within the same time period as the clinical searches.

Health economics filters

The MEDLINE economic evaluations and quality of life search filters are presented below. They were translated for use in the MEDLINE In-Process and Embase databases.

Economic evaluations filter

1 Economics/

2 exp "Costs and Cost Analysis"/

3 Economics, Dental/

4 exp Economics, Hospital/

5 exp Economics, Medical/

6 Economics, Nursing/

7 Economics, Pharmaceutical/

8 Budgets/

9 exp Models, Economic/

10 Markov Chains/

11 Monte Carlo Method/

12 Decision Trees/

13 econom*.tw.

14 cba.tw.

15 cea.tw.

16 cua.tw.

17 markov*.tw.

18 (monte adj carlo).tw.

19 (decision adj3 (tree* or analys*)).tw.

20 (cost or costs or costing* or costly or costed).tw.

21 (price* or pricing*).tw.

22 budget*.tw.

23 expenditure*.tw.

24 (value adj3 (money or monetary)).tw.

25 (pharmacoeconomic* or (pharmaco adj economic*)).tw.

26 or/1-25

Quality of life filter

1. "Quality of Life"/
2. quality of life.tw.
3. "Value of Life"/
4. Quality-Adjusted Life Years/
5. quality adjusted life.tw.
6. (qaly* or qald* or qale* or qtime*).tw.
7. disability adjusted life.tw.
8. daly*.tw.
9. Health Status Indicators/
10. (sf36 or sf 36 or short form 36 or shortform 36 or sf thirtysix or sf thirty six or shortform thirtysix or shortform thirty six or short form thirtysix or short form thirty six).tw.
11. (sf6 or sf 6 or short form 6 or shortform 6 or sf six or sfsix or shortform six or short form six).tw.
12. (sf12 or sf 12 or short form 12 or shortform 12 or sf twelve or sftwelve or shortform twelve or short form twelve).tw.
13. (sf16 or sf 16 or short form 16 or shortform 16 or sf sixteen or sfsixteen or shortform sixteen or short form sixteen).tw.
14. (sf20 or sf 20 or short form 20 or shortform 20 or sf twenty or sftwenty or shortform twenty or short form twenty).tw.
15. (euroqol or euro qol or eq5d or eq 5d).tw.
16. (qol or hql or hqol or hrqol).tw.
17. (hye or hyes).tw.
18. health* year* equivalent*.tw.
19. utilit*.tw.
20. (hui or hui1 or hui2 or hui3).tw.
21. disutili*.tw.

22. rosser.tw.

23. quality of wellbeing.tw.

24. quality of well-being.tw.

25. qwb.tw.

26. willingness to pay.tw.

27. standard gamble*.tw.

28. time trade off.tw.

29. time tradeoff.tw.

30. tto.tw.

31. or/1-30

C.2 Review questions and review protocols

C.2.1 Prescribing controlled drugs

	Details	Additional comments
Review question a)	In line with legislation and regulation for scheduled 2, 3, 4 and 5 controlled drugs, what interventions, systems and processes are effective and cost effective for the **prescribing process** to reduce **controlled drugs related incidents**, including **patient-safety incidents**?	
Objectives	To determine the effectiveness of interventions, systems and processes that can be used when prescribing controlled drugs to reduce controlled drugs related incidents, including patient-safety incidents. For the purpose of this review question prescribing in line with legislation and regulation includes: • prescribing • safety in relation to prescribed dosages and instructions • involving patients when prescribing controlled drugs • keeping contemporaneous records when prescribing controlled drugs • sharing information in line with data protection.	
Type of review	Intervention.	
Language	English only.	
Legislation and regulation	Misuse of Drugs (Supply to Addicts) Regulations1997, and subsequent amendments). Misuse of Drugs Regulations 2001 and subsequent amendments). The Controlled Drugs (Supervision of Management and Use) Regulations 2013. Home Office	

	Details	Additional comments
Policy	Controlled Drugs (Supervision of management and use) Regulations 2013: Information about the Regulations. Care Quality Commission (CQC). Medicines and Healthcare products Regulatory Agency (MHRA). NHS Protect. NHS England.	
Study design/ evidence type	• NICE accredited guidance. • Systematic review of randomised controlled trials (RCTs). • RCTs. It is unlikely that there will be RCTs found for this review question. If insufficient evidence is available progress to: • Other national guidance from the UK, Europe and other countries with similar developed health systems, for example Australia, Canada and New Zealand. • Systematic reviews of non-randomised controlled trials. • Non-randomised controlled trials. • Observational studies. • Pre and post intervention studies (before and after). • Time series studies. • Case series. • Qualitative studies. • Audit reports.	
Status	Published papers.	
Population	Health professionals who prescribe scheduled 2, 3, 4 and 5 controlled drugs as part of their practice. Prescribing in different care settings.	
Interventions, systems and processes	The following interventions, systems or processes relating to prescribing should be included within the review: • interventions that may impact on the effectiveness of prescribing of controlled drugs (including calculation of doses) • patient and carer involvement when prescribing controlled dugs including advice on use and handling • review and follow-up of controlled drug use and subsequent issue of prescriptions • prescribing (and communication) of controlled drugs by more than one health professional • use of NHS England patient safety guidance or other relevant guidance when prescribing or other alerts • prescribing of more than 1 controlled drug or more than one formulation of the same controlled drug for the same person • repeat prescribing for Scheduled 4 and 5 controlled drugs • anticipatory prescribing.	
Comparator	Other intervention groups using different systems/processes or control groups. Usual care.	
Outcomes	• Controlled drug related **patient-safety incidents** relating to prescribing including: ○ prescribing errors	Critical and important outcomes:

	Details	Additional comments
	○ over-prescribing or under-prescribing ○ inadequate review or follow up of the person taking the controlled drug ○ potentially avoidable adverse events, including controlled drugs-related hospital admissions and readmissions, fatalities and serious harm ○ near misses (a prevented medicines related patient safety incident which could have led to patient harm). • Patient and carer reported outcomes such as shared decision making, quality of life, medicines adherence, concordance and compliance, patient experience and patient satisfaction. • Controlled drug related **incidents** related to prescribing as reported in the study or guidance including: ○ diversion (obtaining controlled drugs to sell on and theft) ○ health and social care practitioner misuse ○ controlled stationery for example, prescriptions used to prescribe controlled drugs. • Monitoring prescribing (includes analysing, reporting incidents, recording harms, sharing information, sharing learning, addressing concerns and feedback) – included in this protocol as an outcome, the details of the process will be included in review question e). • Compliance with legislation, regulation and national policy.	• Diversion • Potentially avoidable adverse events • Prescribing errors • Quality of life • Misuse • Inadequate review • Legislation and compliance
Other criteria for inclusion / exclusion of studies	Inclusion criteria: • Studies from the UK, Europe and other countries with similar developed health systems, for example Australia, Canada and New Zealand.	
Search strategies	A search has already been completed in August 2014 to identify secondary sources. The following additional secondary sources will be searched: • General Medical Council • General Dental Council • General Pharmaceutical Council • Public Health England • Nursing and Midwifery Council • Health Professional Council To identify primary literature the following databases will be searched: • Medline • Medline in Process • Embase • Cochrane (includes: CDSR, CENTRAL, DARE, HTA and NHS EED) To identify information on current practice the following will be searched: • Audit Commission • Guidelines & Audit Implementation Network	

	Details	Additional comments
	• Health & Social Care Information Centre • National Clinical Audit and Patient Outcomes Programme • National Audit Office • Bibliographic databases where required The following will be searched for information on statistics: • Health & Social Care Information Centre • UK Data Service • UK National Statistics To identify patient information, PsycInfo will be searched. No study design or other kinds of filters will be applied to the searches other than to identify any health economic literature, exclude animal studies and restrict to English language.	
Review strategies	Appraisal of evidence quality: • Legislation and national policy will not be appraised for quality. • For guidelines, these will be assessed for quality using the AGREE II criteria. • For studies, appropriate NICE methodology checklists will be used to appraise the quality of individual studies. All key outcomes from evidence will be presented in GRADE profiles, where possible. Synthesis of data: • Data on all included studies will be extracted into evidence tables. • Where possible, data may be pooled to give an overall summary effect. • Where data cannot be pooled, narrative summaries of the data will be presented.	
Identified papers from scoping search and GDG experience for background.		

C.2.2 Obtaining and supplying controlled drugs

	Details	Additional comments
Review question b)	In line with legislation and regulation for scheduled 2, 3, 4 and 5 controlled drugs, what interventions, systems and processes are effective and cost effective for **obtaining and supplying** (including dispensing and requisitions) controlled drugs to reduce **controlled drugs-related incidents**, including **patient-safety incidents**?	
Objectives	To determine the effectiveness of interventions, systems and processes that can be used for obtaining and supplying controlled drugs.	

	Details	Additional comments
	For the purpose of this review question obtaining and supplying of controlled drugs in line with legislation and regulation includes: • obtaining - that is purchasing from wholesalers or pharmacies for practice use or stock • supplying (including supply to people who buy over-the-counter Schedule 5 controlled drugs) • dispensing • use of requisitions for controlled drugs • record keeping.	
Type of review	Intervention.	
Language	English only.	
Legislation and regulation	Misuse of Drugs (Supply to Addicts) Regulations1997, and subsequent amendments). Misuse of Drugs Regulations 2001 and subsequent amendments). The Controlled Drugs (Supervision of Management and Use) Regulations 2013. Home Office	
Policy	Controlled Drugs (Supervision of management and use) Regulations 2013: Information about the Regulations. Care Quality Commission (CQC). Medicines and Healthcare products Regulatory Agency (MHRA). NHS Protect. NHS England.	
Study design/ evidence type	• NICE accredited guidance. • Systematic review of randomised controlled trials (RCTs). • RCTs. It is unlikely that there will be RCTs found for this review question. If insufficient evidence is available progress to: • Other national guidance UK, Europe and other countries with similar developed health systems, for example Australia, Canada and New Zealand. • Systematic reviews of non-randomised controlled trials. • Non-randomised controlled trials. • Observational studies. • Pre and post intervention studies (before and after). • Time series studies. • Case series. • Qualitative studies. • Audit reports.	
Status	Published papers.	
Population	Anyone who is involved in the obtaining and supply of scheduled 2, 3, 4 and 5 controlled drugs. Obtaining and supplying in different care settings.	
Interventions, systems and processes	The following interventions, systems or processes relating to obtaining/supplying of controlled drugs should be included within the review: • use and completion of controlled drugs requisitions	

	Details	Additional comments
	• dispensing controlled drugs prescriptions • appropriateness of prescription/requisition: clinical appropriateness (e.g. formulation), appropriate dispensing checks to ensure the controlled drug is being provided to the right person as intended • obtaining/supplying controlled drugs • record keeping in relation to the obtaining and supply of controlled drugs • supplying controlled drugs where the total quantity initially requested cannot be supplied (where an owing is generated due to the quantity prescribed not being available) – this applies to both requisitions and prescriptions • supply of controlled drugs to those prescribed them (including appropriateness of medicine compliance aids) • Patient information, asking for ID/additional processes that the patient may be asked to undertake as it is a controlled drug.	
Comparator	Other intervention groups using different systems/processes or control groups. Usual care.	
Outcomes	• Controlled drugs related **patient-safety incidents** relating to obtaining and supplying including: ○ over or under supply of stock ○ dispensing delays ○ dispensing errors ○ insufficient or inaccurate recording relating to obtaining and supplying. • Controlled drug related **incidents** relating to obtaining and supplying as reported in the study or guidance, including: ○ fraud ○ diversion (obtaining controlled drugs to sell on and theft) ○ health and social care practitioner misuse ○ inadequate storage of obtained and supplied controlled drugs ○ stock discrepancies in supply ○ monitoring use, reporting concerns (including concerns about patterns of prescribing) ○ controlled stationery for example, prescriptions used to prescribe controlled drugs. • Patient and carer reported outcomes such as shared decision making, quality of life, medicines adherence, concordance and compliance, patient experience and patient satisfaction. • Compliance with legislation, regulation and national policy.	Critical and important outcomes: • Dispensing errors • Fraud • Diversion • Legislation • Access to medicines (delays) • Practitioner misuse • Monitoring use, reporting concerns (including concerns about patterns of prescribing)
Other criteria for inclusion / exclusion of studies	Inclusion criteria: • Studies from the UK, Europe and other countries with similar developed health systems, for example Australia, Canada and New Zealand.	
Search strategies	A search has already been completed in August 2014 to identify secondary sources. The following additional secondary sources will be searched: • General Medical Council	

	Details	Additional comments
	• General Dental Council • General Pharmaceutical Council • Public Health England • Nursing and Midwifery Council • Health Professional Council To identify primary literature the following databases will be searched: • Medline • Medline in Process • Embase • Cochrane (includes: CDSR, CENTRAL, DARE, HTA and NHS EED) To identify information on current practice the following will be searched: • Audit Commission • Guidelines & Audit Implementation Network • Health & Social Care Information Centre • National Clinical Audit and Patient Outcomes Programme • National Audit Office • Bibliographic databases where required The following will be searched for information on statistics: • Health & Social Care Information Centre • UK Data Service • UK National Statistics To identify patient information, PsycInfo will be searched. No study design or other kinds of filters will be applied to the searches other than to identify any health economic literature, exclude animal studies and restrict to English language.	
Review strategies	Appraisal of evidence quality: • Legislation and national policy will not be appraised for quality. • For guidelines, these will be assessed for quality using the AGREE II criteria. • For studies, appropriate NICE methodology checklists will be used to appraise the quality of individual studies. All key outcomes from evidence will be presented in GRADE profiles, where possible. Synthesis of data: • Data on all included studies will be extracted into evidence tables. • Where possible, data may be pooled to give an overall summary effect. • Where data cannot be pooled, narrative summaries of the data will be presented.	
Identified papers from		

	Details	Additional comments
scoping search and GDG experience for background		

C.2.3 Administering controlled drugs

	Details	Additional comments
Review question c)	In line with legislation and regulation for scheduled 2, 3, 4 and 5 controlled drugs, what interventions, systems and processes are effective and cost effective for **administering** controlled drugs to reduce **controlled drugs related incidents**, including **patient-safety incidents**?	
Objectives	To determine the effectiveness of interventions, systems and processes that can be used for administering (including self-administration, supervised self-administration and administration by others) controlled drugs. For the purposes of this review question administering in line with legislation and regulation includes: • review of prescriptions by those administering the controlled drugs (e.g. using clinical judgement to determine the prescription is appropriate for the individual) • checking of correct controlled drug, dose, expiry, route of administration (including single, double checking) • record keeping • stock checking, prior to and after administration • administration by designated individuals or carers • self-administration/ supervised self-administration/ consumption • different routes of administration • syringe driver administration • intravenous administration.	
Type of review	Intervention.	
Language	English only.	
Legislation and regulation	Misuse of Drugs (Supply to Addicts) Regulations1997, and subsequent amendments). Misuse of Drugs Regulations 2001, and subsequent amendments). The Controlled Drugs (Supervision of Management and Use) Regulations 2013. Home Office	
Policy	Controlled Drugs (Supervision of management and use) Regulations 2013: Information about the Regulations. Care Quality Commission (CQC). Medicines and Healthcare products Regulatory Agency (MHRA). NHS Protect. NHS England.	
Study design/ evidence type	• NICE accredited guidance. • Systematic review of randomised controlled trials (RCTs).	

	Details	Additional comments
	• RCTs. It is unlikely that there will be RCTs found for this review question. If insufficient evidence is available progress to: • Other national guidance UK, Europe and other countries with similar developed health systems, for example Australia, Canada and New Zealand. • Systematic reviews of non-randomised controlled trials. • Non-randomised controlled trials. • Observational studies. • Pre and post intervention studies (before and after). • Time series studies. • Case series. • Qualitative studies. • Audit reports.	
Status	Published papers.	
Population	Anyone who is involved in the administration of prescribed scheduled 2, 3, 4 and 5 controlled drugs. Administration of controlled drugs in different care settings.	
Interventions, systems and processes	The following interventions, systems or processes relating to the administration of controlled drugs should be included within the review: • facilitating those administering controlled drugs to query prescriptions where appropriate • support for safe administration, including calculation of doses • measuring doses that are proportions of single dose units (such as sachets or ampoules) or measuring doses from multiple dose bottles (including processes for disposing of and recording unused proportions) • handling spillages, unused or refused/partially administered controlled drugs • handling of used products that may have residual product such as (transdermal patches) • administration of different formulations of controlled drugs for example transdermal patches, intravenous, and oral. • syringe drivers or other pumps to administer controlled drugs, including patient controlled analgesia • record keeping • stock checking prior to administration • witnessing administration.	
Comparator	Other intervention groups using different systems/processes or control groups. Usual care.	
Outcomes	• Controlled drugs related **patient-safety incidents** relating to administration including: ○ administration errors ○ recording errors ○ insufficient or inaccurate stock control related to administration ○ potentially avoidable adverse events, including controlled drugs-related hospital admissions and readmissions,	Critical and important outcomes: • Potentially avoidable adverse events • Administration errors

	Details	Additional comments
	fatalities and serious harm ○ delayed and/or missed doses ○ near misses ○ misuse ○ fatalities and serious harm. • Controlled drug related **incidents** relating to administration as reported in the study or guidance, including: ○ fraud ○ diversion (obtaining controlled drugs to sell on and theft) ○ health and social care practitioner misuse ○ inadequate storage of controlled drugs ○ inadequate record keeping during and following administration of controlled drugs ○ controlled stationery for example, prescriptions used to prescribe controlled drugs ○ stock discrepancies following administration of a controlled drug. • Patient and carer reported outcomes such as shared decision making, quality of life, medicines adherence, concordance and compliance, patient experience and patient satisfaction. • Compliance with legislation, regulation and national policy.	• Fraud • Diversion • Legislation • Access to medicines (delays) • Record keeping • Quality of life
Other criteria for inclusion / exclusion of studies	Inclusion criteria: • Studies from the UK, Europe and other countries with similar developed health systems, for example Australia, Canada and New Zealand.	
Search strategies	A search has already been completed in August 2014 to identify secondary sources. The following additional secondary sources will be searched: • General Medical Council • General Dental Council • General Pharmaceutical Council • Public Health England • Nursing and Midwifery Council • Health Professional Council To identify primary literature the following databases will be searched: • Medline • Medline in Process • Embase • Cochrane (includes: CDSR, CENTRAL, DARE, HTA and NHS EED) To identify information on current practice the following will be searched: • Audit Commission • Guidelines & Audit Implementation Network • Health & Social Care Information Centre • National Clinical Audit and Patient Outcomes Programme	

	Details	Additional comments
	• National Audit Office • Bibliographic databases where required The following will be searched for information on statistics: • Health & Social Care Information Centre • UK Data Service • UK National Statistics To identify patient information, PsycInfo will be searched. No study design or other kinds of filters will be applied to the searches other than to identify any health economic literature, exclude animal studies and restrict to English language.	
Review strategies	Appraisal of evidence quality: • Legislation and national policy will not be appraised for quality. • For guidelines, these will be assessed for quality using the AGREE II criteria. • For studies, appropriate NICE methodology checklists will be used to appraise the quality of individual studies. All key outcomes from evidence will be presented in GRADE profiles, where possible. Synthesis of data: • Data on all included studies will be extracted into evidence tables. • Where possible, data may be pooled to give an overall summary effect. • Where data cannot be pooled, narrative summaries of the data will be presented.	
Identified papers from scoping search and GDG experience for background		

C.2.4 Handling controlled drugs

	Details	Additional comments
Review question d)	In line with legislation and regulation for scheduled 2, 3, 4 and 5 controlled drugs, what interventions, systems and processes are effective and cost effective for **handling** (including, storing, transporting, possessing, disposing and destroying) of controlled drugs to reduce **controlled drugs-related incidents**, including **patient-safety incidents**?	
Objectives	To determine the effectiveness of interventions, systems and processes that can be used to ensure the safe handling of controlled drugs. For the purpose of this review question handling of controlled drugs in line with regulation and legislation includes:	

	Details	Additional comments
	• storing (including stock checking) • transporting • possessing • disposing • destroying • record keeping.	
Type of review	Intervention.	
Language	English only.	
Legislation and regulation	Misuse of Drugs (Safe Custody) Regulations 1973. Misuse of Drugs Regulations 2001, and subsequent amendments). The Controlled Drugs (Supervision of Management and Use) Regulations 2013. Home Office Waste Management Regulations 2006.	
Policy	Controlled Drugs (Supervision of management and use) Regulations 2013: Information about the Regulations. Care Quality Commission (CQC). Medicines and Healthcare products Regulatory Agency (MHRA). NHS Protect. NHS England.	
Study design/ evidence type	• NICE accredited guidance. • Systematic review of randomised controlled trials (RCTs). • RCTs. It is unlikely that there will be RCTs found for this review question. If insufficient evidence is available progress to: • Other national guidance UK, Europe and other countries with similar developed health systems, for example Australia, Canada and New Zealand. • Systematic reviews of non-randomised controlled trials. • Non-randomised controlled trials. • Observational studies. • Pre and post intervention studies (before and after). • Time series studies. • Case series. • Qualitative studies. • Audit reports.	
Status	Published papers	
Population	Anyone who is involved in the handling of scheduled 2, 3, 4 and 5 controlled drugs. Handling in different care settings.	
Interventions, systems and processes	The following interventions, systems or processes relating to the handling of controlled drugs should be included within the review: • for ensuring controlled drugs are stored in line with regulations (including storage of expired controlled drugs and in doctor's bags) • for transporting controlled drugs	

	Details	Additional comments
	• for ensuring transfer records are appropriately completed and accessibility of records • for maintaining and reviewing stock balances of controlled drugs (maintaining a running balance of stock and physical reconciliation with stock levels) • for disposing of controlled drugs • for destroying controlled drugs • for handling expired stock • for the handling of patient returned controlled drugs and when patients have passed away, including record keeping • to protect against unauthorised access to controlled drugs, (including keys and key holders).	
Comparator	Other intervention groups using different systems/processes or control groups. Usual care.	
Outcomes	• Controlled drugs related **patient-safety incidents** relating to handling including: ○ recording errors ○ potentially avoidable adverse events, including controlled drugs-related hospital admissions and readmissions, fatalities and serious harm ○ missed doses/delayed of medicines ○ near misses (a prevented medicines related patient safety incident which could have led to patient harm) ○ misuse ○ fatalities and serious harm ○ unauthorised access to stored controlled drugs or incorrectly stored controlled drugs ○ insufficient or inaccurate recording relating to handling. • Patient and carer reported outcomes such as shared decision making, quality of life, medicines adherence, concordance and compliance, patient experience and patient satisfaction. • Controlled drug related **incidents** relating to handling as reported in the study or guidance, including: ○ diversion (obtaining controlled drugs to sell on and theft) ○ inadequate, incorrect or unsafe disposing of controlled drugs ○ inadequate, incorrect or unsafe destroying of controlled drugs ○ discrepancies in controlled drugs stock control related to handling ○ health and social care practitioner misuse ○ misuse of controlled stationery for example, prescriptions used to prescribe controlled drugs. • Compliance with legislation, regulation and national policy.	Critical/important outcomes: • Unauthorised access • Disposal • Destroying • Missed doses/delayed of medicines • Quality of life • Patient reported missed/delayed doses
Other criteria for inclusion / exclusion of studies	Inclusion criteria: • Studies from the UK, Europe and other countries with similar developed health systems, for example New Zealand, Australia and Canada	
Search strategies	A search has already been completed in August 2014 to identify secondary sources.	

	Details	Additional comments
	The following additional secondary sources will be searched: • General Medical Council • General Dental Council • General Pharmaceutical Council • Public Health England • Nursing and Midwifery Council • Health Professional Council To identify primary literature the following databases will be searched: • Medline • Medline in Process • Embase • Cochrane (includes: CDSR, CENTRAL, DARE, HTA and NHS EED) To identify information on current practice the following will be searched: • Audit Commission • Guidelines & Audit Implementation Network • Health & Social Care Information Centre • National Clinical Audit and Patient Outcomes Programme • National Audit Office • Bibliographic databases where required The following will be searched for information on statistics: • Health & Social Care Information Centre • UK Data Service • UK National Statistics To identify patient information, PsycInfo will be searched. No study design or other kinds of filters will be applied to the searches other than to identify any health economic literature, exclude animal studies and restrict to English language.	
Review strategies	Appraisal of evidence quality: • Legislation and national policy will not be appraised for quality. • For guidelines, these will be assessed for quality using the AGREE II criteria. • For studies, appropriate NICE methodology checklists will be used to appraise the quality of individual studies. All key outcomes from evidence will be presented in GRADE profiles, where possible. Synthesis of data: • Data on all included studies will be extracted into evidence tables. • Where possible, data may be pooled to give an overall summary effect.	

	Details	Additional comments
	• Where data cannot be pooled, narrative summaries of the data will be presented.	
Identified papers from scoping search and GDG experience for background		

C.2.5 Monitoring controlled drugs

	Details	Additional comments
Review question e)	In line with legislation and regulation for scheduled 2, 3, 4 and 5 controlled drugs, what interventions, systems and processes are effective and cost effectiveness for **monitoring** use (including, analysing, identifying and reporting incidents, recording harms, sharing information, sharing learning, addressing concerns, feedback) of controlled drugs to reduce **controlled drugs-related incidents**, including **patient-safety incidents**?	
Objectives	To determine the effectiveness of interventions, systems and processes that can be used for monitoring controlled drugs. For the purpose of this review question monitoring of controlled drugs in line with legislation and regulation includes: • analysing • identifying and reporting incidents • recording • sharing information • sharing learning • addressing concerns • feedback.	
Type of review	Intervention.	
Language	English only.	
Legislation and regulation	Misuse of Drugs (Supply to Addicts) Regulations1997, and subsequent amendments). Misuse of Drugs Regulations 2001, and subsequent amendments). The Controlled Drugs (Supervision of Management and Use) Regulations 2013. Home Office	
Policy	• Controlled Drugs (Supervision of management and use) Regulations 2013: Information about the Regulations. • Care Quality Commission (CQC). • Medicines and Healthcare products Regulatory Agency (MHRA). • NHS Protect. • NHS England.	
Study design/ evidence type	• NICE accredited guidance. • Systematic review of randomised controlled trials (RCTs). • RCTs.	

	Details	Additional comments
	It is unlikely that there will be RCTs found for this review question. If insufficient evidence is available progress to: • Other national guidance UK, Europe and other countries with similar developed health systems, for example Australia, Canada and New Zealand. • Systematic reviews of non-randomised controlled trials. • Non-randomised controlled trials. • Observational studies. • Pre and post intervention studies (before and after). • Time series studies. • Case series. • Qualitative studies. • Audit reports.	
Status	Published papers.	
Population	Health and social care practitioners and other designated individuals who are involved in the monitoring of scheduled 2, 3, 4 and 5 controlled drugs. Monitoring across different care settings.	
Interventions, systems and processes	The following interventions, systems or processes relating to monitoring of controlled drugs should be included within the review: • establishing and operating Local Intelligence Networks (LINs) • facilitating local and national intelligence gathering and sharing (information sharing), for example between different care settings and/or organisations or controlled drugs accountable officers (CD AOs) • incident reporting by health and social care practitioners or people prescribed controlled drugs (both national and local systems) • record keeping at organisational level and/or national level • analysis of prescribing data and/or reports of incidents to highlight any areas for concern with review of incidents and any required actions taken • addressing concerns and responding to untoward incidents • review of incidents including trends, and identifying any possible barriers to reporting • review of outcomes of incidents and feedback for health and social care practitioners and designated individuals of reported incidents • review of audit reports and implementation of any possible system improvements.	
Comparator	Other intervention groups using different systems/processes or control groups. Usual care.	
Outcomes	Clarity for organisations and health and social care practitioners around what constitutes an incident and a concern relating to controlled drugs and how these are managed internally and externally. • Controlled drug related **patient-safety incidents** relating to monitoring including:	Critical and important outcomes: • Identifying and reporting of

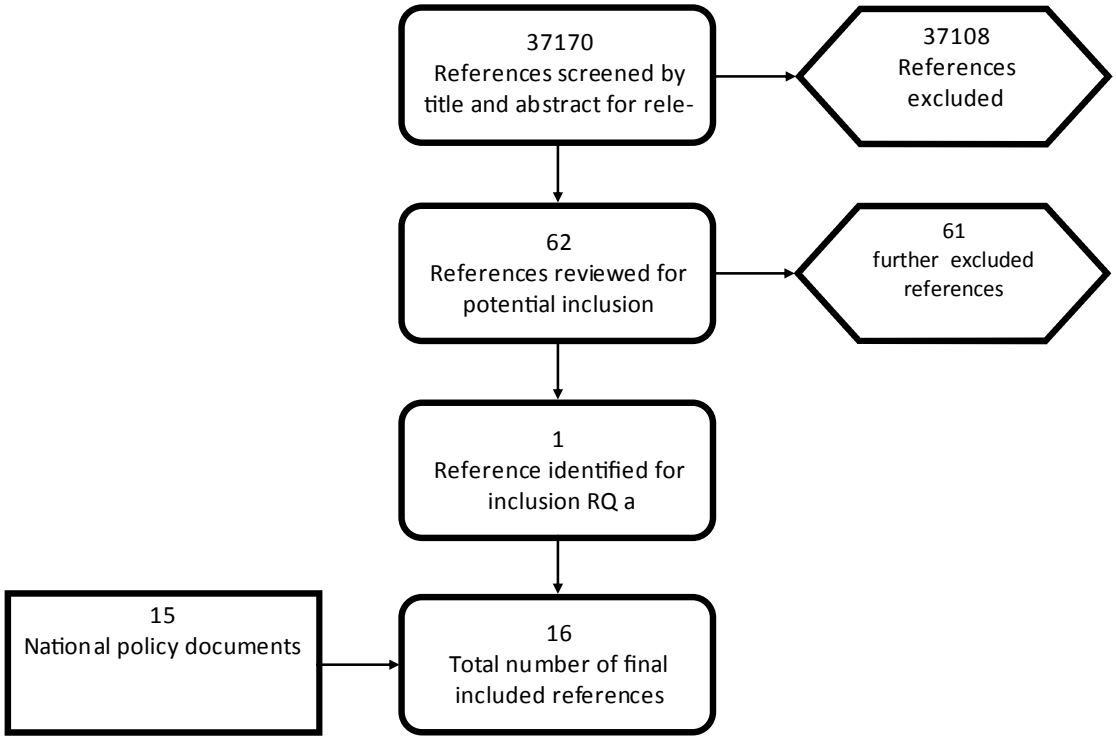
	Details	Additional comments
	○ identifying and reporting of incidents (or potential incidents) ○ reporting of concerns ○ insufficient or inaccurate recording ○ potentially avoidable adverse events ○ near misses ○ fatalities and serious harm. • Process measures as reported in the study or guidance, for example time taken to investigate controlled drugs related incident. • Controlled drug related **incidents** relating to monitoring as reported in the study or guidance, including: ○ diversion (obtaining controlled drugs to sell on and theft) ○ health and social care practitioner misuse ○ inadequate review of incidents (or potential incidents) ○ monitoring use (for example, excess controlled drug waste or controlled drugs obtained repetitively by the same person) ○ controlled stationery for example, prescriptions used to prescribe controlled drugs. • Health and social care practitioner reported outcomes such as satisfaction and collaborative working. • Compliance with legislation, regulation and national policy.	incidents (or potential incidents) • Diversion • Monitoring use • Misuse • Potentially avoidable adverse events • Health and social care practitioner reported outcomes • Process measures
Other criteria for inclusion / exclusion of studies	Inclusion criteria: • Studies from the UK, Europe and other countries with similar developed health systems, for example Australia, Canada and New Zealand.	
Search strategies	A search has already been completed in August 2014 to identify secondary sources. The following additional secondary sources will be searched: • General Medical Council • General Dental Council • General Pharmaceutical Council • Public Health England • Nursing and Midwifery Council • Health Professional Council To identify primary literature the following databases will be searched: • Medline • Medline in Process • Embase • Cochrane (includes: CDSR, CENTRAL, DARE, HTA and NHS EED) To identify information on current practice the following will be searched: • Audit Commission • Guidelines & Audit Implementation Network • Health & Social Care Information Centre • National Clinical Audit and Patient Outcomes Programme • National Audit Office	

	Details	Additional comments
	• Bibliographic databases where required The following will be searched for information on statistics: • Health & Social Care Information Centre • UK Data Service • UK National Statistics To identify patient information, PsycInfo will be searched. No study design or other kinds of filters will be applied to the searches other than to identify any health economic literature, exclude animal studies and restrict to English language.	
Review strategies	Appraisal of evidence quality: • Legislation and national policy will not be appraised for quality. • For guidelines, these will be assessed for quality using the AGREE II criteria. • For studies, appropriate NICE methodology checklists will be used to appraise the quality of individual studies. All key outcomes from evidence will be presented in GRADE profiles, where possible. Synthesis of data: • Data on all included studies will be extracted into evidence tables. • Where possible, data may be pooled to give an overall summary effect. • Where data cannot be pooled, narrative summaries of the data will be presented.	
Identified papers from scoping search and GDG experience for background		

C.3 Clinical consort diagrams

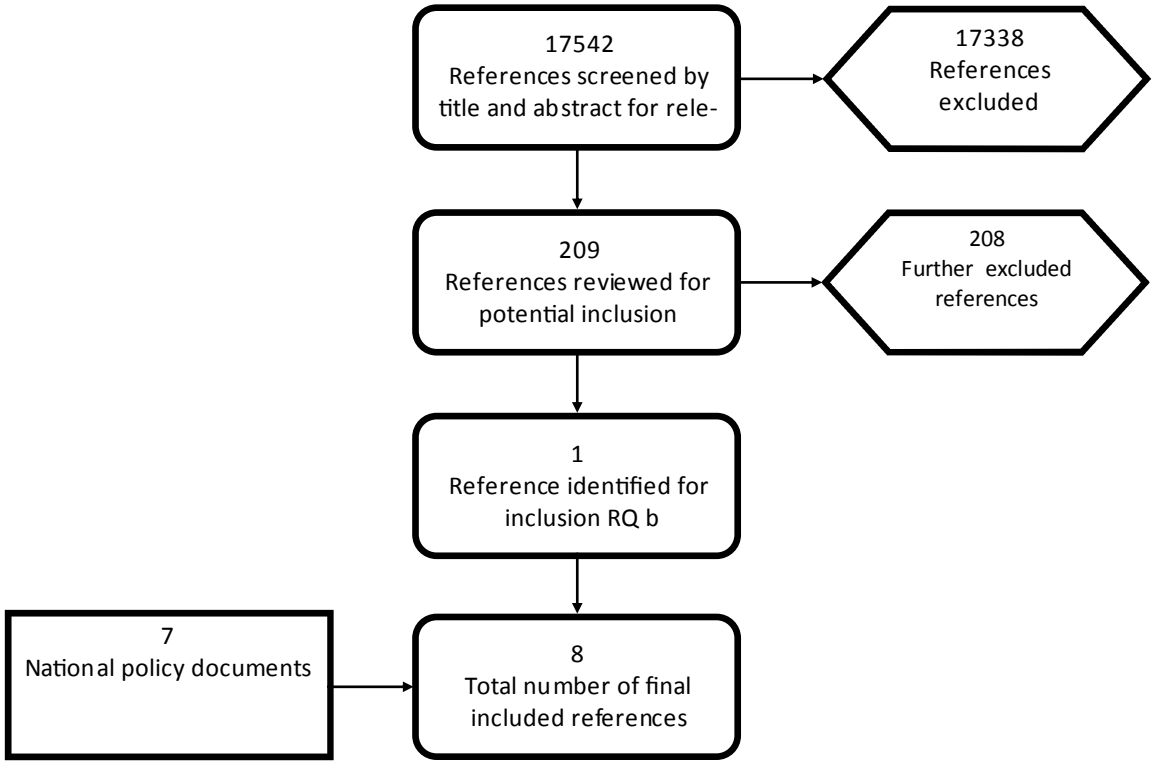
C.3.1 Prescribing of controlled drugs

Figure 1: Inclusion and exclusion of evidence identified from the literature search



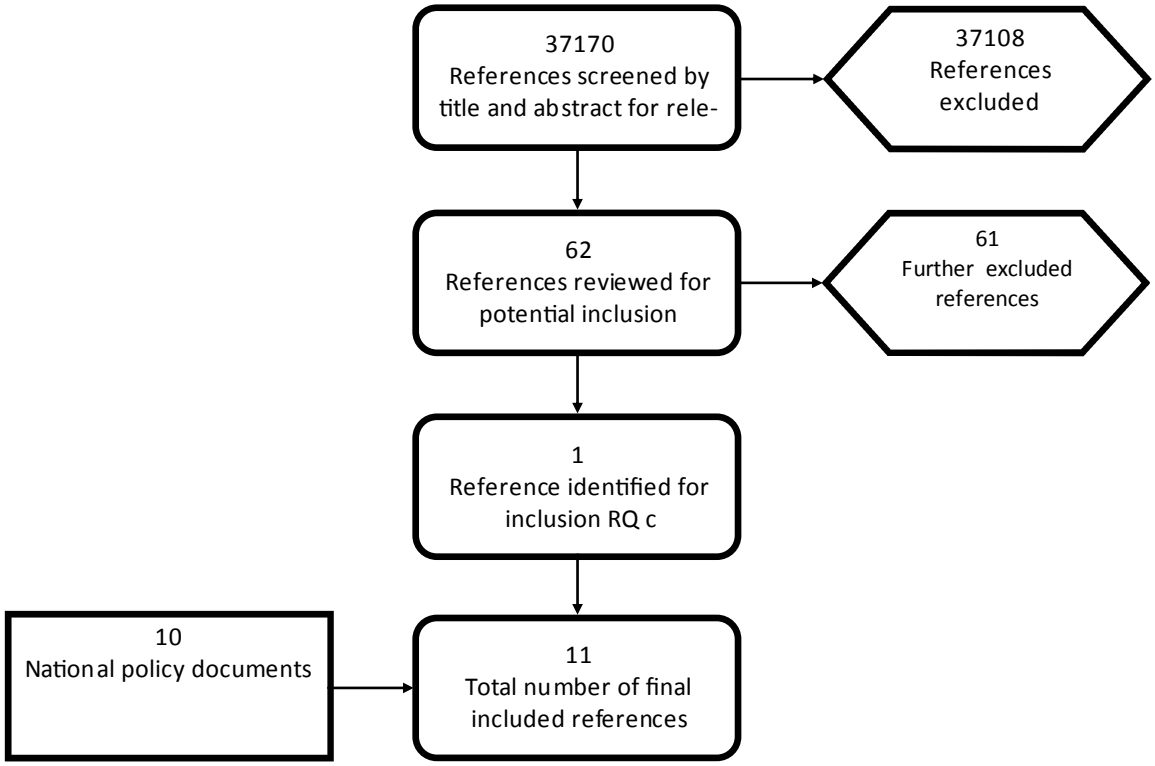
C.3.2 Obtaining and supplying of controlled drugs

Figure 2: Inclusion and exclusion of evidence identified from the literature search



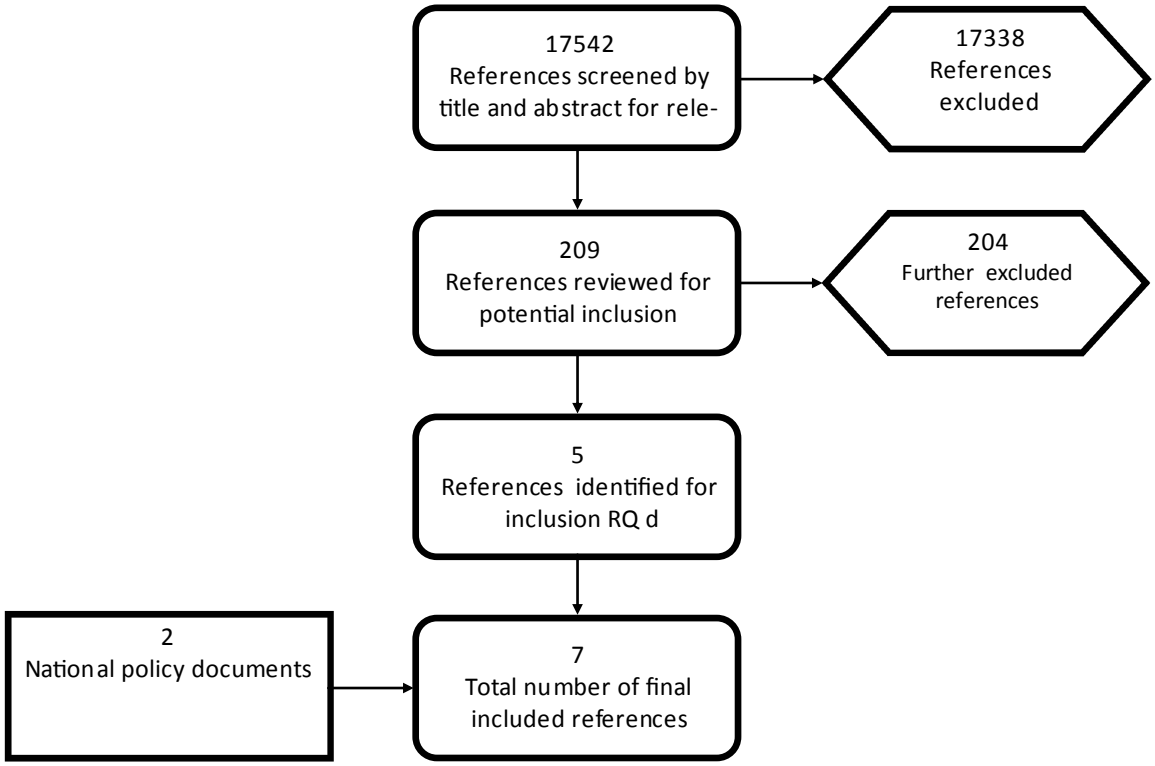
C.3.3 Administration of controlled drugs

Figure 3: Inclusion and exclusion of evidence identified from the literature search



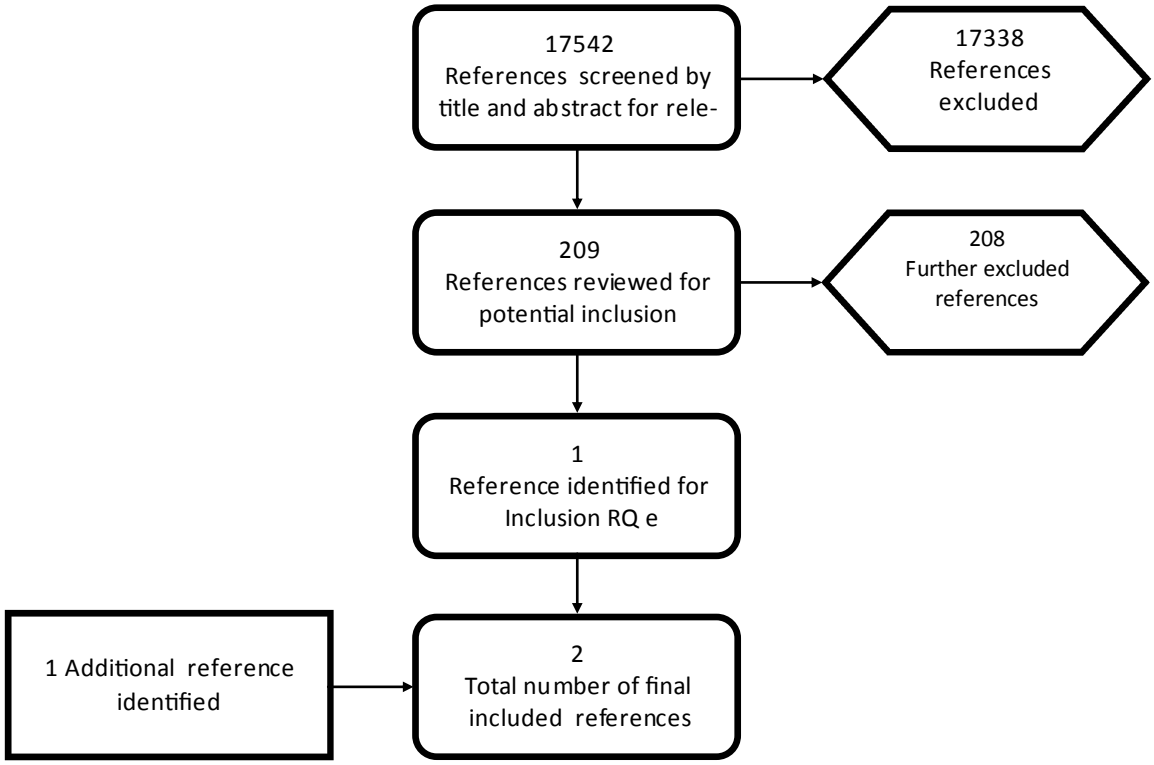
C.3.4 Handling of controlled drugs

Figure 4: Inclusion and exclusion of evidence identified from the literature search



C.3.5 Monitoring of controlled drugs

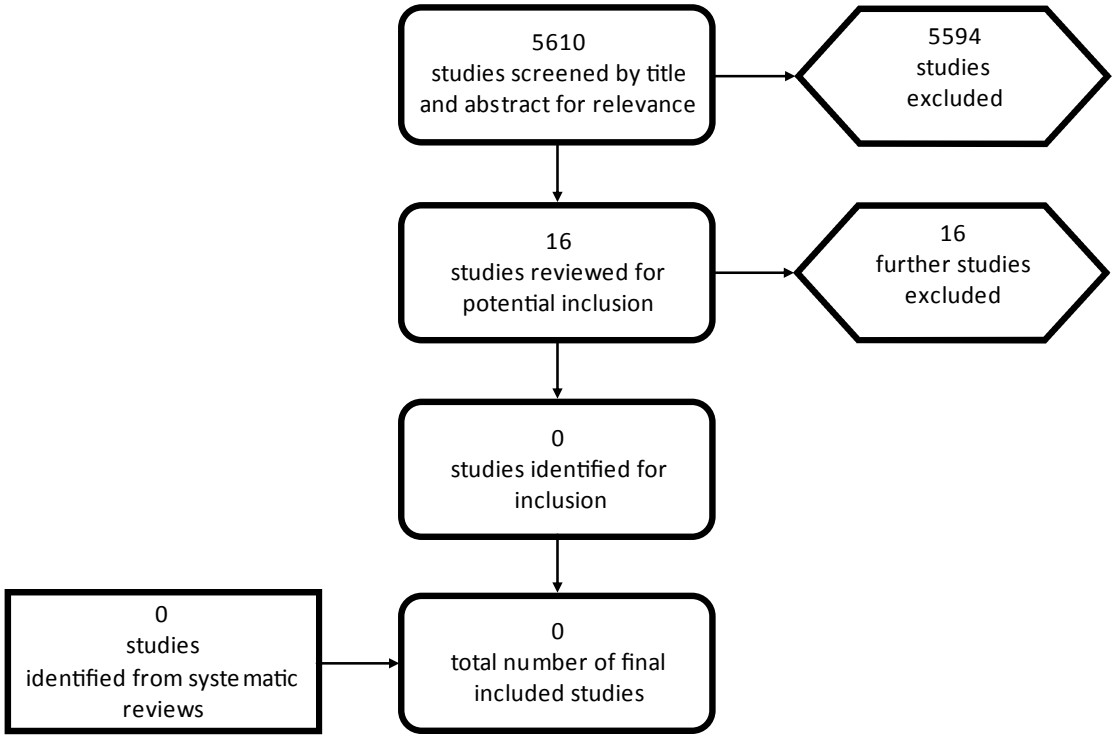
Figure 5: Inclusion and exclusion of evidence identified from the literature search



C.4 Economic consort diagrams

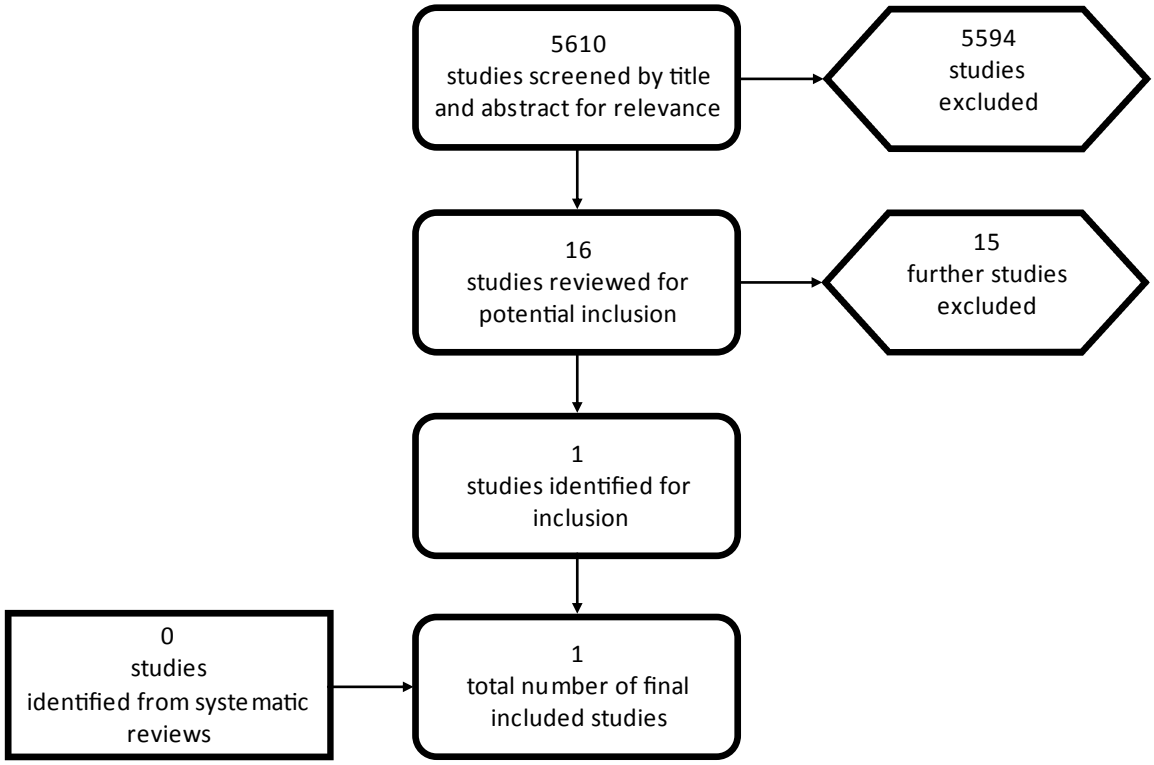
C.4.1 Prescribing of controlled drugs

Figure 6: Inclusion and exclusion of evidence identified from the literature search



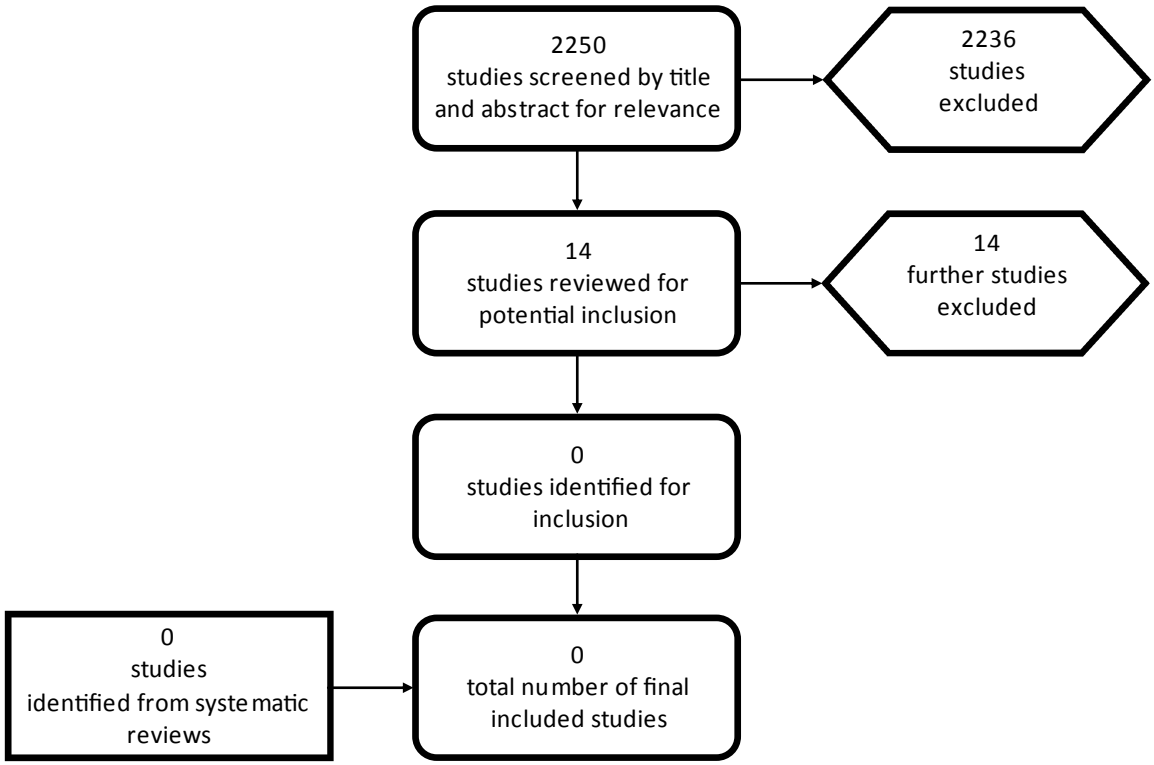
C.4.2 Administration of controlled drugs

Figure 7: Inclusion and exclusion of evidence identified from the literature search



C.4.3 Obtaining, handling and monitoring of controlled drugs

Figure 8: Inclusion and exclusion of evidence identified from the literature search



C.5 Clinical excluded studies

C.5.1 Prescribing controlled drugs

Author	Reason for exclusion
Anon (2004) What's wrong with prescribing hypnotics? Drug & Therapeutics Bulletin 42(12): 89-93	Not relevant evidence type or study design.
Anthierens S, Habraken H, Petrovic M, et al. (2007) The lesser evil? Initiating a benzodiazepine prescription in general practice: a qualitative study on GPs' perspectives. Scandinavian Journal of Primary Health Care 25(4): 214-19	No relevant outcomes
Balter MB, Uhlenhuth EH (1992) Prescribing and use of benzodiazepines: an epidemiologic perspective. Journal of Psychoactive Drugs 24(1): 63-4	Commentary article
Baros AM, Latham PK, Moak DH, et al. (2007) What role does measuring medication compliance play in evaluating the efficacy of naltrexone? Alcoholism, clinical and experimental research. 31(4): 596-603	Not relevant intervention
Bartlett A, Dholakia N, England R, et al. (2014) Prison prescribing practice: Practitioners' perspectives on why prison is different. International Journal of Clinical Practice 68(4): 413-17	Not relevant evidence type or study design.
Bates C, Laciak R, Southwick A, et al. (2011) Overprescription of postoperative narcotics: a look at postoperative pain medication delivery, consumption and disposal in urological practice. Journal of Urology 185(2) 551-55	No relevant comparator
Batty GM, Grant RL, Aggarwal R, et al. (2003) Using prescribing indicators to measure the quality of prescribing to elderly medical in-patients. Age & Ageing 32(3): 292-8	Not relevant intervention
Becker WC, Fiellin DA (2012) Prescriber education on opioids. Annals of Internal Medicine 157(12): 917	Not relevant evidence type.
Bell JR, Ryan A, Mutch C, et al. (2008) Optimising the benefits of unobserved dose administration for stable opioid maintenance patients: follow-up of a randomised trial. Drug & Alcohol Dependence 96 (1-2):183-6	No relevant outcomes
Bell J, Shanahan M, Mutch C, et al. (2007) A randomized trial of effectiveness and cost-effectiveness of observed versus unobserved administration of buprenorphine-naloxone for heroin dependence. Addiction 102(12) 1899-1907	Not relevant
Bendtsen P, Hensing G, McKenzie L et al. (1999) Prescribing benzodiazepines--a critical incident study of a physician dilemma. Social Science & Medicine 49(4):459-67	No relevant comparator
Broekmans S, Vanderschueren S, Morlion B, et al. (2004) Nurses' attitudes toward pain treatment with opioids: a survey in a Belgian University Hospital. International Journal of Nursing Studies 41(2): 183-9	Not relevant
Broglio K, Cole BE (1937) Prescribing opioids in primary care: avoiding perils and pitfalls. Nurse Practitioner 39(6): 30-7	Review article
Comerford D (2008) Techniques of opioid administration. Anaesthesia and Intensive Care Medicine 9(1):21-6	Not relevant intervention
Cormack MA, Howells E (1992) Factors linked to the prescribing of benzodiazepines by general practice principals and trainees. Family Practice 9(4): 466-71	Not relevant evidence type or study design.
Dalleur O, Spinewine A, Henrard S, et al. (2012) Inappropriate prescribing and related hospital admissions in frail older persons according to the STOPP and START criteria. Drugs & Aging 29(10): 829-37	Not relevant intervention.

Author	Reason for exclusion
Dalleur O, Boland B, Losseau C, et al. (2014) Reduction of potentially inappropriate medications using the STOPP criteria in frail older inpatients: A randomised controlled study. Drugs and Aging 31(4):291-8	Not relevant intervention.
de Leon J, Chambers A, Hyatt M, et al. (2012) A practitioner's guide to prescribing clonazepam for adults with intellectual disabilities. de Leon, Jose [Ed] 507-74	Unable to source
de Leon J, Chambers A, Hyatt M, et al. (2012) A practitioner's guide to prescribing diazepam for adults with intellectual disabilities. [References] de Leon, Jose [Ed] 507-94	Unable to source
de Leon J, Chambers A, Hyatt M et al. (2012) A practitioner's guide to prescribing lorazepam for adults with intellectual disabilities. [References] de Leon, Jose [Ed] (2012) 507-254	Unable to source
Denison DE, Schneider F, Childs S, et al. (2011) A prevalence study of errors in opioid prescribing in a large teaching hospital. International Journal of Clinical Practice 65(9): 923-9	Not relevant evidence type or study design.
Derby S, Chin J, Portenoy RK. (1998) Systemic opioid therapy for chronic cancer pain. Practical guidelines for converting drugs and routes of administration. CNS Drugs 9(2): 99-109	Not relevant evidence type or study design.
Dybwad TB, Kjolsrod L, Eskerud J et al. (1997) Why are some doctors high-prescribers of benzodiazepines and minor opiates? A qualitative study of GPs in Norway. Family Practice 14(5) 361-8	Not relevant evidence type.
Gunningberg L, Poder U, Donaldson N, et al. (2014) Medication administration accuracy: Using clinical observation and review of patient records to assess safety and guide performance improvement. Journal of Evaluation in Clinical Practice 20(4): 411-16	No relevant comparator.
Huang AR, Mallet L. (2013) Prescribing opioids in older people. Maturitas 74(2): 123-9	Not relevant intervention
Kahan M, Wilson L, Wenghofer EF, et al. (2011) Pharmacists' experiences with dispensing opioids: provincial survey. Canadian Family Physician 57(11): e448-54	Not relevant evidence type or study design.
Lader M. (1986) A practical guide to prescribing hypnotic benzodiazepines. British Medical Journal 293 (6554) 1048-9	Not relevant evidence type or study design.
Lamont T, Matthew L, Cousins D, et al. (2009) Avoiding midazolam overdose: summary of a safety report from the National Patient Safety Agency. British Medical Journal 339: 4459	Not relevant evidence type or study design.
Lampert A, Seiberth J, Haefeli WE, et al. (2014) A systematic review of medication administration errors with transdermal patches (Provisional abstract). Database of Abstracts of Reviews of Effects (1): 1101-14	No relevant intervention
Lange A, Lasser KE, Xuan Z, et al. (2015) Variability in opioid prescription monitoring and evidence of aberrant medication taking behaviors in urban safety-net clinics. Pain 156(2): 335-40	No relevant comparator
Lesar TS, Smith HS (2011) Making opioid prescribing safer: Time for a checklist? Pain Management 1(4): 279-85	Not relevant evidence type or study design.
Lesar TS, Lomaestro BM, Pohl H. (1997) Medication-prescribing errors in a teaching hospital. A 9-year experience. Archives of Internal Medicine 157(14):1569-76	No relevant intervention
Loder E. (2003) Who will prescribe? A proposal for specialized opioid management clinics. Pain Practice 3(3): 218-21	Review article only describing a model for prescribing opioids with no outcomes reported.

Author	Reason for exclusion
Logan J, Liu Y, Paulozzi L, et al. (2013) Opioid prescribing in emergency departments: the prevalence of potentially inappropriate prescribing and misuse. Medical Care 51(8):646-53	Not a relevant intervention.
Logan M, Fothergill-Bourbonnais F. (1990) Continuous subcutaneous infusion of narcotics. CSCI Canadian Nurse 86(4): 31-2	Not relevant evidence type or study design.
Lum PJ, Little S, Botsko M, et al. (2011) Opioid-prescribing practices and provider confidence recognizing opioid analgesic abuse in HIV primary care settings. Journal of Acquired Immune Deficiency Syndromes 56 (Suppl. 1) S91-7	No relevant outcome measures.
Lynas K (2005) New Rx monitoring system tracks narcotics. Canadian Pharmacists Journal 138 (6):18	Not relevant evidence type or study design, review article only.
Lynas K (2013) Pharmacists can play a key role in implementing new national strategy to combat prescription drug abuse. Canadian Pharmacists Journal 146(3):128-9	Not relevant evidence type or study design, review article only.
Mc DC. (2011) Opioid medication errors in pediatric practice: four years' experience of voluntary safety reporting. Pain Research & Management 16(2): 93-8	No relevant comparator
Mettner J. (2013) The opioid crisis: combating misuse through better prescribing. Minnesota Medicine 96(3): 20-5	Not relevant evidence type or study design, review article only.
Miller MM, Brown RT. (2007) Prescription drug monitoring programs. American Family Physician 75(6): 810-12	Not relevant evidence type or study design, review article only.
Morgan LA, Weaver MF. (2010) Preventing prescription opioid overdose. Journal of Clinical Outcomes Management 17(11): 33-42	Not relevant evidence type or study design, review article only.
Murnion BP, Gnjidic D, Hilmer SN. (2010) Prescription and administration of opioids to hospital in-patients, and barriers to effective use. Pain Medicine 11(1) 58-66	No relevant intervention
Newgreen DB, George LJ, Lloyd AI. (1986) Prescribing and dispensing of benzodiazepines by pharmacists Medical Journal of Australia 144(7) 370-1	Not relevant intervention.
Nutt DJ. (2005) Dr Shipman's last legacy: E-surveillance of the medical profession. Journal of Psychopharmacology 19(5):441	Not relevant evidence type or study design.
Penko J, Mattson J, Miaskowski C et al. (2012) Do patients know they are on pain medication agreements? Results from a sample of high-risk patients on chronic opioid therapy. Pain Medicine 13(9): 1174-80	No relevant intervention.
Peota C. (2014) Opioid prescribing primer. Doctors urged to become knowledgeable about risk Minnesota Medicine 97(4): 9	Not relevant evidence type or study design.
Prewitt J, Schneider S, Horvath M, et al. (2013) PCA safety data review after clinical decision support and smart pump technology implementation. Journal of patient safety 9(2):103-9	No relevant intervention
Rastegar DA, Walley AY. (2013) Preventing prescription opioid overdose deaths. Journal of General Internal Medicine 28(10): 1258-9	Not relevant evidence type or study design, review article only.
Reifler LM, Droz D, Bailey JE, et al. (2012) Do Prescription Monitoring Programs Impact State Trends in Opioid Abuse/Misuse? Pain Medicine 13(3) 434-42	No relevant outcome measures.
Reisfield GM, Sloan PA (2012) Physician identification of opioid diversion: a difficult diagnosis. Journal of Opioid Management 8(1):5-6	Not relevant evidence type or study design. Editorial only.

Author	Reason for exclusion
Rhodes WB, Ball KD. (1989) Benzodiazepine prescribing Lancet 2(8671): 1103	Not relevant evidence type or study design, review article only.
Rothschild JM, Keohane CA, Cook EF, et al. (2005) A controlled trial of smart infusion pumps to improve medication safety in critically ill patients Critical Care Medicine 33(3): 533-40	The study does not mention the use of controlled drugs in the infusion pump, but refers to other medicines.
Salmenlainen P. (2000) Inappropriate prescribing of benzodiazepines by doctors in New South Wales. New South Wales Public Health Bill 11(4): 57-8	No relevant intervention.
Siderov J, Zalcberg JR (1994) Prescribing opioids - A painful experience.Medical Journal of Australia 161(9): 515-16	Not relevant evidence type or study design, review article only.
Sketris IS, Meldrum M, Lacey D, et al. (1987) Effect of a two-day stop-order policy on benzodiazepine prescribing American Journal of Hospital Pharmacy 44(12): 2736-8	No relevant outcomes
Smith AJ, Tett SE. (2010) Improving the use of benzodiazepines--is it possible? A non-systematic review of interventions tried in the last 20 years. BMC Health Services Research 10: 321	No relevant interventions
Strang J, Sheridan J (2003) Effect of national guidelines on prescription of methadone: analysis of NHS prescription data, England 1990-2001 BMJ 327(7410): 321-22	No relevant outcomes reported in the study.
Strang J, Sheridan J (2001) Methadone prescribing to opiate addicts by private doctors: comparison with NHS practice in south east England Addiction 96 (4) 567-576	No relevant outcomes
Strang J, Sheridan J, Hunt C, et al. (2005) The prescribing of methadone and other opioids to addicts: national survey of GPs in England and Wales. British Journal of General Practice 55(515):444-51	No relevant outcomes
Turk DC, Swanson KS, Gatchel RJ (2008) Predicting opioid misuse by chronic pain patients: A systematic review and literature synthesis. Clinical Journal of Pain 24(6): 497-508	No relevant outcome measures reported.

C.5.2 Obtaining and supplying controlled drugs

Author	Reason for exclusion
Anon (1977) 12 tips for prescribers of controlled drugs. Bulletin of the Philadelphia County Dental Society 42(6):14	Unable to source
Anon (1997) A guide to prescribing, administering and dispensing controlled substances in Missouri. Missouri Medicine 94 (2): 76-81	Not relevant to UK practice
Anon (1977) A medical society's guidelines for prescribing controlled drugs. Hospital Formulary 12(10): 677	Not relevant to the review question
Anon (1991) ASHP statement on the pharmacist's responsibility for distribution and control of drugs. American Journal of Hospital Pharmacy 48(8): 1782	Not relevant to UK practice
Anon (1987) ASHP technical assistance bulletin on institutional use of controlled substances. American Journal of Hospital Pharmacy 44(3): 580-9	Duplicate guideline
Anon (2004) CD registers are to be centralised at Prescription Pricing Authority. Pharmaceutical Journal 273 (7330): 874	Not relevant evidence type or study design.
Anon (2003) Check CD prescriptions Pharmaceutical Journal	Brief guidance issued within the

Author	Reason for exclusion
271 (7264): 258	journal
Anon (2013) Codeine care: Mitigating abuse and misuse. SA Pharmaceutical Journal.80 (5): 46-7	No relevant outcomes reported
Anon (1968) Control of amphetamine preparations. British Medical Journal 4(5630): 572-3	Review article.
Anon (1970) Control of amphetamines and L.S.D. Lancet 1(7649): 708	Not relevant evidence type or study design
Anon (1974) Control of habit forming drugs. Illinois Medical Journal 145(4): 348-9	Not relevant evidence type or study design
Anon (1961) Controlled Drugs. Canadian Medical Association Journal 85(11): 661	Editorial only
Anon (2004) Controlled Drugs guide. Pharmaceutical Journal 272 (7304): 756	Abstract only
Anon (2005) Controlled drugs in primary care: An update. MeReC Bulletin 15(3): 1-4	Unable to source
Anon (1987) Controlled substances from the emergency room. North Carolina Medical Journal 48(7):372-6	Not relevant evidence type or study design.
Anon (1967) Dependence on alcohol and other drugs. WHO Chronicle 21(6): 219-6	Not relevant evidence type or study design
Anon (2002) Destruction of controlled drugs Pharmaceutical Journal.269(7218): 475	Brief description of guidance for destruction of controlled drugs
Anon (2004) Destruction of out-of-date Controlled Drugs. Pharmaceutical Journal 272 (7292):395	Brief description of guidance for destruction of controlled drugs
Anon (1982) Detecting and preventing drug abuse and diversion. Hospital Security & Safety Management 3(5): 5-9	Unable to source.
Anon (1972) Division of drug abuse control. Journal of the Arkansas Medical Society 69(7): 214-5	Not relevant evidence type or study design
Anon (1983) Doctors for drug addicts. British Medical Journal Clinical Research Ed 286 (6381):1844	Not relevant to the review question.
Anon (2007) Drug diversion in healthcare: risks and prevention. Healthcare Hazard Management Monitor 21(4):1-8	Unable to source
Anon (1971) Drug trafficking and drug abuse. Medical Journal of Australia 1(22):1151-3	Not relevant evidence type or study design
Anon (2005) E-prescribing for controlled substances. Tennessee Medicine 98(12): 561	Not relevant to the review question
Anon (2010) Electronic prescriptions for controlled substances. Optometry St Louis (7): 367-72	Not relevant to the review question
Anon (1999) Emergency situations and controlled medicines. WHO Drug Information 13(3): 147-8	Not relevant evidence type or study design
Anon (1979) Federal strategy for drug abuse and drug traffic prevention. Contemporary Drug Problems 8(2): 227-49	Not relevant to UK practice
Anon (1980) Guidelines for controlled substances. Journal of the Medical Association of the State of Alabama 50(4): 12-17	Newsletter only
Anon (1980) Guidelines for prescribers of controlled substances. Journal of the American Podiatry Association 70(9): 481-2	Not relevant to the review question
Anon (1978) How nurses should handle matters related to controlled substances. Pharmacy Times 44(1): 38-40	Unable to source
Anon (2000) How one hospital tackles the drug theft/diversion problem head-on. Hospital Security & Safety Management 20(11): 8-10	Unable to source
Anon (2002) How to monitor drug diversion from automated	Unable to source

Author	Reason for exclusion
dispensing cabinets. Healthcare Hazard Management Monitor 15(11): 6-7	
Anon (1990) Managing controlled drugs in the office. Ohio Medicine 86(4): 315	Not relevant evidence type or study design.
Anon (2005) National templates should be produced for CD assessment Pharmaceutical. Journal 275 (7369): 399	Review article only.
Anon (1973) New state drug law seen affecting doctors' prescribing procedures N.Y.MED 29(11): 434	Reason for exclusion: Unable to source
Anon (1970) O-T-C preparations--potential for misuse. Panel discussion. American Journal of Pharmacy & the Sciences Supporting Public Health 142(1): 46-60	Discussion article only.
Anon (1987) PADS: a program to identify and diagnose prescription drug diversion in Indiana. Indiana Medicine 80 (9):874-6	Reason for exclusion: not relevant
Anon (2007) Pain, opioids, and addiction: An urgent problem for doctors and patients. Journal of Pain & Palliative Care Pharmacotherapy 21(4): 45-9	Reason for exclusion: Not relevant to the review question.
Anon (2005) Pharmacies to make annual CD use declarations. Pharmaceutical Journal 275(7358): 71	Review article only
Anon (1972) Possession of rediscovered drugs British Medical Journal 1 (5794) 259-260	Review protocol criteria not met.
Anon (1996) Prescription drug diversion. Virginia Medical Quarterly 123(2): 132	Not relevant
Anon (1986) Reducing employee drug diversion in hospitals. Hospital Security & Safety Management 7(2): 5-9	Unable to source
Anon (1980) Rule on prescribing, dispensing of amphetamines. Wisconsin Medical Journal 79(6):47	Not relevant intervention
Anon (1979) Safe use of psychotropic and narcotic substances. WHO Chronicle 33(1): 12-15	Not relevant evidence type or study design
Anon (1968) Safety of drugs. British Medical Journal 3 (5621):758	Not relevant evidence type or study design
Anon (1972) Safety of medicines British Medical Journal 4 (5834): 192	Editorial only.
Anon (1997) Stockpiling painkillers Nursing 27 (10): 32	Editorial only.
Anon (1969) The misuse of pentazocine. Its dependence-producing potential. JAMA 209(10) 1518-9	Not relevant evidence type or study design
Anon (1968) The physician and the drug abuse laws. JAMA 205 (11): 788-9	Commentary article
Anon (1976) The supply of opium derivatives. Medical Journal of Australia 1(24): 899-900	Not relevant evidence type or study design.
Anon (1976) The use and misuse of psychotropic drugs. (Afrikaans) South African Medical Journal.50 (21): 793-4	Not English language
Anon (1967) Use and misuse of drugs. Nursing Times 63 (48): 1612-3	Unable to source
Anon. (1993) ASHP technical assistance bulletin on use of controlled substances in organized health care settings. American Journal of Hospital Pharmacy 50(3): 489-501	Not relevant
Anon. (2005) Maintaining running balances of stock in Controlled Drug registers. Pharmaceutical Journal.274 (7351): 660	Not relevant

Author	Reason for exclusion
Abedtash H, Finnell JT. (2014) Emergency physician assessment of opiate risk from prescription drug monitoring program data [Abstract]. In: Academic Emergency Medicine Conference Publication 2014. Annual Meeting of the Society for Academic Emergency Medicine 13 – 17 May 2014 Dallas, United States. 21 (5): (Suppl.1): S270-1	Abstract only
Abrams PC. (1948) Cross-check for narcotics solution control. Hospitals 22(3):50	Unable to source
Ahmed I, Majeed A. (2007) The safe and responsible disposal of unused controlled drugs. British Journal of Nursing 16(21): 1318-22	Not relevant
Akici A, Demircan D, Topcu I, et al. (2011) Assessment of controlled medicines prescription patterns in the context of green and red coloured scripts [Abstract]. Basic and Clinical Pharmacology and Toxicology. Congress of the European Association for Clinical Pharmacology and Therapeutics Publication, 10th Conference 26 – 29 June 2011 Budapest, Hungary. 141	Abstract only
Akins K. (1972) Amphetamine controls. Canadian Medical Association Journal 107(2): 113	Not relevant to UK practice
Alldred A. (2007) Managing controlled drugs - Taking ownership of the new agenda. Hospital Pharmacist14(6): 178	Commentary article
Austin LH. (1967) A simplified narcotic distribution system. American Journal of Hospital Pharmacy 24(10): 561-5	No relevant outcomes reported from the system.
Baker K. (2003) How do you dispose of a controlled substance? Drug Topics 147 (4): 58	Not relevant evidence type or study design
Baker KR. (2010) Monitoring controlled substances. Drug Topics 154(9)	not relevant evidence type or study design
Baker R, Moss P, Upton D. et al. (2004) Investigation of systems to prevent diversion of opiate drugs in general practice in the UK. Quality & Safety in Health Care 13(1): 21-5	Not relevant
Barclay J, Clarkson B, Blackhall L, et al. (2013) Substance abuse and diversion in palliative care. (TH341) safety net. SIG Journal of Pain and Symptom management. Conference of the Annual Assembly of the American Academy of Hospice and Palliative Medicine and the Hospice and Palliative Nurses Association. 13 March 2013 New Orleans, United States. 361-2	Not relevant evidence type or study design.
Barnard D. (2002) World Health Organization guidelines for national narcotics control policies. Journal of Palliative Medicine 5(4): 575-7	Not relevant evidence type or study design
Barnea Z, Teichman M. (1994) Substance misuse and abuse among the elderly: Implications for social work intervention. Journal of Gerontological Social Work 21 (3-4): 133-48	Not relevant
Beatty Y. (2005) Controlled substance tracking. Tennessee Medicine 98(10): 467	Not relevant evidence type or study design
Belcher J, Nielsen S, Campbell G, et al. (2014) Diversion of prescribed opioids by people living with chronic pain: Results from an Australian community sample. Drug and Alcohol Review 33(1): 27-32	No relevant intervention
Bell DM, McDonough JP, Ellison JS, et al. (1999) Controlled drug misuse by Certified Registered Nurse Anesthetists. Journal 67(2): 133-40	Not relevant to the review question
Bell J. (2010) The global diversion of pharmaceutical drugs: opiate treatment and the diversion of pharmaceutical opiates: a clinician's perspective. Addiction 105(9): 1531-7	Not relevant study

Author	Reason for exclusion
Bellizzi JJ. (1970) Legal prescription of narcotics. New York State Journal of Medicine 70(12): 1677-80	Not relevant to the review question.
Benjamin DM (2007) Prosecution of physicians for prescribing opioids to patients. Clinical Pharmacology & Therapeutics 81(6): 797-8	Not relevant to the review question
Berge KH, Dillon KR, Sikkink KM, et al. (2012) Diversion of drugs within health care facilities, a multiple-victim crime: patterns of diversion, scope, consequences, detection, and prevention. Mayo Clinic Proceedings 87(7) 674-82	Not relevant study
Bergman U, Griffiths RR (1986) Relative abuse of diazepam and oxazepam: prescription forgeries and theft/loss reports in Sweden. Drug & Alcohol Dependence 16(4): 293-301	Not relevant
Bizer JE (1972) A study to evaluate the controlled substance distribution system at Hendrick Memorial Hospital, Abilene, Texas. Abstracts of Hospital Management Studies 9 (309469)	Abstract only
Black HJ (1983) How much control for controlled substances? American Journal of Hospital Pharmacy 40 (5): 788	Not relevant evidence type or study design
Bogardus DE (2005) Hospital security response to narcotics theft. Journal of Healthcare Protection Management 21(1): 97-100	Not relevant
Bourne PG (1973) Methadone diversion. In: Proceedings of National Conference on Methadone Treatment 2 839-41	Not relevant
Brands B, Blake J, Sproule B, et al. (2004) Prescription opioid abuse in patients presenting for methadone maintenance treatment. Drug and Alcohol Dependence 73(2): 199-207	No relevant intervention
Brent NJ (1989) Administering controlled substances in the home: minimizing the risk of potential diversion. Home Healthcare Nurse 7(4): 6-7	Not relevant to the review question
Burgess FW, Pawasauskas J (2008) Opioid therapy and prescription drug diversion. Medicine & Health, Rhode Island 91(9): 268-70	Not relevant study
Burton J, Echternach J, Rodgers J, et al. (2014) Controlled substance prescribing for discharged emergency patients: Effects of a prescription reporting initiative on physician prescribing. Academic Emergency Medicine. Annual 21 (Suppl.1): S101-2	Not relevant to the review question
Buttram ME, Kurtz SP, Surratt HL, et al. (2014) Health and social problems associated with prescription opioid misuse among a diverse sample of substance-using MSM. Substance Use & Misuse 49(3): 277-84	Not relevant
Calesnick B (1977) Controlled substances. American Family Physician 16(4): 180-1	Not relevant for UK practice
Carlson GM, Castile JA, Janousek JP (1988) Guidelines for the prevention and detection of controlled substance diversion. Hospital Pharmacy 23(12): 1057-9	Not relevant
Carmody G, Vogel D (1986) Unit dose distribution of controlled substances for the operating room. American Journal of Hospital Pharmacy 43(2): 413-415	No relevant outcomes reported from the system used.
Cerda M, Ransome Y, Keyes KM, et al. (2013) Prescription opioid mortality trends in New York City, 1990-2006: Examining the emergence of an epidemic. Drug and Alcohol Dependence 132(1-2): 53-62	Not relevant
Chan K, Groves RL (1979) The use of 'controlled drugs' in general practice. Journal of Clinical Pharmacy 4(2): 101-13	Not relevant to the review question

Author	Reason for exclusion
Chi J (2004) Who is registered to handle controlled substances? Drug Topics 148 (15): 148	Not relevant evidence type or study design
Chisholm AB, Harrison MJ (2009) Opioid abuse amongst anaesthetists: A system to detect personal usage. Anaesthesia & Intensive Care 37(2): 267-71	No relevant outcomes
Chua SM, Lee TS (2006) Abuse of prescription buprenorphine, regulatory controls and the role of the primary physician. Annals of the Academy of Medicine Singapore 35(7): 492-5	Not relevant evidence type or study design.
Clark J (2013) E-prescribing controlled substances moves closer to reality Health Management Technology 34(11): 24	Review article only
Clarke H, MacDougall P, Fraser J et al. (2013) Safe and effective prescribing controlled substances for pain management: Strategies from the office to the community Pain Research and Management. Proceedings of the 2013 Annual Conference of the Canadian Pain Society, Winnipeg, Canada. 8 May – 10 May 2013.18(2): e1-2	Not relevant to the review question
Clayton R (2007) CD guidance for secondary care - Ensuring procedures are fit for purpose. Pharmaceutical Journal 278 (7451): 555-6	Commentary article
Cleary JF, Cherny N (2014) Is opioid over-regulation hurting cancer patients? Clinical Practice.11(2): 125-9	Not relevant as out of scope.
Cohen J (1991) Prescribing controlled drugs. Practitioner 235(1502): 452-4	Not relevant to the review question
Cohen S (1979) The prescription of controlled substances: what's right and what's wrong. NIDA Research Monograph 27: 11-16	Not relevant to the review question
Coletti CM, Nomura JT, Farley H (2011) Opioid prescriptions from the emergency department: A descriptive analysis. In proceedings of Annals of Emergency Medicine Conference: American College of Emergency Physicians, Research Forum. 15 – 16 January 2011 San Francisco, United States. 58(4) (Suppl.1): S228	No relevant outcomes.
Coplan P (2014) Controlling controlled substances abuse and misuse by managed care payers: a new generation of risk management initiatives? Pharmacoepidemiology & Drug Safety 23(4): 428-30	Commentary article
Curran RE (1962) Canada and controlled drugs. Medical Services Journal 18: 415-30	Not relevant to UK practice
Dasgupta N (2014) Opioid analgesic prescribing and overdose mortality in North Carolina. Dissertation Abstracts International: The Sciences and Engineering 75	Not relevant to the review question
Davies K (2011) Identifying unprescribed controlled medication use: A database analysis. Journal of Pain 12 (4) Suppl. 1): 61	Abstract only
Davis WR, Johnson BD (2008) Prescription opioid use, misuse, and diversion among street drug users in New York City. Drug and Alcohol Dependence 92 (1-3): 267-76	Not relevant
Demircan D, Gulmez SE, Donertas B, et al. (2013) Use of drugs subject to controlled prescriptions: a retrospective analysis. Balkan Medical Journal 30(1) 46-53	No relevant outcomes
Dobscha SK (2013) Prescription opioids and benzodiazepines: Moving beyond "just say no". Pain Medicine 14(10): 1447-9	Not relevant to the review question
Doig I, Cordy C (2004) A review of controlled substances.	Not relevant to UK practice

Author	Reason for exclusion
Medicine & Health, Rhode Island 87(6): 186-188	
Duffy P, Mackridge AJ (2014) Use and diversion of illicit methadone-Under what circumstances does it occur, and potential risks associated with continued use of other substances. Journal of Substance Use 19(1-2): 48-55	Not relevant
DuPont RL (1993) Benzodiazepines, addiction, and public policy. New Jersey Medicine 90(11) 823-6	Not relevant evidence type or study design
Eckel FM (2009) Are we using controlled substances properly? Pharmacy Times 75(11): 1	Not relevant to the review question
Eckel FM (2014) Controlled substance misuse and abuse: Solving the problem of opioid safety. Pharmacy Times 80 (7)	Commentary article
Eggen AE, Andrew M (1994) Use of codeine analgesics in a general population. A Norwegian study of moderately strong analgesics. European Journal of Clinical Pharmacology 46(6): 491-6	Not relevant
Ehrhardt HE, Schroder O (1977) The effects of prescription orders on the control of narcotic drugs. Bulletin on Narcotics 29(2): 1-7	Not relevant to UK practice
Eidson K (2010) Controlled Substance Monitoring Database (CSMD) Journal of the Tennessee Dental Association 90(2): 14-6	Not relevant study
El-Aneed A, Alaghehbandan R, Gladney N, et al. (2009) Prescription drug abuse and methods of diversion: The potential role of a pharmacy network. Journal of Substance Use 14(2):75-83	Not relevant study
Feldman SM, Bingham TC (2012) Misuse and abuse associated with buprenorphine utilization for the treatment of opioid dependency. Journal of Managed Care Pharmacy 18: 188	Abstract only
Finlayson RE (1995) Misuse of prescription drugs. International Journal of the Addictions 30 (13-14) 1871-901	Review article only
Fishman SM, Papazian JS, Gonzalez S, et al. (2004) Regulating opioid prescribing through prescription monitoring programs: balancing drug diversion and treatment of pain. Pain Medicine 5(3): 309-24	Not relevant to UK practice
Foote FM (1972) Patient requests for controlled drugs. Connecticut Medicine 36 (2): 85-6	Not relevant evidence type or study design
Fornili K, Simoni-Wastila L (2011) Prescription monitoring programs: Striking the balance between medical use and diversion. Journal of Addictions Nursing 22(1-2): 77-82	Not relevant
Forsyth B (1983) Computer controlled drug abuse Computers in Healthcare 4 (4) 22-26	Not relevant evidence type or study design.
Fountain J, Griffiths P, Farrell M, et al. (1998) Diversion tactics: How a sample of drug misusers in treatment obtained surplus drugs to sell on the illicit market. International Journal of Drug Policy 9(3): 159-67	No relevant interventions, systems or processes included within the paper. Findings summarised to highlight problems
Fox SL (1976) The physician and the controlled drug laws Maryland State Medical Journal 25(2): 64-70	Not relevant to UK practice
Foxhall K (2005) Controlled substances can now be ordered electronically. Drug Topics.149 (12)	Not relevant to UK practice
Fraser J (2013) Effective monitoring of controlled substance prescribing. Pain Research and Management 18(2): e2	Not relevant to the review question.
Freeman PR, Talbert J, Blumenschein K (2011) Impact of	Abstract only

Author	Reason for exclusion
prescription monitoring programs on controlled substance prescribing behaviour. Proceedings of 16th Annual International Meeting of the International Society for Pharmacoeconomics and Outcomes Research(ISPOR) 21 – 25 May 2011, Baltimore, United States. A27	
Gardner JR (1985) Are your controlled substances controlled? Texas Hospitals 40(11): 30-3	Unable to source
Giltrow J (2006) Monitoring and inspection of controlled drugs: Role of the society's inspectors Pharmaceutical Journal.277 (7430): 702-7	Not relevant study
Greenwald BD, Narcessian EJ (1999) Opioids for managing patients with chronic pain: Community pharmacists' perspectives and concerns. Journal of Pain and Symptom Management 17(5): 369-75)	Not relevant evidence type or study design.
Griffith R (2007) Legal requirements for the prescribing and administration of medicines. British Journal of Community Nursing 12(10): 477-81	Limited information relating to controlled drugs
Griffith R, Tengnah C (2011) Prescription of controlled drugs by non-medical prescribers. British Journal of Community Nursing 16(11): 558-62	Not a relevant intervention
Gwira Baumblatt JA, Wiedeman C, Dunn JR, et al. (2014) High-risk use by patients prescribed opioids for pain and its role in overdose deaths. JAMA Internal Medicine 174 (5): 796-801	Not relevant to the review question.
Hagemeier NE, Gray JA, Pack RP (2013) Prescription drug abuse: A comparison of prescriber and pharmacist perspectives. Substance Use & Misuse 48(9): 783-90	Not relevant intervention
Hagen T (2012) Review of a pharmacist-implemented controlled substance refill program in a patient-centered medical home. Journal of the American Pharmacists Association 52(2): 258	Not a relevant intervention
Halldorsson A (2007) Prescribing of controlled substances for non-patients in the educational setting: Review of the ethical, legal, and moral dilemma for residents. Medical Education Online 12: 1-6	No relevant intervention
Hallinan R, Osborn M, Cohen M et al. (2011) Increasing the benefits and reducing the harms of prescription opioid analgesics. Drug and Alcohol Review 30(3): 315-23	No interventions discussed as part of the review article
Hamrick LC (1978) Prescription blanks in group practice: a strategy for control. Group Practice 27(3) 28-9	Not relevant to the review question.
Harrison B (2006) Prescription drug monitoring programs. Ncsl Legisbrief 14(4):1-2	Review article only.
Hayes P, Hickey K, Lovell S, et al. (1976) The storage of drugs in homes. Medical Journal of Australia 1(8): 235-6	Not relevant evidence type or study design
Hazebrook LS, Ross TW, Ploetz PA (1991) Computer system for determining trends in controlled-substance discrepancies. American Journal of Hospital Pharmacy 48 (6):1262-4	No relevant comparator. A new system is implemented, however its effect was not compared in the study to the previous system used to identify trends.
Hibbard FJ, Bair JN, Sylvester KL (1983) Pharmacy-based controlled substances distribution for a university campus. American Journal of Hospital Pharmacy 40(1): 74-7	Not relevant
Hoover RC, McCormick WC, Harrison WL (1981) Pilferage of controlled substances in hospitals American Journal of Hospital Pharmacy 38(7): 1007-10	Not relevant

Author	Reason for exclusion
Hoppe J, Howland MA, Nelson L (2014) The role of pharmacies and pharmacists in managing controlled substance dispensing. Pain Medicine 15(12) 1996-8	Commentary article
Horgan C, Prottas J, Tompkins C et al. (1993) Summary and conclusions of a review of prescription drug diversion control methods. NIDA Research Monograph 131: 206-23	Not relevant
Hurwitz W (2005) The challenge of prescription drug misuse: A review and commentary. Pain Medicine 6(2): 152-61	Not relevant
Inciardi JA, Surratt HL, Kurtz SP, et al. (2007) Mechanisms of prescription drug diversion among drug-involved club- and street-based populations. Pain Medicine 8(2): 171-83	Not relevant
Inciardi JA, Surratt HL, Cicero TJ, et al. (2009) Prescription opioid abuse and diversion in an urban community: The results of an ultrarapid assessment. Pain Medicine 10(3): 537-548	Not relevant
Inciardi JA, Surratt HL, Cicero TJ et al. (2009) The "black box" of prescription drug diversion. Journal of Addictive Diseases 28(4): 332-47	Not relevant
Inciardi JA, Surratt HL, Kurtz SP, et al. (2006) The diversion of prescription drugs by health care workers in Cincinnati, Ohio. Substance Use & Misuse 41(2): 255-64	Not relevant
Irvine JM, Hallvik SE, Hildebran C et al. (2014) Who uses a prescription drug monitoring program and how? Insights from a statewide survey of Oregon clinicians. Journal of Pain 15(7): 747-55	Not relevant
Jaramillo JE, Farrar RD (2011) Unused medications: A case report - show me the money. Clinical Toxicology 49 (6): 607	Not relevant
Jatav VS, Saggu JS, Jat RK et al. (2011) Recent advances in development of transdermal patches Pharmacophore 2(6): 287-97)	Not relevant
Jay MP (2008) E-prescribing of controlled substances: Safer than paper. Drug Benefit Trends 20(7): 287-8	Commentary article
Johnson BD (2003) Patterns of drug distribution: implications and issues. Substance Use & Misuse 38 (11-13):1789-1806	Review article
Johnson JA, Code WE, Duncan PG (1990) "An improved system for narcotic control in the operating room" Canadian Journal of Anaesthesia 37 (4:Pt 2)	Not relevant
Johnson KW, Grube JW, Ogilvie KA, et al. (2012) A community prevention model to prevent children from inhaling and ingesting harmful legal products. Evaluation and Program Planning 35(1): 113-23	Not relevant
Johnson K, Courser M, Holder H et al. (2007) A community prevention intervention to reduce youth from inhaling and ingesting harmful legal products. Journal of Drug Education 37(3): 227-47	Not relevant
Johnson PE (2011) Drug shortages: impact and strategies. Journal of the National Comprehensive Cancer Network 9 (8): 815-9	Commentary article
Johnson RE (1973) Present and projected drug system services in a highly developed HMO structure. Health Service Rep 88(9): 873-7	Not relevant
Joranson DE (1993) Availability of opioids for cancer pain: recent trends, assessment of system barriers. New World Health Organization guidelines and the risk of diversion. Journal of Pain & Symptom Management 8(6): 353-60	Not relevant study

Author	Reason for exclusion
Joranson DE (1993) Guiding principles of international and federal laws pertaining to medical use and diversion of controlled substances. NIDA Research Monograph 131:18-34	Not relevant to UK practice
Joranson DE, Gilson AM (2006) Wanted: a public health approach to prescription opioid abuse and diversion Pharmacoepidemiology & Drug Safety 15(9): 632-4	Not relevant
Joranson DE, Gilson AM (2005) Drug crime is a source of abused pain medications in the United States. [References] Journal of Pain and Symptom Management 30(4): 299-301	Commentary article
Kage A (2012) Audit on prescription of controlled drug Archives of Disease in Childhood. Proceedings of 4th Congress of the European Academy of Paediatric Societies, 5 – 9 January 2012 Istanbul Turkey 97: 436	Abstract
Kern SI (2010) Controlled drugs: how to minimize the risks to you and your patients. Medical Economics 87(15): 50-1	Commentary article
Kern SI (2008) Perils when prescribing controlled drugs. Medical Economics 85(3): 20	Commentary article
Lien CA (2012) A need to establish programs to detect and prevent drug diversion. Mayo Clinic Proceedings 87 (7): 607-9	Commentary article
Longo LP, Parran T Jr., Johnson B, et al. (2000) Addiction: part II. Identification and management of the drug-seeking patient. American Family Physician 61(8): 2401-8	Not relevant
Longo LP (1999) Resting assured: risk management in the prescription of controlled substances. WMJ 98(1) 23-9	Not relevant study
Lurie P, Lee PR (1991) Fifteen solutions to the problems of prescription drug abuse. Journal of Psychoactive Drugs 23(4): 349-57	Not relevant study
Lynas K (2012) Pharmacists not part of current regulatory change on prescribing controlled substances. Canadian Pharmacists Journal 145(4): 156	Commentary article
Mackintosh D, Molloy V (2002) Reconciling drug accountability records Good Clinical Practice Journal 9(4): 24-5	Not relevant study
Martin ES, Dzierba SH, Jones DM (2013) Preventing large-scale controlled substance diversion from within the pharmacy. Hospital Pharmacy 48(5) 406-12	Not relevant
McClary B, Cable DW (1999) A guide to prescribing, administering, and dispensing controlled substances in Missouri. Missouri Medicine 96(2) 47-54	Not relevant study
McCormick CG (2006) Regulatory challenges for new formulations of controlled substances in today's environment. Drug and Alcohol Dependence 83 (Suppl.1): S63-7	Not relevant
Miller NS (2006) Failure of enforcement controlled substance laws in health policy for prescribing opiate medications: a painful assessment of morbidity and mortality. American Journal of Therapeutics 13(6): 527-33	Not relevant to UK practice
Miller NS (2004) Prescription opiate medications: Medical uses and consequences, laws and controls. Psychiatric Clinics of North America.27(4): 689-708	Not relevant to UK practice
Miller NSE (2006) This Issue: Prescription Opiate Medications Psychiatric Annals 36(6): 378-82	Commentary article
Miller NS (2010) Legal authority, medical basis and public policy for controlling and scheduling controlled substances.	Not relevant to UK practice
Miller NS (2006) Physicians and the Controlled Substance Laws for Prescription Opiate Medications. Psychiatric Annals 36(6):	Not relevant study

Author	Reason for exclusion
422-9	
Mitchell M, Veitch B (2000) Responsibility for controlled drugs in operating departments. British Journal of Nursing 9(17): 1139-43	Not relevant
Moore AP (1995) Pharmacy costs associated with handling of controlled drugs. British Journal of Medical Economics 9(1): 69-72	Not relevant
O'Neal BC (2004) Controlled-substance diversion detection: Go the extra mile Hospital Pharmacy 39(9): 868-70	Not relevant
Phillips D (1985) Guidelines for prescribers of controlled drugs Journal of the Arkansas Medical Society 81(9) 463-4	Not relevant to UK practice
Phillips D (1990) Physician controlled drug records. Journal of the Arkansas Medical Society 86(12): 513	Commentary article
Phillips J (2013) Prescription drug abuse: problem, policies and implications. Nursing Outlook 61(2) 78-4	Not relevant to UK practice
Poon SJ, Greenwood-Ericksen MB (2014) The opioid prescription epidemic and the role of emergency medicine. Annals of Emergency Medicine 64(5): 490-5	Not relevant
Portenoy RK (1993) Therapeutic use of opioids: prescribing and control issues. Research Monograph 131: 35-50	Not relevant
Primeaux B, Chelette C, Smith C (2012) Pharmacists' involvement in the use of a prescription monitoring program. Journal of the American Pharmacists Association 52(2): 236	Abstract only
Reisfield G, Paulian G, Merlo L, et al. (2010) Opioid prescription under filling among retail pharmacies. Pain Medicine 11(4): 586-90	Not relevant
Sigler KA, Guernsey BG, Ingrim NB, et al. (1984) Effect of a triplicate prescription law on prescribing of Schedule II drugs. American Journal of Hospital Pharmacy 41(1): 108-11	Not relevant to the review question.
Sigmon SC, Dunn KE, Saulsgiver K, et al. (2013) A randomized, double-blind evaluation of buprenorphine taper duration in primary prescription opioid abusers. JAMA Psychiatry 70(12): 1347-1354	No relevant intervention
Sihvo S, Hemminki E, Ahonen R (1999) Physicians' attitudes toward reclassifying drugs as over-the-counter. Medical Care 37(5): 518-26	Opinion article.
Smith DE, Wesson DR (1972) Legitimate and illegitimate distribution of amphetamines and barbiturates. Journal of Psychedelic Drugs 5(2): 177-81	Unable to source
Smith M, Rosenblum A, Parrino M, et al. (2010) Validity of self-reported misuse of prescription opioid analgesics. Substance Use & Misuse 45(10) 1509-24	No relevant intervention
Smolarek RT, Roffe BD, Solomon DK (801) Types of selected security devices for hospital pharmacies. Hospital Pharmacy 19(12) 795-7	No relevant interventions, systems or processes included within the paper.
Sokalska ME (1984) Legal measures to combat drug-related problems in Poland. Bulletin on Narcotics 36 (3)19-25	Not relevant to UK practice
Sprague K (2014) DEA issues final rule on disposal of controlled substances. Consultant Pharmacist 29(11): 772	Not relevant to UK practice
Springer R (2005) Managing controlled substances in the office surgical setting. Plastic Surgical Nursing 25(2) 100-4	Not relevant evidence type or study design.

Author	Reason for exclusion
Stanos SP, Fishbain DA, Fishman SM (2009) Pain management with opioid analgesics: Balancing risk & benefit. American Journal of Physical Medicine and Rehabilitation 88(3)(Suppl 2): S69-99	Not relevant as out of scope.
Stephens AE (1985) Implementing an inventory control of alcohol, controlled substances, and pharmaceutical supplies. Hospital Materiel Management Quarterly 7(2) 38-49	Not relevant evidence type or study design.
Twillman RK, Kirch R, Gilson A (2014) Efforts to control prescription drug abuse: Why clinicians should be concerned and take action as essential advocates for rational policy. CA Cancer Journal for Clinicians 64(6): 369-76	Not relevant to the review question.
Viliunas A (1971) Prescribing barbiturates Medical Journal of Australia 2(13): 684	Not relevant intervention, system or processes included in the paper.
Volkow ND, Frieden TR, Hyde PS, et al. (2014) Medication-assisted therapies--tackling the opioid-overdose epidemic. New England Journal of Medicine 370(22): 2063-6	No relevant intervention
Wellman GS, Hammond RL, Talmage R (2001) Computerized controlled-substance surveillance: application involving automated storage and distribution cabinets. American Journal of Health-System Pharmacy 58(19): 1830-5	Not relevant
Whalen RP, Silverman R (1975) Diversion of narcotic and stimulant drugs. New York State Journal of Medicine 75 (5): 735-7	Not relevant
Wilford BB (1990) Prescription drug abuse and control. Hospital Pharmacy 25(8): 796	Bibliography only.
Wolfert MZ, Gilson AM, Dahl JL et al. (2010) Opioid analgesics for pain control: Wisconsin physicians' knowledge, beliefs, attitudes, and prescribing practices. Pain Medicine 11 (3) 425-434	No relevant intervention

C.5.3 Administering controlled drugs

Author	Reason for exclusion
Anon (2004) What's wrong with prescribing hypnotics? Drug & Therapeutics Bulletin 42(12): 89-93	Not relevant evidence type or study design.
Anthierens S, Habraken H, Petrovic M, et al. (2007) The lesser evil? Initiating a benzodiazepine prescription in general practice: a qualitative study on GPs' perspectives. Scandinavian Journal of Primary Health Care 25(4): 214-19	No relevant outcomes
Balter MB, Uhlenhuth EH (1992) Prescribing and use of benzodiazepines: an epidemiologic perspective. Journal of Psychoactive Drugs 24(1): 63-4	Commentary article
Baros AM, Latham PK, Moak DH, et al. (2007) What role does measuring medication compliance play in evaluating the efficacy of naltrexone? Alcoholism, clinical and experimental research. 31(4): 596-603	Not relevant intervention
Bartlett A, Dholakia N, England R, et al. (2014) Prison prescribing practice: Practitioners' perspectives on why prison is different. International Journal of Clinical Practice 68(4): 413-17	Not relevant evidence type or study design.
Bates C, Laciak R, Southwick A, et al. (2011) Overprescription of postoperative narcotics: a look at postoperative pain medication	No relevant comparator

Author	Reason for exclusion
delivery, consumption and disposal in urological practice. Journal of Urology 185(2) 551-55	
Batty GM, Grant RL, Aggarwal R, et al. (2003) Using prescribing indicators to measure the quality of prescribing to elderly medical in-patients. Age & Ageing 32(3): 292-8	Not relevant intervention
Becker WC, Fiellin DA (2012) Prescriber education on opioids. Annals of Internal Medicine 157(12): 917	Not relevant evidence type.
Bell JR, Ryan A, Mutch C, et al. (2008) Optimising the benefits of unobserved dose administration for stable opioid maintenance patients: follow-up of a randomised trial. Drug & Alcohol Dependence 96 (1-2):183-6	No relevant outcomes
Bendtsen P, Hensing G, McKenzie L et al. (1999) Prescribing benzodiazepines--a critical incident study of a physician dilemma. Social Science & Medicine 49(4):459-67	No relevant comparator
Broekmans S, Vanderschueren S, Morlion B, et al. (2004) Nurses' attitudes toward pain treatment with opioids: a survey in a Belgian University Hospital. International Journal of Nursing Studies 41(2): 183-9	Not relevant
Broglio K, Cole BE (1937) Prescribing opioids in primary care: avoiding perils and pitfalls. Nurse Practitioner 39(6): 30-7	Review article
Comerford D (2008) Techniques of opioid administration. Anaesthesia and Intensive Care Medicine 9(1):21-6	Not relevant intervention
Cormack MA, Howells E (1992) Factors linked to the prescribing of benzodiazepines by general practice principals and trainees. Family Practice 9(4): 466-71	Not relevant evidence type or study design.
Dalleur O, Spinewine A, Henrard S, et al. (2012) Inappropriate prescribing and related hospital admissions in frail older persons according to the STOPP and START criteria. Drugs & Aging 29(10): 829-37	Not relevant intervention.
Dalleur O, Boland B, Losseau C, et al. (2014) Reduction of potentially inappropriate medications using the STOPP criteria in frail older inpatients: A randomised controlled study. Drugs and Aging 31(4):291-8	Not relevant intervention.
de Leon J, Chambers A, Hyatt M, et al. (2012) A practitioner's guide to prescribing clonazepam for adults with intellectual disabilities. de Leon, Jose [Ed] 507-74	Unable to source
de Leon J, Chambers A, Hyatt M, et al. (2012) A practitioner's guide to prescribing diazepam for adults with intellectual disabilities. [References] de Leon, Jose [Ed] 507-94	Unable to source
de Leon J, Chambers A, Hyatt M et al. (2012) A practitioner's guide to prescribing lorazepam for adults with intellectual disabilities. [References] de Leon, Jose [Ed] (2012) 507-254	Unable to source
Denison DE, Schneider F, Childs S, et al. (2011) A prevalence study of errors in opioid prescribing in a large teaching hospital. International Journal of Clinical Practice 65(9): 923-9	Not relevant evidence type or study design.
Derby S, Chin J, Portenoy RK. (1998) Systemic opioid therapy for chronic cancer pain. Practical guidelines for converting drugs and routes of administration. CNS Drugs 9(2): 99-109	Not relevant evidence type or study design.
Dybwad TB, Kjolsrod L, Eskerud J et al. (1997) Why are some doctors high-prescribers of benzodiazepines and minor opiates? A qualitative study of GPs in Norway. Family Practice 14(5) 361-8	Not relevant evidence type.
Gunningberg L, Poder U, Donaldson N, et al. (2014) Medication administration accuracy: Using clinical observation and review of patient records to assess safety and guide performance	No relevant comparator.

Author	Reason for exclusion
improvement. Journal of Evaluation in Clinical Practice 20(4): 411-16	
Huang AR, Mallet L. (2013) Prescribing opioids in older people. Maturitas 74(2): 123-9	Not relevant intervention
Humphries CA, Counsell DJ, Pediani RC, et al. (1997) Audit of opioid prescribing: the effect of hospital guidelines. Anaesthesia 52 (8) 745-49	Not relevant
Kahan M, Wilson L, Wenghofer EF, et al. (2011) Pharmacists' experiences with dispensing opioids: provincial survey. Canadian Family Physician 57(11): e448-54	Not relevant evidence type or study design.
Lader M. (1986) A practical guide to prescribing hypnotic benzodiazepines. British Medical Journal 293 (6554) 1048-9	Not relevant evidence type or study design.
Lamont T, Matthew L, Cousins D, et al. (2009) Avoiding midazolam overdose: summary of a safety report from the National Patient Safety Agency. British Medical Journal 339: 4459	Not relevant evidence type or study design.
Lampert A, Seiberth J, Haefeli WE, et al. (2014) A systematic review of medication administration errors with transdermal patches (Provisional abstract). Database of Abstracts of Reviews of Effects (1): 1101-14	No relevant intervention
Lange A, Lasser KE, Xuan Z, et al. (2015) Variability in opioid prescription monitoring and evidence of aberrant medication taking behaviors in urban safety-net clinics. Pain 156(2): 335-40	No relevant comparator
Lesar TS, Smith HS (2011) Making opioid prescribing safer: Time for a checklist? Pain Management 1(4): 279-85	Not relevant evidence type or study design.
Lesar TS, Lomaestro BM, Pohl H. (1997) Medication-prescribing errors in a teaching hospital. A 9-year experience. Archives of Internal Medicine 157(14):1569-76	No relevant intervention
Loder E. (2003) Who will prescribe? A proposal for specialized opioid management clinics. Pain Practice 3(3): 218-21	Review article only describing a model for prescribing opioids with no outcomes reported.
Logan J, Liu Y, Paulozzi L, et al. (2013) Opioid prescribing in emergency departments: the prevalence of potentially inappropriate prescribing and misuse. Medical Care 51(8):646-53	Not a relevant intervention.
Logan M, Fothergill-Bourbonnais F. (1990) Continuous subcutaneous infusion of narcotics. CSCI Canadian Nurse 86(4): 31-2	Not relevant evidence type or study design.
Lum PJ, Little S, Botsko M, et al. (2011) Opioid-prescribing practices and provider confidence recognizing opioid analgesic abuse in HIV primary care settings. Journal of Acquired Immune Deficiency Syndromes 56 (Suppl. 1) S91-7	No relevant outcome measures.
Lynas K (2005) New Rx monitoring system tracks narcotics. Canadian Pharmacists Journal 138 (6):18	Not relevant evidence type or study design, review article only.
Lynas K (2013) Pharmacists can play a key role in implementing new national strategy to combat prescription drug abuse. Canadian Pharmacists Journal 146(3):128-9	Not relevant evidence type or study design, review article only.
Mc DC. (2011) Opioid medication errors in pediatric practice: four years' experience of voluntary safety reporting. Pain Research & Management 16(2): 93-8	No relevant comparator
Mettner J. (2013) The opioid crisis: combating misuse through	Not relevant evidence type or

Author	Reason for exclusion
better prescribing. Minnesota Medicine 96(3): 20-5	study design, review article only.
Miller MM, Brown RT. (2007) Prescription drug monitoring programs. American Family Physician 75(6): 810-12	Not relevant evidence type or study design, review article only.
Morgan LA, Weaver MF. (2010) Preventing prescription opioid overdose. Journal of Clinical Outcomes Management 17(11): 33-42	Not relevant evidence type or study design, review article only.
Murnion BP, Gnjidic D, Hilmer SN. (2010) Prescription and administration of opioids to hospital in-patients, and barriers to effective use. Pain Medicine 11(1) 58-66	No relevant intervention
Newgreen DB, George LJ, Lloyd AI. (1986) Prescribing and dispensing of benzodiazepines by pharmacists Medical Journal of Australia 144(7) 370-1	Not relevant intervention.
Nutt DJ. (2005) Dr Shipman's last legacy: E-surveillance of the medical profession. Journal of Psychopharmacology 19(5):441	Not relevant evidence type or study design.
Penko J, Mattson J, Miaskowski C et al. (2012) Do patients know they are on pain medication agreements? Results from a sample of high-risk patients on chronic opioid therapy. Pain Medicine 13(9): 1174-80	No relevant intervention.
Peota C. (2014) Opioid prescribing primer. Doctors urged to become knowledgeable about risk Minnesota Medicine 97(4): 9	Not relevant evidence type or study design.
Prewitt J, Schneider S, Horvath M, et al. (2013) PCA safety data review after clinical decision support and smart pump technology implementation. Journal of patient safety 9(2):103-9	No relevant intervention
Rastegar DA, Walley AY. (2013) Preventing prescription opioid overdose deaths. Journal of General Internal Medicine 28(10): 1258-9	Not relevant evidence type or study design, review article only.
Reifler LM, Droz D, Bailey JE, et al. (2012) Do Prescription Monitoring Programs Impact State Trends in Opioid Abuse/Misuse? Pain Medicine 13(3) 434-42	No relevant outcome measures.
Reisfield GM, Sloan PA (2012) Physician identification of opioid diversion: a difficult diagnosis. Journal of Opioid Management 8(1):5-6	Not relevant evidence type or study design. Editorial only.
Rhodes WB, Ball KD. (1989) Benzodiazepine prescribing Lancet 2(8671): 1103	Not relevant evidence type or study design, review article only.
Rothschild JM, Keohane CA, Cook EF, et al. (2005) A controlled trial of smart infusion pumps to improve medication safety in critically ill patients Critical Care Medicine 33(3): 533-40	The study does not mention the use of controlled drugs in the infusion pump, but refers to other medicines.
Salmenlainen P. (2000) Inappropriate prescribing of benzodiazepines by doctors in New South Wales. New South Wales Public Health Bill 11(4): 57-8	No relevant intervention.
Siderov J, Zalcberg JR (1994) Prescribing opioids - A painful experience.Medical Journal of Australia 161(9): 515-16	Not relevant evidence type or study design, review article only.
Sketris IS, Meldrum M, Lacey D, et al. (1987) Effect of a two-day stop-order policy on benzodiazepine prescribing American	No relevant outcomes

Author	Reason for exclusion
Journal of Hospital Pharmacy 44(12): 2736-8	
Smith AJ, Tett SE. (2010) Improving the use of benzodiazepines--is it possible? A non-systematic review of interventions tried in the last 20 years. BMC Health Services Research 10: 321	No relevant interventions
Strang J, Sheridan J (2003) Effect of national guidelines on prescription of methadone: analysis of NHS prescription data, England 1990-2001 BMJ 327(7410): 321-22	No relevant outcomes reported in the study.
Strang J, Sheridan J (2001) Methadone prescribing to opiate addicts by private doctors: comparison with NHS practice in south east England Addiction 96 (4) 567-576	No relevant outcomes
Strang J, Sheridan J, Hunt C, et al. (2005) The prescribing of methadone and other opioids to addicts: national survey of GPs in England and Wales. British Journal of General Practice 55(515):444-51	No relevant outcomes
Turk DC, Swanson KS, Gatchel RJ (2008) Predicting opioid misuse by chronic pain patients: A systematic review and literature synthesis. Clinical Journal of Pain 24(6): 497-508	No relevant outcome measures reported.

C.5.4 Handling controlled drugs

Author	Reason for exclusion
Anon (1977) 12 tips for prescribers of controlled drugs. Bulletin of the Philadelphia County Dental Society 42(6):14	Unable to source
Anon (1997) A guide to prescribing, administering and dispensing controlled substances in Missouri. Missouri Medicine 94 (2): 76-81	Not relevant to UK practice
Anon (1977) A medical society's guidelines for prescribing controlled drugs. Hospital Formulary 12(10): 677	Not relevant to the review question
Anon (1991) ASHP statement on the pharmacist's responsibility for distribution and control of drugs. American Journal of Hospital Pharmacy 48(8): 1782	Not relevant to UK practice
Anon (1987) ASHP technical assistance bulletin on institutional use of controlled substances. American Journal of Hospital Pharmacy 44(3): 580-9	Duplicate guideline
Anon (2004) CD registers are to be centralised at Prescription Pricing Authority. Pharmaceutical Journal 273 (7330): 874	Not relevant evidence type or study design.
Anon (2003) Check CD prescriptions Pharmaceutical Journal 271 (7264): 258	Brief guidance issued within the journal
Anon (2013) Codeine care: Mitigating abuse and misuse. SA Pharmaceutical Journal.80 (5): 46-7	No relevant outcomes reported
Anon (1968) Control of amphetamine preparations. British Medical Journal 4(5630): 572-3	Review article.
Anon (1970) Control of amphetamines and L.S.D. Lancet 1(7649): 708	Not relevant evidence type or study design
Anon (1974) Control of habit forming drugs. Illinois Medical Journal 145(4): 348-9	Not relevant evidence type or study design
Anon (1961) Controlled Drugs. Canadian Medical Association Journal 85(11): 661	Editorial only
Anon (2004) Controlled Drugs guide. Pharmaceutical Journal 272 (7304): 756	Abstract only
Anon (2005) Controlled drugs in primary care: An update. MeReC Bulletin 15(3): 1-4	Unable to source

Author	Reason for exclusion
Anon (1987) Controlled substances from the emergency room. North Carolina Medical Journal 48(7):372-6	Not relevant evidence type or study design.
Anon (1967) Dependence on alcohol and other drugs. WHO Chronicle 21(6): 219-6	Not relevant evidence type or study design
Anon (2002) Destruction of controlled drugs Pharmaceutical Journal.269(7218): 475	Brief description of guidance for destruction of controlled drugs
Anon (2004) Destruction of out-of-date Controlled Drugs. Pharmaceutical Journal 272 (7292):395	Brief description of guidance for destruction of controlled drugs
Anon (1982) Detecting and preventing drug abuse and diversion. Hospital Security & Safety Management 3(5): 5-9	Unable to source.
Anon (1972) Division of drug abuse control. Journal of the Arkansas Medical Society 69(7): 214-5	Not relevant evidence type or study design
Anon (1983) Doctors for drug addicts. British Medical Journal Clinical Research Ed 286 (6381):1844	Not relevant to the review question.
Anon (2007) Drug diversion in healthcare: risks and prevention. Healthcare Hazard Management Monitor 21(4):1-8	Unable to source
Anon (1971) Drug trafficking and drug abuse. Medical Journal of Australia 1(22):1151-3	Not relevant evidence type or study design
Anon (2005) E-prescribing for controlled substances. Tennessee Medicine 98(12): 561	Not relevant to the review question
Anon (2010) Electronic prescriptions for controlled substances. Optometry St Louis (7): 367-72	Not relevant to the review question
Anon (1999) Emergency situations and controlled medicines. WHO Drug Information 13(3): 147-8	Not relevant evidence type or study design
Anon (1979) Federal strategy for drug abuse and drug traffic prevention. Contemporary Drug Problems 8(2): 227-49	Not relevant to UK practice
Anon (1980) Guidelines for controlled substances. Journal of the Medical Association of the State of Alabama 50(4): 12-17	Newsletter only
Anon (1980) Guidelines for prescribers of controlled substances. Journal of the American Podiatry Association 70(9): 481-2	Not relevant to the review question
Anon (1978) How nurses should handle matters related to controlled substances. Pharmacy Times 44(1): 38-40	Unable to source
Anon (2000) How one hospital tackles the drug theft/diversion problem head-on. Hospital Security & Safety Management 20(11): 8-10	Unable to source
Anon (2002) How to monitor drug diversion from automated dispensing cabinets. Healthcare Hazard Management Monitor 15(11): 6-7	Unable to source
Anon (1990) Managing controlled drugs in the office. Ohio Medicine 86(4): 315	Not relevant evidence type or study design.
Anon (2005) National templates should be produced for CD assessment Pharmaceutical. Journal 275 (7369): 399	Review article only.
Anon (1973) New state drug law seen affecting doctors' prescribing procedures N.Y.MED 29(11): 434	Reason for exclusion: Unable to source
Anon (1970) O-T-C preparations--potential for misuse. Panel discussion. American Journal of Pharmacy & the Sciences Supporting Public Health 142(1): 46-60	Discussion article only.
Anon (1987) PADS: a program to identify and diagnose prescription drug diversion in Indiana. Indiana Medicine 80(9):874-6	Reason for exclusion: not relevant
Anon (2007) Pain, opioids, and addiction: An urgent problem for	Reason for exclusion: Not

Author	Reason for exclusion
doctors and patients. Journal of Pain & Palliative Care Pharmacotherapy 21(4): 45-9	relevant to the review question.
Anon (2005) Pharmacies to make annual CD use declarations. Pharmaceutical Journal 275(7358): 71	Review article only
Anon (1972) Possession of rediscovered drugs British Medical Journal 1 (5794) 259-260	Review protocol criteria not met.
Anon (1996) Prescription drug diversion. Virginia Medical Quarterly 123(2): 132	Not relevant
Anon (1986) Reducing employee drug diversion in hospitals. Hospital Security & Safety Management 7(2): 5-9	Unable to source
Anon (1980) Rule on prescribing, dispensing of amphetamines. Wisconsin Medical Journal 79(6):47	Not relevant intervention
Anon (1979) Safe use of psychotropic and narcotic substances. WHO Chronicle 33(1): 12-15	Not relevant evidence type or study design
Anon (1968) Safety of drugs. British Medical Journal 3 (5621):758	Not relevant evidence type or study design
Anon (1972) Safety of medicines British Medical Journal 4 (5834): 192	Editorial only.
Anon (1997) Stockpiling painkillers Nursing 27 (10): 32	Editorial only.
Anon (1969) The misuse of pentazocine. Its dependence-producing potential. JAMA 209(10) 1518-9	Not relevant evidence type or study design
Anon (1968) The physician and the drug abuse laws. JAMA 205 (11): 788-9	Commentary article
Anon (1976) The supply of opium derivatives. Medical Journal of Australia 1(24): 899-900	Not relevant evidence type or study design.
Anon (1976) The use and misuse of psychotropic drugs. (Afrikaans) South African Medical Journal.50 (21): 793-4	Not English language
Anon (1967) Use and misuse of drugs. Nursing Times 63 (48): 1612-3	Unable to source
Abedtash H, Finnell JT. (2014) Emergency physician assessment of opiate risk from prescription drug monitoring program data [Abstract]. In: Academic Emergency Medicine Conference Publication 2014. Annual Meeting of the Society for Academic Emergency Medicine 13 – 17 May 2014 Dallas, United States. 21 (5): (Suppl.1): S270-1	Abstract only
Abrams PC. (1948) Cross-check for narcotics solution control. Hospitals 22(3):50	Unable to source
Akici A, Demircan D, Topcu I, et al. (2011) Assessment of controlled medicines prescription patterns in the context of green and red coloured scripts [Abstract]. Basic and Clinical Pharmacology and Toxicology. Congress of the European Association for Clinical Pharmacology and Therapeutics Publication, 10th Conference 26 – 29 June 2011 Budapest, Hungary. 141	Abstract only
Akins K. (1972) Amphetamine controls. Canadian Medical Association Journal 107(2): 113	Not relevant to UK practice
Alldred A. (2007) Managing controlled drugs - Taking ownership of the new agenda. Hospital Pharmacist14(6): 178	Commentary article
Austin LH. (1967) A simplified narcotic distribution system. American Journal of Hospital Pharmacy 24(10): 561-5	No relevant outcomes reported from the system.
Baker K. (2003) How do you dispose of a controlled substance? Drug Topics 147 (4): 58	Not relevant evidence type or study design
Baker KR. (2010) Monitoring controlled substances. Drug Topics	not relevant evidence type or

Author	Reason for exclusion
154(9)	study design
Barclay J, Clarkson B, Blackhall L, et al. (2013) Substance abuse and diversion in palliative care. (TH341) safety net. SIG Journal of Pain and Symptom management. Conference of the Annual Assembly of the American Academy of Hospice and Palliative Medicine and the Hospice and Palliative Nurses Association. 13 March 2013 New Orleans, United States. 361-2	Not relevant evidence type or study design.
Barnard D. (2002) World Health Organization guidelines for national narcotics control policies. Journal of Palliative Medicine 5(4): 575-7	Not relevant evidence type or study design
Barnea Z, Teichman M. (1994) Substance misuse and abuse among the elderly: Implications for social work intervention. Journal of Gerontological Social Work 21 (3-4): 133-48	Not relevant
Beatty Y. (2005) Controlled substance tracking. Tennessee Medicine 98(10): 467	Not relevant evidence type or study design
Belcher J, Nielsen S, Campbell G, et al. (2014) Diversion of prescribed opioids by people living with chronic pain: Results from an Australian community sample. Drug and Alcohol Review 33(1): 27-32	No relevant intervention
Bell DM, McDonough JP, Ellison JS, et al. (1999) Controlled drug misuse by Certified Registered Nurse Anesthetists. Journal 67(2): 133-40	Not relevant to the review question
Bell J. (2010) The global diversion of pharmaceutical drugs: opiate treatment and the diversion of pharmaceutical opiates: a clinician's perspective. Addiction 105(9): 1531-7	Not relevant study
Bellizzi JJ. (1970) Legal prescription of narcotics. New York State Journal of Medicine 70(12): 1677-80	Not relevant to the review question.
Benjamin DM (2007) Prosecution of physicians for prescribing opioids to patients. Clinical Pharmacology & Therapeutics 81(6): 797-8	Not relevant to the review question
Berge KH, Dillon KR, Sikkink KM, et al. (2012) Diversion of drugs within health care facilities, a multiple-victim crime: patterns of diversion, scope, consequences, detection, and prevention. Mayo Clinic Proceedings 87(7) 674-82	Not relevant study
Bergman U, Griffiths RR (1986) Relative abuse of diazepam and oxazepam: prescription forgeries and theft/loss reports in Sweden. Drug & Alcohol Dependence 16(4): 293-301	Not relevant
Bizer JE (1972) A study to evaluate the controlled substance distribution system at Hendrick Memorial Hospital, Abilene, Texas. Abstracts of Hospital Management Studies 9 (309469)	Abstract only
Black HJ (1983) How much control for controlled substances? American Journal of Hospital Pharmacy 40 (5): 788	Not relevant evidence type or study design
Bogardus DE (2005) Hospital security response to narcotics theft. Journal of Healthcare Protection Management 21(1): 97-100	Not relevant
Bourne PG (1973) Methadone diversion. In: Proceedings of National Conference on Methadone Treatment 2 839-41	Not relevant
Brands B, Blake J, Sproule B, et al. (2004) Prescription opioid abuse in patients presenting for methadone maintenance treatment. Drug and Alcohol Dependence 73(2): 199-207	No relevant intervention
Brent NJ (1989) Administering controlled substances in the	Not relevant to the review

Author	Reason for exclusion
home: minimizing the risk of potential diversion. Home Healthcare Nurse 7(4): 6-7	question
Burgess FW, Pawasauskas J (2008) Opioid therapy and prescription drug diversion. Medicine & Health, Rhode Island 91(9): 268-70	Not relevant study
Burton J, Echternach J, Rodgers J, et al. (2014) Controlled substance prescribing for discharged emergency patients: Effects of a prescription reporting initiative on physician prescribing. Academic Emergency Medicine. Annual 21 (Suppl.1): S101-2	Not relevant to the review question
Buttram ME, Kurtz SP, Surratt HL, et al. (2014) Health and social problems associated with prescription opioid misuse among a diverse sample of substance-using MSM. Substance Use & Misuse 49(3): 277-84	Not relevant
Calesnick B (1977) Controlled substances. American Family Physician 16(4): 180-1	Not relevant for UK practice
Carlson GM, Castile JA, Janousek JP (1988) Guidelines for the prevention and detection of controlled substance diversion. Hospital Pharmacy 23(12): 1057-9	Not relevant
Carmody G, Vogel D (1986) Unit dose distribution of controlled substances for the operating room. American Journal of Hospital Pharmacy 43(2): 413-415	No relevant outcomes reported from the system used.
Cerda M, Ransome Y, Keyes KM, et al. (2013) Prescription opioid mortality trends in New York City, 1990-2006: Examining the emergence of an epidemic. Drug and Alcohol Dependence 132(1-2): 53-62	Not relevant
Chan K, Groves RL (1979) The use of 'controlled drugs' in general practice. Journal of Clinical Pharmacy 4(2): 101-13	Not relevant to the review question
Chi J (2004) Who is registered to handle controlled substances? Drug Topics 148 (15): 148	Not relevant evidence type or study design
Chisholm AB, Harrison MJ (2009) Opioid abuse amongst anaesthetists: A system to detect personal usage. Anaesthesia & Intensive Care 37(2): 267-71	No relevant outcomes
Chua SM, Lee TS (2006) Abuse of prescription buprenorphine, regulatory controls and the role of the primary physician. Annals of the Academy of Medicine Singapore 35(7): 492-5	Not relevant evidence type or study design.
Clark J (2013) E-prescribing controlled substances moves closer to reality Health Management Technology 34(11): 24	Review article only
Clarke H, MacDougall P, Fraser J et al. (2013) Safe and effective prescribing controlled substances for pain management: Strategies from the office to the community Pain Research and Management. Proceedings of the 2013 Annual Conference of the Canadian Pain Society, Winnipeg, Canada. 8 May – 10 May 2013.18(2): e1-2	Not relevant to the review question
Clayton R (2007) CD guidance for secondary care - Ensuring procedures are fit for purpose. Pharmaceutical Journal 278 (7451): 555-6	Commentary article
Cleary JF, Cherny N (2014) Is opioid over-regulation hurting cancer patients? Clinical Practice.11(2): 125-9	Not relevant as out of scope.
Cohen J (1991) Prescribing controlled drugs. Practitioner 235(1502): 452-4	Not relevant to the review question
Cohen S (1979) The prescription of controlled substances: what's right and what's wrong. NIDA Research Monograph 27: 11-16	Not relevant to the review question

Author	Reason for exclusion
Coletti CM, Nomura JT, Farley H (2011) Opioid prescriptions from the emergency department: A descriptive analysis. In proceedings of Annals of Emergency Medicine Conference: American College of Emergency Physicians, Research Forum. 15 – 16 January 2011 San Francisco, United States. 58(4) (Suppl.1): S228	No relevant outcomes.
Coplan P (2014) Controlling controlled substances abuse and misuse by managed care payers: a new generation of risk management initiatives? Pharmacoepidemiology & Drug Safety 23(4): 428-30	Commentary article
Curran RE (1962) Canada and controlled drugs. Medical Services Journal 18: 415-30	Not relevant to UK practice
Dasgupta N (2014) Opioid analgesic prescribing and overdose mortality in North Carolina. Dissertation Abstracts International: The Sciences and Engineering 75	Not relevant to the review question
Davies K (2011) Identifying unprescribed controlled medication use: A database analysis. Journal of Pain 12 (4) Suppl. 1): 61	Abstract only
Davis WR, Johnson BD (2008) Prescription opioid use, misuse, and diversion among street drug users in New York City. Drug and Alcohol Dependence 92 (1-3): 267-76	Not relevant
Demircan D, Gulmez SE, Donertas B, et al. (2013) Use of drugs subject to controlled prescriptions: a retrospective analysis. Balkan Medical Journal 30(1) 46-53	No relevant outcomes
Dobscha SK (2013) Prescription opioids and benzodiazepines: Moving beyond "just say no". Pain Medicine 14(10): 1447-9	Not relevant to the review question
Doig I, Cordy C (2004) A review of controlled substances. Medicine & Health, Rhode Island 87(6): 186-188	Not relevant to UK practice
Duffy P, Mackridge AJ (2014) Use and diversion of illicit methadone-Under what circumstances does it occur, and potential risks associated with continued use of other substances. Journal of Substance Use 19(1-2): 48-55	Not relevant
DuPont RL (1993) Benzodiazepines, addiction, and public policy. New Jersey Medicine 90(11) 823-6	Not relevant evidence type or study design
Eckel FM (2009) Are we using controlled substances properly? Pharmacy Times 75(11): 1	Not relevant to the review question
Eckel FM (2014) Controlled substance misuse and abuse: Solving the problem of opioid safety. Pharmacy Times 80 (7)	Commentary article
Eggen AE, Andrew M (1994) Use of codeine analgesics in a general population. A Norwegian study of moderately strong analgesics. European Journal of Clinical Pharmacology 46(6): 491-6	Not relevant
Ehrhardt HE, Schroder O (1977) The effects of prescription orders on the control of narcotic drugs. Bulletin on Narcotics 29(2): 1-7	Not relevant to UK practice
Eidson K (2010) Controlled Substance Monitoring Database (CSMD) Journal of the Tennessee Dental Association 90(2):14-6	Not relevant study
El-Aneed A, Alaghehbandan R, Gladney N, et al. (2009) Prescription drug abuse and methods of diversion: The potential role of a pharmacy network. Journal of Substance Use 14(2):75-83	Not relevant study
Feldman SM, Bingham TC (2012) Misuse and abuse associated with buprenorphine utilization for the treatment of opioid dependency. Journal of Managed Care Pharmacy 18: 188	Abstract only
Finlayson RE (1995) Misuse of prescription drugs. International	Review article only

Author	Reason for exclusion
Journal of the Addictions 30 (13-14) 1871-901	
Fishman SM, Papazian JS, Gonzalez S, et al. (2004) Regulating opioid prescribing through prescription monitoring programs: balancing drug diversion and treatment of pain. Pain Medicine 5(3): 309-24	Not relevant to UK practice
Foote FM (1972) Patient requests for controlled drugs. Connecticut Medicine 36 (2): 85-6	Not relevant evidence type or study design
Fornili K, Simoni-Wastila L (2011) Prescription monitoring programs: Striking the balance between medical use and diversion. Journal of Addictions Nursing 22(1-2): 77-82	Not relevant
Forsyth B (1983) Computer controlled drug abuse Computers in Healthcare 4 (4) 22-26	Not relevant evidence type or study design.
Fountain J, Griffiths P, Farrell M, et al. (1998) Diversion tactics: How a sample of drug misusers in treatment obtained surplus drugs to sell on the illicit market. International Journal of Drug Policy 9(3): 159-67	No relevant interventions, systems or processes included within the paper. Findings summarised to highlight problems
Fox SL (1976) The physician and the controlled drug laws Maryland State Medical Journal 25(2): 64-70	Not relevant to UK practice
Foxhall K (2005) Controlled substances can now be ordered electronically. Drug Topics.149 (12)	Not relevant to UK practice
Fraser J (2013) Effective monitoring of controlled substance prescribing. Pain Research and Management 18(2): e2	Not relevant to the review question.
Freeman PR, Talbert J, Blumenschein K (2011) Impact of prescription monitoring programs on controlled substance prescribing behaviour. Proceedings of 16th Annual International Meeting of the International Society for Pharmacoeconomics and Outcomes Research(ISPOR) 21 – 25 May 2011, Baltimore, United States. A27	Abstract only
Gardner JR (1985) Are your controlled substances controlled? Texas Hospitals 40(11): 30-3	Unable to source
Giltrow J (2006) Monitoring and inspection of controlled drugs: Role of the society's inspectors Pharmaceutical Journal.277 (7430): 702-7	Not relevant study
Greenwald BD, Narcessian EJ (1999) Opioids for managing patients with chronic pain: Community pharmacists' perspectives and concerns. Journal of Pain and Symptom Management 17(5): 369-75)	Not relevant evidence type or study design.
Griffith R (2007) Legal requirements for the prescribing and administration of medicines. British Journal of Community Nursing 12(10): 477-81	Limited information relating to controlled drugs
Griffith R, Tengnah C (2011) Prescription of controlled drugs by non-medical prescribers. British Journal of Community Nursing 16(11): 558-62	Not a relevant intervention
Gwira Baumblatt JA, Wiedeman C, Dunn JR, et al. (2014) High-risk use by patients prescribed opioids for pain and its role in overdose deaths. JAMA Internal Medicine 174 (5): 796-801	Not relevant to the review question.
Hagemeier NE, Gray JA, Pack RP (2013) Prescription drug abuse: A comparison of prescriber and pharmacist perspectives. Substance Use & Misuse 48(9): 783-90	Not relevant intervention
Hagen T (2012) Review of a pharmacist-implemented controlled substance refill program in a patient-centered medical home. Journal of the American Pharmacists Association 52(2): 258	Not a relevant intervention

Author	Reason for exclusion
Halldorsson A (2007) Prescribing of controlled substances for non-patients in the educational setting: Review of the ethical, legal, and moral dilemma for residents. Medical Education Online 12: 1-6	No relevant intervention
Hallinan R, Osborn M, Cohen M et al. (2011) Increasing the benefits and reducing the harms of prescription opioid analgesics. Drug and Alcohol Review 30(3): 315-23	No interventions discussed as part of the review article
Hamrick LC (1978) Prescription blanks in group practice: a strategy for control. Group Practice 27(3) 28-9	Not relevant to the review question.
Harrison B (2006) Prescription drug monitoring programs. Ncsl Legisbrief 14(4):1-2	Review article only.
Hayes P, Hickey K, Lovell S, et al. (1976) The storage of drugs in homes. Medical Journal of Australia 1(8): 235-6	Not relevant evidence type or study design
Hazebrook LS, Ross TW, Ploetz PA (1991) Computer system for determining trends in controlled-substance discrepancies. American Journal of Hospital Pharmacy 48 (6):1262-4	No relevant comparator. A new system is implemented, however its effect was not compared in the study to the previous system used to identify trends.
Hibbard FJ, Bair JN, Sylvester KL (1983) Pharmacy-based controlled substances distribution for a university campus. American Journal of Hospital Pharmacy 40(1): 74-7	Not relevant
Hoover RC, McCormick WC, Harrison WL (1981) Pilferage of controlled substances in hospitals American Journal of Hospital Pharmacy 38(7): 1007-10	Not relevant
Hoppe J, Howland MA, Nelson L (2014) The role of pharmacies and pharmacists in managing controlled substance dispensing. Pain Medicine 15(12) 1996-8	Commentary article
Horgan C, Prottas J, Tompkins C et al. (1993) Summary and conclusions of a review of prescription drug diversion control methods. NIDA Research Monograph 131: 206-23	Not relevant
Hurwitz W (2005) The challenge of prescription drug misuse: A review and commentary. Pain Medicine 6(2): 152-61	Not relevant
Inciardi JA, Surratt HL, Kurtz SP, et al. (2007) Mechanisms of prescription drug diversion among drug-involved club- and street-based populations. Pain Medicine 8(2): 171-83	Not relevant
Inciardi JA, Surratt HL, Cicero TJ, et al. (2009) Prescription opioid abuse and diversion in an urban community: The results of an ultrarapid assessment. Pain Medicine 10(3): 537-548	Not relevant
Inciardi JA, Surratt HL, Cicero TJ et al. (2009) The "black box" of prescription drug diversion. Journal of Addictive Diseases 28(4): 332-47	Not relevant
Inciardi JA, Surratt HL, Kurtz SP, et al. (2006) The diversion of prescription drugs by health care workers in Cincinnati, Ohio. Substance Use & Misuse 41(2): 255-64	Not relevant
Irvine JM, Hallvik SE, Hildebran C et al. (2014) Who uses a prescription drug monitoring program and how? Insights from a statewide survey of Oregon clinicians. Journal of Pain 15(7): 747-55	Not relevant
Jaramillo JE, Farrar RD (2011) Unused medications: A case report - show me the money. Clinical Toxicology 49 (6): 607	Not relevant
Jatav VS, Saggu JS, Jat RK et al. (2011) Recent advances in development of transdermal patches Pharmacophore 2(6): 287-	Not relevant

Author	Reason for exclusion
97)	
Jay MP (2008) E-prescribing of controlled substances: Safer than paper. Drug Benefit Trends 20(7): 287-8	Commentary article
Johnson BD (2003) Patterns of drug distribution: implications and issues. Substance Use & Misuse 38 (11-13):1789-1806	Review article
Johnson JA, Code WE, Duncan PG (1990) "An improved system for narcotic control in the operating room" Canadian Journal of Anaesthesia 37 (4:Pt 2)	Not relevant
Johnson KW, Grube JW, Ogilvie KA, et al. (2012) A community prevention model to prevent children from inhaling and ingesting harmful legal products. Evaluation and Program Planning 35(1): 113-23	Not relevant
Johnson K, Courser M, Holder H et al. (2007) A community prevention intervention to reduce youth from inhaling and ingesting harmful legal products. Journal of Drug Education 37(3): 227-47	Not relevant
Johnson PE (2011) Drug shortages: impact and strategies. Journal of the National Comprehensive Cancer Network 9 (8): 815-9	Commentary article
Johnson RE (1973) Present and projected drug system services in a highly developed HMO structure. Health Service Rep 88(9): 873-7	Not relevant
Joranson DE (1993) Availability of opioids for cancer pain: recent trends, assessment of system barriers. New World Health Organization guidelines and the risk of diversion. Journal of Pain & Symptom Management 8(6): 353-60	Not relevant study
Joranson DE (1993) Guiding principles of international and federal laws pertaining to medical use and diversion of controlled substances. NIDA Research Monograph 131:18-34	Not relevant to UK practice
Joranson DE, Gilson AM (2006) Wanted: a public health approach to prescription opioid abuse and diversion Pharmacoepidemiology & Drug Safety 15(9): 632-4	Not relevant
Joranson DE, Gilson AM (2005) Drug crime is a source of abused pain medications in the United States. [References] Journal of Pain and Symptom Management 30(4): 299-301	Commentary article
Kage A (2012) Audit on prescription of controlled drug Archives of Disease in Childhood. Proceedings of 4th Congress of the European Academy of Paediatric Societies, 5 – 9 January 2012 Istanbul Turkey 97: 436	Abstract
Kern SI (2010) Controlled drugs: how to minimize the risks to you and your patients. Medical Economics 87(15): 50-1	Commentary article
Kern SI (2008) Perils when prescribing controlled drugs. Medical Economics 85(3): 20	Commentary article
Lien CA (2012) A need to establish programs to detect and prevent drug diversion. Mayo Clinic Proceedings 87 (7): 607-9	Commentary article
Longo LP, Parran T Jr., Johnson B, et al. (2000) Addiction: part II. Identification and management of the drug-seeking patient. American Family Physician 61(8): 2401-8	Not relevant
Longo LP (1999) Resting assured: risk management in the prescription of controlled substances. WMJ 98(1) 23-9	Not relevant study
Lurie P, Lee PR (1991) Fifteen solutions to the problems of prescription drug abuse. Journal of Psychoactive Drugs 23(4): 349-57	Not relevant study

Author	Reason for exclusion
Lynas K (2012) Pharmacists not part of current regulatory change on prescribing controlled substances. Canadian Pharmacists Journal 145(4): 156	Commentary article
Mackintosh D, Molloy V (2002) Reconciling drug accountability records Good Clinical Practice Journal 9(4): 24-5	Not relevant study
Martin ES, Dzierba SH, Jones DM (2013) Preventing large-scale controlled substance diversion from within the pharmacy. Hospital Pharmacy 48(5) 406-12	Not relevant
McClary B, Cable DW (1999) A guide to prescribing, administering, and dispensing controlled substances in Missouri. Missouri Medicine 96(2) 47-54	Not relevant study
McCormick CG (2006) Regulatory challenges for new formulations of controlled substances in today's environment. Drug and Alcohol Dependence 83 (Suppl.1): S63-7	Not relevant
Miller NS (2006) Failure of enforcement controlled substance laws in health policy for prescribing opiate medications: a painful assessment of morbidity and mortality. American Journal of Therapeutics 13(6): 527-33	Not relevant to UK practice
Miller NS (2004) Prescription opiate medications: Medical uses and consequences, laws and controls. Psychiatric Clinics of North America.27(4): 689-708	Not relevant to UK practice
Miller NSE (2006) This Issue: Prescription Opiate Medications Psychiatric Annals 36(6): 378-82	Commentary article
Miller NS (2010) Legal authority, medical basis and public policy for controlling and scheduling controlled substances.	Not relevant to UK practice
Miller NS (2006) Physicians and the Controlled Substance Laws for Prescription Opiate Medications. Psychiatric Annals 36(6): 422-9	Not relevant study
Mitchell M, Veitch B (2000) Responsibility for controlled drugs in operating departments. British Journal of Nursing 9(17): 1139-43	Not relevant
Moore AP (1995) Pharmacy costs associated with handling of controlled drugs. British Journal of Medical Economics 9(1): 69-72	Not relevant
O'Neal BC (2004) Controlled-substance diversion detection: Go the extra mile Hospital Pharmacy 39(9): 868-70	Not relevant
Phillips D (1985) Guidelines for prescribers of controlled drugs Journal of the Arkansas Medical Society 81(9) 463-4	Not relevant to UK practice
Phillips D (1990) Physician controlled drug records. Journal of the Arkansas Medical Society 86(12): 513	Commentary article
Phillips J (2013) Prescription drug abuse: problem, policies and implications. Nursing Outlook 61(2) 78-4	Not relevant to UK practice
Poon SJ, Greenwood-Ericksen MB (2014) The opioid prescription epidemic and the role of emergency medicine. Annals of Emergency Medicine 64(5): 490-5	Not relevant
Portenoy RK (1993) Therapeutic use of opioids: prescribing and control issues. Research Monograph 131: 35-50	Not relevant
Primeaux B, Chelette C, Smith C (2012) Pharmacists' involvement in the use of a prescription monitoring program. Journal of the American Pharmacists Association 52(2): 236	Abstract only
Reisfield G, Paulian G, Merlo L, et al. (2010) Opioid prescription under filling among retail pharmacies. Pain Medicine 11(4): 586-	Not relevant

Author	Reason for exclusion
90	
Sigler KA, Guernsey BG, Ingrim NB, et al. (1984) Effect of a triplicate prescription law on prescribing of Schedule II drugs. American Journal of Hospital Pharmacy 41(1): 108-11	Not relevant to the review question.
Sigmon SC, Dunn KE, Saulsgiver K, et al. (2013) A randomized, double-blind evaluation of buprenorphine taper duration in primary prescription opioid abusers. JAMA Psychiatry 70(12): 1347-1354	No relevant intervention
Sihvo S, Hemminki E, Ahonen R (1999) Physicians' attitudes toward reclassifying drugs as over-the-counter. Medical Care 37(5): 518-26	Opinion article.
Smith DE, Wesson DR (1972) Legitimate and illegitimate distribution of amphetamines and barbiturates. Journal of Psychedelic Drugs 5(2): 177-81	Unable to source
Smith M, Rosenblum A, Parrino M, et al. (2010) Validity of self-reported misuse of prescription opioid analgesics. Substance Use & Misuse 45(10) 1509-24	No relevant intervention
Smolarek RT, Roffe BD, Solomon DK (801) Types of selected security devices for hospital pharmacies. Hospital Pharmacy 19(12) 795-7	No relevant interventions, systems or processes included within the paper.
Sokalska ME (1984) Legal measures to combat drug-related problems in Poland. Bulletin on Narcotics 36 (3)19-25	Not relevant to UK practice
Sprague K (2014) DEA issues final rule on disposal of controlled substances. Consultant Pharmacist 29(11): 772	Not relevant to UK practice
Springer R (2005) Managing controlled substances in the office surgical setting. Plastic Surgical Nursing 25(2) 100-4	Not relevant evidence type or study design.
Stanos SP, Fishbain DA, Fishman SM (2009) Pain management with opioid analgesics: Balancing risk & benefit. American Journal of Physical Medicine and Rehabilitation 88(3)(Suppl 2): S69-99	Not relevant as out of scope.
Stephens AE (1985) Implementing an inventory control of alcohol, controlled substances, and pharmaceutical supplies. Hospital Materiel Management Quarterly 7(2) 38-49	Not relevant evidence type or study design.
Twillman RK, Kirch R, Gilson A (2014) Efforts to control prescription drug abuse: Why clinicians should be concerned and take action as essential advocates for rational policy. CA Cancer Journal for Clinicians 64(6): 369-76	Not relevant to the review question.
Viliunas A (1971) Prescribing barbiturates Medical Journal of Australia 2(13): 684	Not relevant intervention, system or processes included in the paper.
Volkow ND, Frieden TR, Hyde PS, et al. (2014) Medication-assisted therapies--tackling the opioid-overdose epidemic. New England Journal of Medicine 370(22): 2063-6	No relevant intervention
Wellman GS, Hammond RL, Talmage R (2001) Computerized controlled-substance surveillance: application involving automated storage and distribution cabinets. American Journal of Health-System Pharmacy 58(19): 1830-5	Not relevant
Whalen RP, Silverman R (1975) Diversion of narcotic and stimulant drugs. New York State Journal of Medicine 75 (5): 735-7	Not relevant
Wilford BB (1990) Prescription drug abuse and control. Hospital	Bibliography only.

Author	Reason for exclusion
Pharmacy 25(8): 796	
Wolfert MZ, Gilson AM, Dahl JL et al. (2010) Opioid analgesics for pain control: Wisconsin physicians' knowledge, beliefs, attitudes, and prescribing practices. Pain Medicine 11 (3) 425-434	No relevant intervention

C.5.5 Monitoring controlled drugs

Author	Reason for exclusion
Anon (1977) 12 tips for prescribers of controlled drugs. Bulletin of the Philadelphia County Dental Society 42(6):14	Unable to source
Anon (1997) A guide to prescribing, administering and dispensing controlled substances in Missouri. Missouri Medicine 94 (2): 76-81	Not relevant to UK practice
Anon (1977) A medical society's guidelines for prescribing controlled drugs. Hospital Formulary 12(10): 677	Not relevant to the review question
Anon (1991) ASHP statement on the pharmacist's responsibility for distribution and control of drugs. American Journal of Hospital Pharmacy 48(8): 1782	Not relevant to UK practice
Anon (1987) ASHP technical assistance bulletin on institutional use of controlled substances. American Journal of Hospital Pharmacy 44(3): 580-9	Duplicate guideline
Anon (2004) CD registers are to be centralised at Prescription Pricing Authority. Pharmaceutical Journal 273 (7330): 874	Not relevant evidence type or study design.
Anon (2003) Check CD prescriptions Pharmaceutical Journal 271 (7264): 258	Brief guidance issued within the journal
Anon (2013) Codeine care: Mitigating abuse and misuse. SA Pharmaceutical Journal.80 (5): 46-7	No relevant outcomes reported
Anon (1968) Control of amphetamine preparations. British Medical Journal 4(5630): 572-3	Review article.
Anon (1970) Control of amphetamines and L.S.D. Lancet 1(7649): 708	Not relevant evidence type or study design
Anon (1974) Control of habit forming drugs. Illinois Medical Journal 145(4): 348-9	Not relevant evidence type or study design
Anon (1961) Controlled Drugs. Canadian Medical Association Journal 85(11): 661	Editorial only
Anon (2004) Controlled Drugs guide. Pharmaceutical Journal 272 (7304): 756	Abstract only
Anon (2005) Controlled drugs in primary care: An update. MeReC Bulletin 15(3): 1-4	Unable to source
Anon (1987) Controlled substances from the emergency room. North Carolina Medical Journal 48(7):372-6	Not relevant evidence type or study design.
Anon (1967) Dependence on alcohol and other drugs. WHO Chronicle 21(6): 219-6	Not relevant evidence type or study design
Anon (2002) Destruction of controlled drugs Pharmaceutical Journal.269(7218): 475	Brief description of guidance for destruction of controlled drugs
Anon (2004) Destruction of out-of-date Controlled Drugs. Pharmaceutical Journal 272 (7292):395	Brief description of guidance for destruction of controlled drugs
Anon (1982) Detecting and preventing drug abuse and diversion. Hospital Security & Safety Management 3(5): 5-9	Unable to source.
Anon (1972) Division of drug abuse control. Journal of the	Not relevant evidence type or

Author	Reason for exclusion
Arkansas Medical Society 69(7): 214-5	study design
Anon (1983) Doctors for drug addicts. British Medical Journal Clinical Research Ed 286 (6381):1844	Not relevant to the review question.
Anon (2007) Drug diversion in healthcare: risks and prevention. Healthcare Hazard Management Monitor 21(4):1-8	Unable to source
Anon (1971) Drug trafficking and drug abuse. Medical Journal of Australia 1(22):1151-3	Not relevant evidence type or study design
Anon (2005) E-prescribing for controlled substances. Tennessee Medicine 98(12): 561	Not relevant to the review question
Anon (2010) Electronic prescriptions for controlled substances. Optometry St Louis (7): 367-72	Not relevant to the review question
Anon (1999) Emergency situations and controlled medicines. WHO Drug Information 13(3): 147-8	Not relevant evidence type or study design
Anon (1979) Federal strategy for drug abuse and drug traffic prevention. Contemporary Drug Problems 8(2): 227-49	Not relevant to UK practice
Anon (1980) Guidelines for controlled substances. Journal of the Medical Association of the State of Alabama 50(4): 12-17	Newsletter only
Anon (1980) Guidelines for prescribers of controlled substances. Journal of the American Podiatry Association 70(9): 481-2	Not relevant to the review question
Anon (1978) How nurses should handle matters related to controlled substances. Pharmacy Times 44(1): 38-40	Unable to source
Anon (2000) How one hospital tackles the drug theft/diversion problem head-on. Hospital Security & Safety Management 20(11): 8-10	Unable to source
Anon (2002) How to monitor drug diversion from automated dispensing cabinets. Healthcare Hazard Management Monitor 15(11): 6-7	Unable to source
Anon (1990) Managing controlled drugs in the office. Ohio Medicine 86(4): 315	Not relevant evidence type or study design.
Anon (2005) National templates should be produced for CD assessment Pharmaceutical. Journal 275 (7369): 399	Review article only.
Anon (1973) New state drug law seen affecting doctors' prescribing procedures N.Y.MED 29(11): 434	Reason for exclusion: Unable to source
Anon (1970) O-T-C preparations--potential for misuse. Panel discussion. American Journal of Pharmacy & the Sciences Supporting Public Health 142(1): 46-60	Discussion article only.
Anon (1987) PADS: a program to identify and diagnose prescription drug diversion in Indiana. Indiana Medicine 80 (9):874-6	Reason for exclusion: not relevant
Anon (2007) Pain, opioids, and addiction: An urgent problem for doctors and patients. Journal of Pain & Palliative Care Pharmacotherapy 21(4): 45-9	Reason for exclusion: Not relevant to the review question.
Anon (2005) Pharmacies to make annual CD use declarations. Pharmaceutical Journal 275(7358): 71	Review article only
Anon (1972) Possession of rediscovered drugs British Medical Journal 1 (5794) 259-260	Review protocol criteria not met.
Anon (1996) Prescription drug diversion. Virginia Medical Quarterly 123(2): 132	Not relevant
Anon (1986) Reducing employee drug diversion in hospitals. Hospital Security & Safety Management 7(2): 5-9	Unable to source
Anon (1980) Rule on prescribing, dispensing of amphetamines.	Not relevant intervention

Author	Reason for exclusion
Wisconsin Medical Journal 79(6):47	
Anon (1979) Safe use of psychotropic and narcotic substances. WHO Chronicle 33(1): 12-15	Not relevant evidence type or study design
Anon (1968) Safety of drugs. British Medical Journal 3 (5621):758	Not relevant evidence type or study design
Anon (1972) Safety of medicines British Medical Journal 4 (5834): 192	Editorial only.
Anon (1997) Stockpiling painkillers Nursing 27 (10): 32	Editorial only.
Anon (1969) The misuse of pentazocine. Its dependence-producing potential. JAMA 209(10) 1518-9	Not relevant evidence type or study design
Anon (1968) The physician and the drug abuse laws. JAMA 205 (11): 788-9	Commentary article
Anon (1976) The supply of opium derivatives. Medical Journal of Australia 1(24): 899-900	Not relevant evidence type or study design.
Anon (1976) The use and misuse of psychotropic drugs. (Afrikaans) South African Medical Journal.50 (21): 793-4	Not English language
Anon (1967) Use and misuse of drugs. Nursing Times 63 (48): 1612-3	Unable to source
Anon. (1993) ASHP technical assistance bulletin on use of controlled substances in organized health care settings. American Journal of Hospital Pharmacy 50(3): 489-501	Not relevant
Anon. (2005) Maintaining running balances of stock in Controlled Drug registers. Pharmaceutical Journal.274 (7351): 660	Not relevant
Anon. (1980) Principles and guidelines for distribution of narcotic and other psychoactive drugs Canadian Pharmaceutical Journal 113 (9): 289-292	Not relevant
Abedtash H, Finnell JT. (2014) Emergency physician assessment of opiate risk from prescription drug monitoring program data [Abstract]. In: Academic Emergency Medicine Conference Publication 2014. Annual Meeting of the Society for Academic Emergency Medicine 13 – 17 May 2014 Dallas, United States. 21 (5): (Suppl.1): S270-1	Abstract only
Abrams PC. (1948) Cross-check for narcotics solution control. Hospitals 22(3):50	Unable to source
Ahmed I, Majeed A. (2007) The safe and responsible disposal of unused controlled drugs. British Journal of Nursing 16(21): 1318-22	Not relevant
Akici A, Demircan D, Topcu I, et al. (2011) Assessment of controlled medicines prescription patterns in the context of green and red coloured scripts [Abstract]. Basic and Clinical Pharmacology and Toxicology. Congress of the European Association for Clinical Pharmacology and Therapeutics Publication, 10th Conference 26 – 29 June 2011 Budapest, Hungary. 141	Abstract only
Akins K. (1972) Amphetamine controls. Canadian Medical Association Journal 107(2): 113	Not relevant to UK practice
Alldred A. (2007) Managing controlled drugs - Taking ownership of the new agenda. Hospital Pharmacist14(6): 178	Commentary article
Austin LH. (1967) A simplified narcotic distribution system. American Journal of Hospital Pharmacy 24(10): 561-5	No relevant outcomes reported from the system.
Baker K. (2003) How do you dispose of a controlled substance? Drug Topics 147 (4): 58	Not relevant evidence type or study design

Author	Reason for exclusion
Baker KR. (2010) Monitoring controlled substances. Drug Topics 154(9)	not relevant evidence type or study design
Barclay J, Clarkson B, Blackhall L, et al. (2013) Substance abuse and diversion in palliative care. (TH341) safety net. SIG Journal of Pain and Symptom management. Conference of the Annual Assembly of the American Academy of Hospice and Palliative Medicine and the Hospice and Palliative Nurses Association. 13 March 2013 New Orleans, United States. 361-2	Not relevant evidence type or study design.
Barnard D. (2002) World Health Organization guidelines for national narcotics control policies. Journal of Palliative Medicine 5(4): 575-7	Not relevant evidence type or study design
Barnea Z, Teichman M. (1994) Substance misuse and abuse among the elderly: Implications for social work intervention. Journal of Gerontological Social Work 21 (3-4): 133-48	Not relevant
Beatty Y. (2005) Controlled substance tracking. Tennessee Medicine 98(10): 467	Not relevant evidence type or study design
Belcher J, Nielsen S, Campbell G, et al. (2014) Diversion of prescribed opioids by people living with chronic pain: Results from an Australian community sample. Drug and Alcohol Review 33(1): 27-32	No relevant intervention
Bell DM, McDonough JP, Ellison JS, et al. (1999) Controlled drug misuse by Certified Registered Nurse Anesthetists. Journal 67(2): 133-40	Not relevant to the review question
Bell J. (2010) The global diversion of pharmaceutical drugs: opiate treatment and the diversion of pharmaceutical opiates: a clinician's perspective. Addiction 105(9): 1531-7	Not relevant study
Bellizzi JJ. (1970) Legal prescription of narcotics. New York State Journal of Medicine 70(12): 1677-80	Not relevant to the review question.
Benjamin DM (2007) Prosecution of physicians for prescribing opioids to patients. Clinical Pharmacology & Therapeutics 81(6): 797-8	Not relevant to the review question
Berge KH, Dillon KR, Sikkink KM, et al. (2012) Diversion of drugs within health care facilities, a multiple-victim crime: patterns of diversion, scope, consequences, detection, and prevention. Mayo Clinic Proceedings 87(7) 674-82	Not relevant study
Bergman U, Griffiths RR (1986) Relative abuse of diazepam and oxazepam: prescription forgeries and theft/loss reports in Sweden. Drug & Alcohol Dependence 16(4): 293-301	Not relevant
Bizer JE (1972) A study to evaluate the controlled substance distribution system at Hendrick Memorial Hospital, Abilene, Texas. Abstracts of Hospital Management Studies 9 (309469)	Abstract only
Black HJ (1983) How much control for controlled substances? American Journal of Hospital Pharmacy 40 (5): 788	Not relevant evidence type or study design
Bogardus DE (2005) Hospital security response to narcotics theft. Journal of Healthcare Protection Management 21(1): 97-100	Not relevant
Bourne PG (1973) Methadone diversion. In: Proceedings of National Conference on Methadone Treatment 2 839-41	Not relevant
Brands B, Blake J, Sproule B, et al. (2004) Prescription opioid abuse in patients presenting for methadone maintenance treatment. Drug and Alcohol Dependence 73(2): 199-207	No relevant intervention
Brent NJ (1989) Administering controlled substances in the home: minimizing the risk of potential diversion. Home	Not relevant to the review question

Author	Reason for exclusion
Healthcare Nurse 7(4): 6-7	
Burgess FW, Pawasauskas J (2008) Opioid therapy and prescription drug diversion. Medicine & Health, Rhode Island 91(9): 268-70	Not relevant study
Burton J, Echternach J, Rodgers J, et al. (2014) Controlled substance prescribing for discharged emergency patients: Effects of a prescription reporting initiative on physician prescribing. Academic Emergency Medicine. Annual 21 (Suppl.1): S101-2	Not relevant to the review question
Buttram ME, Kurtz SP, Surratt HL, et al. (2014) Health and social problems associated with prescription opioid misuse among a diverse sample of substance-using MSM. Substance Use & Misuse 49(3): 277-84	Not relevant
Calesnick B (1977) Controlled substances. American Family Physician 16(4): 180-1	Not relevant for UK practice
Carlson GM, Castile JA, Janousek JP (1988) Guidelines for the prevention and detection of controlled substance diversion. Hospital Pharmacy 23(12): 1057-9	Not relevant
Carmody G, Vogel D (1986) Unit dose distribution of controlled substances for the operating room. American Journal of Hospital Pharmacy 43(2): 413-415	No relevant outcomes reported from the system used.
Cerda M, Ransome Y, Keyes KM, et al. (2013) Prescription opioid mortality trends in New York City, 1990-2006: Examining the emergence of an epidemic. Drug and Alcohol Dependence 132(1-2): 53-62	Not relevant
Chan K, Groves RL (1979) The use of 'controlled drugs' in general practice. Journal of Clinical Pharmacy 4(2): 101-13	Not relevant to the review question
Chi J (2004) Who is registered to handle controlled substances? Drug Topics 148 (15): 148	Not relevant evidence type or study design
Chisholm AB, Harrison MJ (2009) Opioid abuse amongst anaesthetists: A system to detect personal usage. Anaesthesia & Intensive Care 37(2): 267-71	No relevant outcomes
Chua SM, Lee TS (2006) Abuse of prescription buprenorphine, regulatory controls and the role of the primary physician. Annals of the Academy of Medicine Singapore 35(7): 492-5	Not relevant evidence type or study design.
Clark J (2013) E-prescribing controlled substances moves closer to reality Health Management Technology 34(11): 24	Review article only
Clarke H, MacDougall P, Fraser J et al. (2013) Safe and effective prescribing controlled substances for pain management: Strategies from the office to the community Pain Research and Management. Proceedings of the 2013 Annual Conference of the Canadian Pain Society, Winnipeg, Canada. 8 May – 10 May 2013.18(2): e1-2	Not relevant to the review question
Clayton R (2007) CD guidance for secondary care - Ensuring procedures are fit for purpose. Pharmaceutical Journal 278 (7451): 555-6	Commentary article
Cleary JF, Cherny N (2014) Is opioid over-regulation hurting cancer patients? Clinical Practice.11(2): 125-9	Not relevant as out of scope.
Cohen J (1991) Prescribing controlled drugs. Practitioner 235(1502): 452-4	Not relevant to the review question
Cohen S (1979) The prescription of controlled substances: what's right and what's wrong. NIDA Research Monograph 27: 11-16	Not relevant to the review question

Author	Reason for exclusion
Coletti CM, Nomura JT, Farley H (2011) Opioid prescriptions from the emergency department: A descriptive analysis. In proceedings of Annals of Emergency Medicine Conference: American College of Emergency Physicians, Research Forum. 15 – 16 January 2011 San Francisco, United States. 58(4) (Suppl.1): S228	No relevant outcomes.
Coplan P (2014) Controlling controlled substances abuse and misuse by managed care payers: a new generation of risk management initiatives? Pharmacoepidemiology & Drug Safety 23(4): 428-30	Commentary article
Curran RE (1962) Canada and controlled drugs. Medical Services Journal 18: 415-30	Not relevant to UK practice
Dasgupta N (2014) Opioid analgesic prescribing and overdose mortality in North Carolina. Dissertation Abstracts International: The Sciences and Engineering 75	Not relevant to the review question
Davies K (2011) Identifying unprescribed controlled medication use: A database analysis. Journal of Pain 12 (4) Suppl. 1): 61	Abstract only
Davis WR, Johnson BD (2008) Prescription opioid use, misuse, and diversion among street drug users in New York City. Drug and Alcohol Dependence 92 (1-3): 267-76	Not relevant
Demircan D, Gulmez SE, Donertas B, et al. (2013) Use of drugs subject to controlled prescriptions: a retrospective analysis. Balkan Medical Journal 30(1) 46-53	No relevant outcomes
Dobscha SK (2013) Prescription opioids and benzodiazepines: Moving beyond "just say no". Pain Medicine 14(10): 1447-9	Not relevant to the review question
Doig I, Cordy C (2004) A review of controlled substances. Medicine & Health, Rhode Island 87(6): 186-188	Not relevant to UK practice
Duffy P, Mackridge AJ (2014) Use and diversion of illicit methadone-Under what circumstances does it occur, and potential risks associated with continued use of other substances. Journal of Substance Use 19(1-2): 48-55	Not relevant
DuPont RL (1993) Benzodiazepines, addiction, and public policy. New Jersey Medicine 90(11) 823-6	Not relevant evidence type or study design
Eckel FM (2009) Are we using controlled substances properly? Pharmacy Times 75(11): 1	Not relevant to the review question
Eckel FM (2014) Controlled substance misuse and abuse: Solving the problem of opioid safety. Pharmacy Times 80 (7)	Commentary article
Eggen AE, Andrew M (1994) Use of codeine analgesics in a general population. A Norwegian study of moderately strong analgesics. European Journal of Clinical Pharmacology 46(6): 491-6	Not relevant
Ehrhardt HE, Schroder O (1977) The effects of prescription orders on the control of narcotic drugs. Bulletin on Narcotics 29(2): 1-7	Not relevant to UK practice
Eidson K (2010) Controlled Substance Monitoring Database (CSMD) Journal of the Tennessee Dental Association 90(2): 14-6	Not relevant study
El-Aneed A, Alaghehbandan R, Gladney N, et al. (2009) Prescription drug abuse and methods of diversion: The potential role of a pharmacy network. Journal of Substance Use 14(2):75-83	Not relevant study

Author	Reason for exclusion
Feldman SM, Bingham TC (2012) Misuse and abuse associated with buprenorphine utilization for the treatment of opioid dependency. Journal of Managed Care Pharmacy 18: 188	Abstract only
Finlayson RE (1995) Misuse of prescription drugs. International Journal of the Addictions 30 (13-14) 1871-901	Review article only
Fishman SM, Papazian JS, Gonzalez S, et al. (2004) Regulating opioid prescribing through prescription monitoring programs: balancing drug diversion and treatment of pain. Pain Medicine 5(3): 309-24	Not relevant to UK practice
Foote FM (1972) Patient requests for controlled drugs. Connecticut Medicine 36 (2): 85-6	Not relevant evidence type or study design
Fornili K, Simoni-Wastila L (2011) Prescription monitoring programs: Striking the balance between medical use and diversion. Journal of Addictions Nursing 22(1-2): 77-82	Not relevant
Forsyth B (1983) Computer controlled drug abuse Computers in Healthcare 4 (4) 22-26	Not relevant evidence type or study design.
Fountain J, Griffiths P, Farrell M, et al. (1998) Diversion tactics: How a sample of drug misusers in treatment obtained surplus drugs to sell on the illicit market. International Journal of Drug Policy 9(3): 159-67	No relevant interventions, systems or processes included within the paper. Findings summarised to highlight problems
Fox SL (1976) The physician and the controlled drug laws Maryland State Medical Journal 25(2): 64-70	Not relevant to UK practice
Foxhall K (2005) Controlled substances can now be ordered electronically. Drug Topics.149 (12)	Not relevant to UK practice
Fraser J (2013) Effective monitoring of controlled substance prescribing. Pain Research and Management 18(2): e2	Not relevant to the review question.
Freeman PR, Talbert J, Blumenschein K (2011) Impact of prescription monitoring programs on controlled substance prescribing behaviour. Proceedings of 16th Annual International Meeting of the International Society for Pharmacoeconomics and Outcomes Research(ISPOR) 21 – 25 May 2011, Baltimore, United States. A27	Abstract only
Gardner JR (1985) Are your controlled substances controlled? Texas Hospitals 40(11): 30-3	Unable to source
Giltrow J (2006) Monitoring and inspection of controlled drugs: Role of the society's inspectors Pharmaceutical Journal.277 (7430): 702-7	Not relevant study
Greenwald BD, Narcessian EJ (1999) Opioids for managing patients with chronic pain: Community pharmacists' perspectives and concerns. Journal of Pain and Symptom Management 17(5): 369-75)	Not relevant evidence type or study design.
Griffith R (2007) Legal requirements for the prescribing and administration of medicines. British Journal of Community Nursing 12(10): 477-81	Limited information relating to controlled drugs
Griffith R, Tengnah C (2011) Prescription of controlled drugs by non-medical prescribers. British Journal of Community Nursing 16(11): 558-62	Not a relevant intervention
Gwira Baumblatt JA, Wiedeman C, Dunn JR, et al. (2014) High-risk use by patients prescribed opioids for pain and its role in overdose deaths. JAMA Internal Medicine 174 (5): 796-801	Not relevant to the review question.

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Hagemeier NE, Gray JA, Pack RP (2013) Prescription drug abuse: A comparison of prescriber and pharmacist perspectives. Substance Use & Misuse 48(9): 783-90	Not relevant intervention
Hagen T (2012) Review of a pharmacist-implemented controlled substance refill program in a patient-centered medical home. Journal of the American Pharmacists Association 52(2): 258	Not a relevant intervention
Halldorsson A (2007) Prescribing of controlled substances for non-patients in the educational setting: Review of the ethical, legal, and moral dilemma for residents. Medical Education Online 12: 1-6	No relevant intervention
Hallinan R, Osborn M, Cohen M et al. (2011) Increasing the benefits and reducing the harms of prescription opioid analgesics. Drug and Alcohol Review 30(3): 315-23	No interventions discussed as part of the review article
Hamrick LC (1978) Prescription blanks in group practice: a strategy for control. Group Practice 27(3) 28-9	Not relevant to the review question.
Harrison B (2006) Prescription drug monitoring programs. Ncsl Legisbrief 14(4):1-2	Review article only.
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Hazebrook LS, Ross TW, Ploetz PA (1991) Computer system for determining trends in controlled-substance discrepancies. American Journal of Hospital Pharmacy 48 (6):1262-4	No relevant comparator. A new system is implemented, however its effect was not compared in the study to the previous system used to identify trends.
Hibbard FJ, Bair JN, Sylvester KL (1983) Pharmacy-based controlled substances distribution for a university campus. American Journal of Hospital Pharmacy 40(1): 74-7	Not relevant
Hoover RC, McCormick WC, Harrison WL (1981) Pilferage of controlled substances in hospitals American Journal of Hospital Pharmacy 38(7): 1007-10	Not relevant
Hoppe J, Howland MA, Nelson L (2014) The role of pharmacies and pharmacists in managing controlled substance dispensing. Pain Medicine 15(12) 1996-8	Commentary article
Horgan C, Prottas J, Tompkins C et al. (1993) Summary and conclusions of a review of prescription drug diversion control methods. NIDA Research Monograph 131: 206-23	Not relevant
Hurwitz W (2005) The challenge of prescription drug misuse: A review and commentary. Pain Medicine 6(2): 152-61	Not relevant
Inciardi JA, Surratt HL, Kurtz SP, et al. (2007) Mechanisms of prescription drug diversion among drug-involved club- and street-based populations. Pain Medicine 8(2): 171-83	Not relevant
Inciardi JA, Surratt HL, Cicero TJ, et al. (2009) Prescription opioid abuse and diversion in an urban community: The results of an ultrarapid assessment. Pain Medicine 10(3): 537-548	Not relevant
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Inciardi JA, Surratt HL, Kurtz SP, et al. (2006) The diversion of prescription drugs by health care workers in Cincinnati, Ohio. Substance Use & Misuse 41(2): 255-64	Not relevant

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Irvine JM, Hallvik SE, Hildebran C et al. (2014) Who uses a prescription drug monitoring program and how? Insights from a statewide survey of Oregon clinicians. Journal of Pain 15(7): 747-55	Not relevant
Jaramillo JE, Farrar RD (2011) Unused medications: A case report - show me the money. Clinical Toxicology 49 (6): 607	Not relevant
Jatav VS, Saggu JS, Jat RK et al. (2011) Recent advances in development of transdermal patches Pharmacophore 2(6): 287-97)	Not relevant
Jay MP (2008) E-prescribing of controlled substances: Safer than paper. Drug Benefit Trends 20(7): 287-8	Commentary article
Johnson BD (2003) Patterns of drug distribution: implications and issues. Substance Use & Misuse 38 (11-13):1789-1806	Review article
Johnson JA, Code WE, Duncan PG (1990) "An improved system for narcotic control in the operating room" Canadian Journal of Anaesthesia 37 (4:Pt 2)	Not relevant
Johnson KW, Grube JW, Ogilvie KA, et al. (2012) A community prevention model to prevent children from inhaling and ingesting harmful legal products. Evaluation and Program Planning 35(1): 113-23	Not relevant
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Johnson PE (2011) Drug shortages: impact and strategies. Journal of the National Comprehensive Cancer Network 9 (8): 815-9	Commentary article
Johnson RE (1973) Present and projected drug system services in a highly developed HMO structure. Health Service Rep 88(9): 873-7	Not relevant
Joranson DE (1993) Availability of opioids for cancer pain: recent trends, assessment of system barriers. New World Health Organization guidelines and the risk of diversion. Journal of Pain & Symptom Management 8(6): 353-60	Not relevant study
Joranson DE (1993) Guiding principles of international and federal laws pertaining to medical use and diversion of controlled substances. NIDA Research Monograph 131:18-34	Not relevant to UK practice
Joranson DE, Gilson AM (2006) Wanted: a public health approach to prescription opioid abuse and diversion Pharmacoepidemiology & Drug Safety 15(9): 632-4	Not relevant
Joranson DE, Gilson AM (2005) Drug crime is a source of abused pain medications in the United States. [References] Journal of Pain and Symptom Management 30(4): 299-301	Commentary article
Kage A (2012) Audit on prescription of controlled drug Archives of Disease in Childhood. Proceedings of 4th Congress of the European Academy of Paediatric Societies, 5 – 9 January 2012 Istanbul Turkey 97: 436	Abstract
Kern SI (2010) Controlled drugs: how to minimize the risks to you and your patients. Medical Economics 87(15): 50-1	Commentary article
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Lien CA (2012) A need to establish programs to detect and prevent drug diversion. Mayo Clinic Proceedings 87 (7): 607-9	Commentary article

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Longo LP, Parran T Jr., Johnson B, et al. (2000) Addiction: part II. Identification and management of the drug-seeking patient. American Family Physician 61(8): 2401-8	Not relevant
Longo LP (1999) Resting assured: risk management in the prescription of controlled substances. WMJ 98(1) 23-9	Not relevant study
Lurie P, Lee PR (1991) Fifteen solutions to the problems of prescription drug abuse. Journal of Psychoactive Drugs 23(4): 349-57	Not relevant study
Lynas K (2012) Pharmacists not part of current regulatory change on prescribing controlled substances. Canadian Pharmacists Journal 145(4): 156	Commentary article
Mackintosh D, Molloy V (2002) Reconciling drug accountability records Good Clinical Practice Journal 9(4): 24-5	Not relevant study
Martin ES, Dzierba SH, Jones DM (2013) Preventing large-scale controlled substance diversion from within the pharmacy. Hospital Pharmacy 48(5) 406-12	Not relevant
McClary B, Cable DW (1999) A guide to prescribing, administering, and dispensing controlled substances in Missouri. Missouri Medicine 96(2) 47-54	Not relevant study
McCormick CG (2006) Regulatory challenges for new formulations of controlled substances in today's environment. Drug and Alcohol Dependence 83 (Suppl.1): S63-7	Not relevant
Miller NS (2006) Failure of enforcement controlled substance laws in health policy for prescribing opiate medications: a painful assessment of morbidity and mortality. American Journal of Therapeutics 13(6): 527-33	Not relevant to UK practice
Miller NS (2004) Prescription opiate medications: Medical uses and consequences, laws and controls. Psychiatric Clinics of North America.27(4): 689-708	Not relevant to UK practice
Miller NSE (2006) This Issue: Prescription Opiate Medications Psychiatric Annals 36(6): 378-82	Commentary article
Miller NS (2010) Legal authority, medical basis and public policy for controlling and scheduling controlled substances.	Not relevant to UK practice
Miller NS (2006) Physicians and the Controlled Substance Laws for Prescription Opiate Medications. Psychiatric Annals 36(6): 422-9	Not relevant study
Mitchell M, Veitch B (2000) Responsibility for controlled drugs in operating departments. British Journal of Nursing 9(17): 1139-43	Not relevant
Moore AP (1995) Pharmacy costs associated with handling of controlled drugs. British Journal of Medical Economics 9(1): 69-72	Not relevant
O'Neal BC (2004) Controlled-substance diversion detection: Go the extra mile Hospital Pharmacy 39(9): 868-70	Not relevant
Phillips D (1985) Guidelines for prescribers of controlled drugs Journal of the Arkansas Medical Society 81(9) 463-4	Not relevant to UK practice
Phillips D (1990) Physician controlled drug records. Journal of the Arkansas Medical Society 86(12): 513	Commentary article
Phillips J (2013) Prescription drug abuse: problem, policies and implications. Nursing Outlook 61(2) 78-4	Not relevant to UK practice
Poon SJ, Greenwood-Ericksen MB (2014) The opioid prescription epidemic and the role of emergency medicine. Annals of Emergency Medicine 64(5): 490-5	Not relevant

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Portenoy RK (1993) Therapeutic use of opioids: prescribing and control issues. Research Monograph 131: 35-50	Not relevant
Primeaux B, Chelette C, Smith C (2012) Pharmacists' involvement in the use of a prescription monitoring program. Journal of the American Pharmacists Association 52(2): 236	Abstract only
Reisfield G, Paulian G, Merlo L, et al. (2010) Opioid prescription under filling among retail pharmacies. Pain Medicine 11(4): 586-90	Not relevant
Sigler KA, Guernsey BG, Ingrim NB, et al. (1984) Effect of a triplicate prescription law on prescribing of Schedule II drugs. American Journal of Hospital Pharmacy 41(1): 108-11	Not relevant to the review question.
Sigmon SC, Dunn KE, Saulsgiver K, et al. (2013) A randomized, double-blind evaluation of buprenorphine taper duration in primary prescription opioid abusers. JAMA Psychiatry 70(12): 1347-1354	No relevant intervention
Sihvo S, Hemminki E, Ahonen R (1999) Physicians' attitudes toward reclassifying drugs as over-the-counter. Medical Care 37(5): 518-26	Opinion article.
Smith DE, Wesson DR (1972) Legitimate and illegitimate distribution of amphetamines and barbiturates. Journal of Psychedelic Drugs 5(2): 177-81	Unable to source
Smith M, Rosenblum A, Parrino M, et al. (2010) Validity of self-reported misuse of prescription opioid analgesics. Substance Use & Misuse 45(10) 1509-24	No relevant intervention
Smolarek RT, Roffe BD, Solomon DK (801) Types of selected security devices for hospital pharmacies. Hospital Pharmacy 19(12) 795-7	No relevant interventions, systems or processes included within the paper.
Sokalska ME (1984) Legal measures to combat drug-related problems in Poland. Bulletin on Narcotics 36 (3)19-25	Not relevant to UK practice
Sprague K (2014) DEA issues final rule on disposal of controlled substances. Consultant Pharmacist 29(11): 772	Not relevant to UK practice
Springer R (2005) Managing controlled substances in the office surgical setting. Plastic Surgical Nursing 25(2) 100-4	Not relevant evidence type or study design.
Stanos SP, Fishbain DA, Fishman SM (2009) Pain management with opioid analgesics: Balancing risk & benefit. American Journal of Physical Medicine and Rehabilitation 88(3)(Suppl 2): S69-99	Not relevant as out of scope.
Stephens AE (1985) Implementing an inventory control of alcohol, controlled substances, and pharmaceutical supplies. Hospital Materiel Management Quarterly 7(2) 38-49	Not relevant evidence type or study design.
Twillman RK, Kirch R, Gilson A (2014) Efforts to control prescription drug abuse: Why clinicians should be concerned and take action as essential advocates for rational policy. CA Cancer Journal for Clinicians 64(6): 369-76	Not relevant to the review question.
Viliunas A (1971) Prescribing barbiturates Medical Journal of Australia 2(13): 684	Not relevant intervention, system or processes included in the paper.
Volkow ND, Frieden TR, Hyde PS, et al. (2014) Medication-assisted therapies--tackling the opioid-overdose epidemic. New England Journal of Medicine 370(22): 2063-6	No relevant intervention
Wellman GS, Hammond RL, Talmage R (2001) Computerized controlled-substance surveillance: application involving automated storage and distribution cabinets. American Journal	Not relevant

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of Health-System Pharmacy 58(19): 1830-5	
Whalen RP, Silverman R (1975) Diversion of narcotic and stimulant drugs. New York State Journal of Medicine 75 (5): 735-7	Not relevant
Wilford BB (1990) Prescription drug abuse and control. Hospital Pharmacy 25(8): 796	Bibliography only.
Wolfert MZ, Gilson AM, Dahl JL et al. (2010) Opioid analgesics for pain control: Wisconsin physicians' knowledge, beliefs, attitudes, and prescribing practices. Pain Medicine 11 (3) 425-434	No relevant intervention

C.6 Secondary sources excluded from all review questions

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General Medical Council (2015) Consultation on changes to the Indicative Sanctions Guidance and on the role of apologies and warnings [accessed 30 March 2015]	Not relevant
General Medical Council (2015) Guidance on assessing the seriousness of concerns relating to self-prescribing or prescribing to those in personal relationships with doctors [accessed 30 March 2015]	Not relevant
General Medical Council (2015) Review of fitness to practise restriction banks and glossary [accessed 30 March 2015]	Not relevant
General Medical Council (2015) Mapping outcomes against Good medical practice [accessed 30 March 2015]	Not relevant
General Medical Council (2014) The state of medical education and practice in the UK report: 2014 [accessed 30 March 2015]	Not relevant
General Medical Council (2014) Be prepared: are new doctors safe to practise?	Not relevant
General Medical Council (2014) Guidance on making referrals to the disclosure and barring service [accessed 30 March 2015]	Not relevant
Monrouxe, L, Bullock A, Cole J, et al. (2014) How prepared are UK medical graduates for practice? Final report from a programme of research commissioned by the General Medical Council [accessed 30 March 2015]	Not relevant
General Medical Council (2014) Medical practitioners tribunal service interim orders pan conditions bank [accessed 30 March 2015]	Not relevant
General Medical Council (2014) Undertakings bank [accessed 30 March 2015]	Not relevant
General Medical Council (2014) Medical practitioners tribunal service fitness to practise panel conditions bank Not relevant	Not relevant
General Medical Council (2014) Guidance for doctors acting as responsible consultants or clinicians	Not relevant

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[accessed 30 March 2015]	
General Medical Council (2013) Good practice in prescribing and managing medicines and devices [accessed 30 March 2015]	Not relevant
General Medical Council (2013) Professional standards authority performance review report 2012-13 [accessed 30 March 2015]	Not relevant
Mathers, N, Mitchell C, Hunn A (2012) A study to assess the impact of continuing professional development (CPD) on doctors' performance and patient/service outcomes for the General Medical Council [accessed 30 March 2015]	Not relevant
General Medical Council (2012) Protecting children and young people: the responsibilities of all doctors [accessed 30 March 2015]	Not relevant
General Medical Council (2012) Leadership and management for all doctors [accessed 30 March 2015]	Not relevant
General Medical Council (2012) The state of medical education and practice in the UK [accessed 30 March 2015]	Not relevant
General Medical Council (2012) Raising and acting on concerns about patient safety [accessed 30 March 2015]	Not relevant
Avery, T, Barber N, Ghaleb M, et al. (2012) Investigating the prevalence and causes of prescribing errors in general practice: the PRACtICe study: a report for the General Medical Council [accessed 30 March 2015]	Not relevant
The Royal College of Anaesthetists (2012) Acute care common stem core training programme: curriculum and assessment system [accessed 30 March 2015]	Not relevant
The College of Emergency Medicine (2012) Curriculum and assessment systems for core specialty training ACCS CT1-3 & higher specialty training ST4-6 training programmes [accessed 30 March 2015]	Not relevant
Intercollegiate Board for Training in Pre-hospital Emergency Medicine (2011) Sub-specialty training in pre-hospital emergency medicine: curriculum framework [accessed 30 March 2015]	Not relevant
The Royal College of Anaesthetists (2011) Acute care common stem core training programme: curriculum and assessment system [accessed 30 March 2015]	Not relevant
General Medical Council (2010) Treatment and care towards the end of life: good practice in decision making [accessed 30 March 2015]	Not relevant
The Royal College of Anaesthetists (2010) CCT in Anaesthetics: Annex B – basic level training [accessed 30 March 2015]	Not relevant
The Royal College of Anaesthetists (2010) Acute care common stem core training: curriculum and assessment system	Not relevant

Reference	Reason for Exclusion
[accessed 30 March 2015]	
Joint Royal Colleges of Physicians Training Board (2010) Speciality training curriculum for medical oncology [accessed 30 March 2015]	Not relevant
Joint Royal Colleges of Physicians Training Board (2010) Speciality training curriculum for palliative medicine [accessed 30 March 2015]	Not relevant
Royal College of Psychiatrists (2009) A competency based curriculum for specialist training in psychiatry [accessed 30 March 2015]	Not relevant
De Vires H, Rabinovich L, Klautzer L, et al. (2009) International comparison of ten medical regulatory systems [accessed 30 March 2015]	Not relevant
General Medical Council (2009) Confidentiality [accessed 30 March 2015]	Not relevant
Postgraduate Education Board (2009) Foundation programme curriculum [accessed 30 March 2015]	Not relevant
General Medical Council (2008) Consent: patients and doctors making decisions together [accessed 30 March 2015]	Not relevant
The Royal College of Anaesthetists (2007) Acute care common stem core training: a manual for trainees and trainers [accessed 30 March 2015]	Not relevant
General Medical Council (2007) 0-18 years: guidance for all doctors [accessed 30 March 2015]	Not relevant
General Medical Council (2007) Palliative medicine assessment blueprint [accessed 30 March 2015]	Not relevant
General Medical Council (2007) Medical student engagement and registration [accessed 30 March 2015]	Not relevant
PMST Curriculum Working Group: Faculty of Pharmaceutical Medicine (2007) Curriculum for pharmaceutical medicine specialty training (PMST) [accessed 30 March 2015]	Not relevant
Joint Royal Colleges of Physicians Training Board (2007) Specialty training curriculum for palliative medicine [accessed 30 March 2015]	Not relevant
Joint Royal Colleges of Physicians Training Board (2007) Specialty training curriculum for medical oncology [accessed 30 March 2015]	Not relevant
College of Emergency Medicine (2006) Curriculum [accessed 30 March 2015]	Not relevant
General Medical Council Education Committee (2006) Strategic options for undergraduate medical education consultation: Final report [accessed 30 March 2015]	Not relevant
General Medical Council (2005) The Government's response to the fourth report of the Shipman Inquiry: implications for the	Already have as background

Reference	Reason for Exclusion
General Medical Council [accessed 30 March 2015]	
General Medical Council (2005) Strategic options for undergraduate medical education – annex A [accessed 30 March 2015]	Not relevant
Shipman Inquiry (2004) Shipman Inquiry: Fourth Report: summary of proposed government action. Annex B. [accessed 30 March 2015]	Not relevant to the review question but used for scope background.
Shipman Inquiry (2004) Shipman Inquiry: Fourth Report: executive summary (extract from the Government's response to the fourth report of the Shipman Inquiry. Annex A [accessed 30 March 2015]	Not relevant to the review question but used for scope background.
Shipman Inquiry (2004) Shipman Inquiry: Fourth Report: recommendations. Annex A. [accessed 30 March 2015]	Not relevant to the review question but used for scope background.
General Medical Council (1983) Professional conduct and discipline: fitness to practise [accessed 30 March 2015]	Not relevant
(date unknown) Annex B: Recommendation 2: prescribing rights of medical practitioners (see Annex A for full text) [accessed 30 March 2015]	Not relevant
(date unknown) Annex C: The new doctor: recommendations on general clinical training [accessed 30 March 2015]	Not relevant
Vincent C, Woloshynowych M. (date unknown) The assessment of performance: annex A. An analysis of general practitioner cases referred to the General Medical Council following the introduction of the performance procedures [accessed 30 March 2015]	Not relevant
General Medical Council (date unknown) Guidance on assessing the seriousness of concerns relating to self-prescribing, or prescribing to those in close personal relationships with doctors [accessed 30 March 2015]	Not relevant
General Medical Council (date unknown) Good practice in prescribing and managing medicines and devices: draft for consultation [accessed 30 March 2015]	Already captured
Dornan T. (date unknown) An in depth investigation into causes of prescribing errors by foundation trainees in relation to their medical education. EQUIP study. [accessed 30 March 2015]	Background / not relevant
General Dental Council (2013) Standards for the dental team [accessed 30 March 2015]	Not relevant
General Dental Council (2012) Corporate strategy 2013-2015 public confidence in dental regulation [accessed 30 March 2015]	Not relevant
General Dental Council (2009) Developing the dental team: Second edition (Interim) [accessed 30 March 2015]	Not relevant
General Dental Council (2008) The first five years: Third edition (interim)	Not relevant

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[accessed 30 March 2015]	
General Pharmaceutical Council (to be published – date TBA) The safe supply of pharmacy medicines [accessed 30 March 2015]	Not relevant
General Pharmaceutical Council (to be published in 2015) Distance sale and supply [accessed 30 March 2015]	Not relevant
General Pharmaceutical Council (2014) Guidance for registered pharmacies preparing unlicensed medicines [accessed 30 March 2015]	Not relevant
General Pharmaceutical Council (2014) GPhC highlights the requirement for openness and honesty amongst pharmacy professionals [accessed 30 March 2015]	Not relevant
General Pharmaceutical Council (2014) Guidance on tutoring for pharmacists and pharmacy technicians [accessed 30 March 2015]	Not relevant
General Pharmaceutical Council (2013) The standards for registered pharmacies [accessed 30 March 2015]	Not relevant
General Pharmaceutical Council (2013) Developing guidance to support the safe and effective supply of 'Pharmacy (P)' medicines [accessed 30 March 2015]	Not relevant
General Pharmaceutical Council (2013) Prototype inspection model – examples of evidence version 1.0 [accessed 30 March 2015]	Not relevant
General Pharmaceutical Council (2013) Inspection decision making framework version 8.0 [accessed 30 March 2015]	Not relevant
General Pharmaceutical Council (2012) Standards of conduct, ethics and performance [accessed 30 March 2015]	Not relevant
General Pharmaceutical Council (2012) Guidance on consent [accessed 30 March 2015]	Not relevant
General Pharmaceutical Council (2012) Guidance on patient confidentiality [accessed 30 March 2015]	Not relevant
General Pharmaceutical Council (2012) Guidance on raising concerns [accessed 30 March 2015]	Not relevant
General Pharmaceutical Council (2011) Future pharmacists: standards for the initial education and training of pharmacists [accessed 30 March 2015]	Not relevant
General Pharmaceutical Council (2010) Standards for continuing professional development [accessed 30 March 2015]	Not relevant
General Pharmaceutical Council (2010) Guidance for responsible pharmacists [accessed 30 March 2015]	Not relevant
General Pharmaceutical Council (2010) Responding to complaints and concerns	Not relevant

Reference	Reason for Exclusion
[accessed 30 March 2015]	
General Pharmaceutical Council (2010) Guidance for owners and superintendent pharmacists who employ responsible pharmacists [accessed 30 March 2015]	Not relevant
General Pharmaceutical Council (2010) Guidance on the provision of pharmacy services affected by religious and moral beliefs [accessed 30 March 2015]	Not relevant
General Pharmaceutical Council (2010) Standards for the initial education and training of pharmacy technicians [accessed 30 March 2015]	Not relevant
Public Health England (2015) Young people's statistics from the National Drug Treatment Monitoring System: financial year ending 31 March 2014 [accessed 30 March 2015]	Not relevant
Public Health England (2014) Drug statistics from the National Drug Treatment Monitoring System (NDTMS): financial year ending March 2014 [accessed 30 March 2015]	Not relevant
Public Health England (2014) Pregabalin and gabapentin: advice for prescribers on the risk of misuse [accessed 30 March 2015]	Not relevant
Public Health England (2014) Prescribed places of detention: health needs assessment toolkit [accessed 30 March 2015]	Not relevant
Public Health England (2014) Drug misuse and dependence: UK guidelines on clinical management: consultation outcome [accessed 30 March 2015]	Not relevant
National Treatment Agency for Substance Misuse (2013) Falling drug use: the impact of treatment [accessed 30 March 2015]	Not relevant
Nursing & Midwifery Council (2015) The code: professional standards of practice and behaviour for nurses and midwives [accessed 30 March 2015]	Not relevant
Nursing & Midwifery Council (2013) Raising concerns: guidance for nurses and midwives [accessed 30 March 2015]	Not relevant
Nursing & Midwifery Council (2012) Controlled drugs [accessed 30 March 2015]	Mentioned professional registration previously
Nursing & Midwifery Council (2012) Amendments to Home Office Misuse of Drugs Regulations 2001 [accessed 30 March 2015]	Legislation already taken into account
Nursing & Midwifery Council (2012) Midwives exemptions frequently asked questions [accessed 30 March 2015]	Not relevant
Keegan M (2011) Consultation response: Good practice in prescribing and managing medicines and devices [accessed 30 March 2015]	Not relevant
Nursing & Midwifery Council (2010) Nurse and midwife independent prescribing of unlicensed medicines [accessed 30 March 2015]	Not relevant

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Nursing & Midwifery Council (2010) Unlicensed medicines - changes to the indicative content of the independent and supplementary nurse prescribing programme - V300 [accessed 30 March 2015]	Not relevant
Nursing & Midwifery Council (2009) Standards of educational preparation for prescribing from the Nurse Prescribers Formulary for Community Practitioners for nurses without a specialist practitioner qualification - introducing code V150 [accessed 30 March 2015]	Not relevant
Nursing & Midwifery Council (2008) The code: standards of conduct, performance and ethics for nurses and midwives [accessed 30 March 2015]	Not relevant
Nursing & Midwifery Council (2008) Remote assessment and prescribing [accessed 30 March 2015]	Not relevant
Nursing & Midwifery Council (2009) Supply and/or administration of medicine by student nurses and student midwives in relation to Patient Group Directions (PGDs). [accessed 30 March 2015]	Not relevant
Nursing & Midwifery Council (2007) Standards for medicines management [accessed 30 March 2015]	Not relevant
Nursing & Midwifery Council (2007) Prescribing for children and young people [accessed 30 March 2015]	Not relevant
Nursing & Midwifery Council (2007) Strengthened requirements on Criminal Records Bureau checks for eligibility to undertake preparation to prescribe as a Nurse Independent Prescriber [accessed 30 March 2015]	Not relevant
Nursing & Midwifery Council (2007) Integrated V100 prescribing within Specialist Community Public Health Nursing Programmes and SPQ District Nurse Upload [accessed 30 March 2015]	Not relevant
Nursing & Midwifery Council (2007) Additional requirements to include within the Indicative Content of Nurse Independent Prescribing education and training programmes [accessed 30 March 2015]	Not relevant
Nursing & Midwifery Council (2006) Standards of proficiency for nurse and midwife prescribers [accessed 30 March 2015]	Not relevant
Nursing & Midwifery Council (2004) Addition of diamorphine and morphine to the list of exemptions for midwives. The Prescription Only Medicines (Human Use) Amendment Order 2004 [accessed 30 March 2015]	Already taken into account
Health & Care Professions Council (2013) Standards for prescribing	Already covered in intro
Health & Care Professions Council (2012) Independent prescribing for chiropodists/podiatrists and physiotherapists [accessed 30 March 2015]	Not relevant
Health & Care Professions Council (2012) Regulating ethics and conduct at the council for professions supplementary to medicine – 1960 to 2002 [accessed 30 March 2015]	Not relevant

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Health & Care Professions Council (2010) The fitness to practise process - Information for employers and managers [accessed 30 March 2015]	Not relevant
Audit Commission (2008) The Ipswich hospital NHS trust 2007/08 annual audit letter [accessed 30 March 2015]	Not relevant – account audits of trusts Archived content
Audit Commission (2007) Good Hope Hospital NHS Trust: annual audit letter 2006/2007 [accessed 30 March 2015]	Not relevant – account audits of trusts Archived content
Audit Commission (2006) Taunton and Somerset NHS Trust: annual audit letter 2005/2006 [accessed 30 March 2015]	Not relevant – account audits of trusts Archived content
Audit Commission (2006) University Hospitals of Morecambe Bay NHS Trust: annual audit letter 2005/2006 [accessed 30 March 2015]	Not relevant – account audits of trusts Archived content
Audit Commission (2006) University Hospitals of Morecambe Bay NHS Trust: annual audit letter 2005/2006 [accessed 30 March 2015]	Not relevant – account audits of trusts Archived content
Audit Commission (2006) St George's Healthcare NHS Trust: annual audit letter 2005/2006 [accessed 30 March 2015]	Not relevant – account audits of trusts Archived content
Audit Commission (2006) North West Strategic Health Authority - covering Cheshire and Merseyside SHA, Cumbria and Lancashire SHA and Greater Manchester SHA: annual audit letter 2005/2006 [accessed 30 March 2015]	Not relevant – account audits of trusts Archived content
Audit Commission (2004) Drug misuse 2004: reducing the local impact [accessed 30 March 2015]	Not relevant – account audits of trusts Archived content
Audit Commission (2002) Changing habits: The commissioning and management of community drug treatment services for adults [accessed 30 March 2015]	Not relevant – account audits of trusts Archived content
Audit Commission (1996) Tackling crime effectively: management handbook Volume 2 [accessed 30 March 2015]	Not relevant – account audits of trusts Archived content
Audit Commission (1994) A prescription for improvement: towards more rational prescribing in general practice [accessed 30 March 2015]	Not relevant – account audits of trusts Archived content
Care Quality Commission (2014) The safer management of controlled drugs 2013 [accessed 30 March 2015]	Already searched
Care Quality Commission (2014) Section H: Reporting CDs incidents [accessed 30 March 2015]	Already searched
Care Quality Commission (2014) Controlled drugs governance primary care (provider) self-assessment tool [accessed 30 March 2015]	Already searched
Care Quality Commission (2011) The safer management of controlled drugs 2010 [accessed 30 March 2015]	Already searched
Guidelines & Audit Implementation Network (2014) Regional	Not relevant

Reference	Reason for Exclusion
Guidelines for the Supply of "Take-Home Medication" from Northern Ireland Emergency Departments [accessed 30 March 2015]	
Guidelines & Audit Implementation Network (2011) "Take home" medication supply from Northern Ireland emergency departments: audit report by the Northern Ireland regional emergency department pharmacist group [accessed 30 March 2015]	Not relevant
Guidelines & Audit Implementation Network (2011) Guidelines on regional immediate discharge documentation for patients being discharged from secondary into primary care [accessed 30 March 2015]	Not relevant
Guidelines & Audit Implementation Network (2009) Medication administration record card audit report Northern Ireland prison service [accessed 30 March 2015]	Not relevant
Interface Pharmacist Network Specialist Medicines (2008) Surveying the use of regional shared care guidelines in secondary & primary care [accessed 30 March 2015]	Not relevant
Health & Social Care Information Centre (2014) Statistics on drugs misuse: England, 2014 [NS] Previous years dating back to 2006 can be found here [accessed 30 March 2015]	Not relevant
Health & Social Care Information Centre (2015) Prescription Cost Analysis, England - 2014 [NS] [accessed 30 March 2015]	Not relevant
Health & Social Care Information Centre (2014) Hospital Prescribing: England, 2013-14 [accessed 30 March 2015]	Not relevant
Health & Social Care Information Centre (2014) Clinical Commissioning Group Prescribing Data - July to September 2014 [accessed 30 March 2015]	Not relevant
Health & Social Care Information Centre (2014) Prescriptions Dispensed in the Community, Statistics for England - 2003-2013 [NS] [accessed 30 March 2015]	Not relevant
National Clinical Audit and Patient Outcomes Programme [accessed 30 March 2015]	Nothing found clinical audit reports arranged by condition – no reports just on prescribing or management of controlled drugs
National Audit Office (2013) Review of the data systems for the Department of Health [accessed 30 March 2015]	Not relevant
National Audit Office (2012) Review of the data systems for the Department of Health [accessed 30 March 2015]	Not relevant
National Audit Office (2011) The National Programme for IT in the NHS: an update on the delivery of detailed care records systems [accessed 30 March 2015]	Not relevant
National Audit Office (2010) Review of the data systems for	Not relevant

Reference	Reason for Exclusion
Public Service Agreement 18 [accessed 30 March 2015]	
National Audit Office (2010) Review of the data systems for Public Service Agreement 19 [accessed 30 March 2015]	Not relevant
National Audit Office (2010) The Community Pharmacy Contractual Framework and the retained medicine margin [accessed 30 March 2015]	Not relevant
National Audit Office (2008) End of life care [accessed 30 March 2015]	Not relevant
National Audit Office (2008) The National Programme for IT in the NHS: Progress since 2006 [accessed 30 March 2015]	Not relevant
National Audit Office (2007) Prescribing costs in primary care [accessed 30 March 2015]	Not relevant
National Audit Office (2006) The Provision of Out-of-Hours Care in England [accessed 30 March 2015]	Not relevant
National Audit Office (2005) A Safer Place for Patients: learning to improve patient safety [accessed 30 March 2015]	Not relevant
National Audit Office (2004) The Drug Treatment and Testing Order: early lessons [accessed 30 March 2015]	Not relevant
National Audit Office (2003) Safety, Quality, Efficacy: Regulating Medicines in the UK [accessed 30 March 2015]	Not relevant
National Centre for Social Research (2013) Smoking, Drinking and Drug Use among Young People, 2013 Date accessed [08 April 2015]	Not relevant
Pharmaceutical Society (2013) Standards for Pharmacist Prescribers [accessed 30 March 2015]	Not relevant
General Practitioners Committee (2013) Prescribing in general practice [accessed 30 March 2015]	Not relevant
NHS Specialist Pharmacy Service (2015) Reducing medicines waste throughout the patient journey: simple guide and supporting information [accessed 30 March 2015]	Not relevant
NHS Business Services Authority (2014) Controlled drug prescribing [accessed 30 March 2015]	Not relevant
NHS Business Services Authority (2014) Requisitions for schedule 1, 2 and 3 controlled drugs [accessed 30 March 2015]	Not relevant
NHS Business Services Authority (date not known) Background for the safer management of controlled drugs [accessed 30 March 2015]	Not relevant

Reference	Reason for Exclusion
Vowles KE, McEntee ML, Julnes PS, et al. (2015) Rates of opioid misuse, abuse, and addiction in chronic pain: a systematic review and data synthesis. Journal of the International Association for the Study of Pain 156(4): 569-76 [accessed 30 March 2015]	Not relevant

C.7 Economic excluded studies

C.7.1 Prescribing controlled drugs

Author	Reason for exclusion
Anon (1984) Curtailment of prescribing in the National Health Service. Lancet 2 (8412): 1136-7	Not an economic study
Anon (1995) Narcotics are safe for acute and chronic pain Hospital Peer Review 20 (1) 13-15	Not an economic study
Anon (1996) Drug utilisation Australian Prescriber 19(3):68	Article could not be obtained
Anon (2001) Patient-controlled analgesic infusion pumps. Health Devices 30(5): 157-85	Not an economic study
Asselin WM, Leslie JM (1992) Modification of Emit assay reagents for improved sensitivity and cost effectiveness in the analysis of haemolysed whole blood. Journal of Analytical Toxicology 16(6):381-8	Not relevant
Bell J, Shanahan M, Mutch C et al. (2007) A randomized trial of effectiveness and cost-effectiveness of observed versus unobserved administration of buprenorphine-naloxone for heroin dependence Addiction 102 (12) 1899-1907	Included for RQC only
Bloor K, Leese B, Maynard A (1994) The costs of managing severe cancer pain and potential savings from transdermal administration. European Journal of Cancer 30A(4): 463-8	Cost analysis only, not a full economic analysis
Brogan SE, Winter NB, Abiodun A et al. (2013) A cost utilization analysis of intrathecal therapy for refractory cancer pain: identifying factors associated with cost benefit. Pain Medicine 14(4): 478-86	Not a full economic analyses
Byford S, Barrett B, Metrebian N et al. (2013) Cost-effectiveness of injectable opioid treatment v. oral methadone for chronic heroin addiction. British Journal of Psychiatry 203(5):341-9	Not relevant
Dijkgraaf MG, van der Zanden BP, de Borgie CA, et al. (2005) Cost utility analysis of co-prescribed heroin compared with methadone maintenance treatment in heroin addicts in two randomised trials. BMJ 330 (7503):1297	Not relevant
Justad M (148) Continuous subcutaneous infusion: an efficacious, cost-effective analgesia alternative at the end of life. Home Healthcare Nurse 27(3): 140-7	Not an economic analysis
Kumar K, Hunter G, Demeria DD (2002) Treatment of chronic pain by using intrathecal drug therapy compared with conventional pain therapies: a cost-effectiveness analysis. Journal of Neurosurgery 97(4): 803-10	Not relevant
Lugo RA, Chester EA, Cash J, et al. (1999) A cost analysis of enterally administered lorazepam in the pediatric intensive care unit. Critical Care Medicine 27 (2): 417-21	Cost analysis only, not a full economic analysis
Montesano F, Mellace V (2013) The effects of a novel take-home treatment strategy in patients with opioid-dependence receiving long-term opioid replacement therapy with buprenorphine/naloxone in Italy: A cost analysis. Heroin	Cost analysis only, not a full economic analysis

Author	Reason for exclusion
Addiction and Related Clinical Problems 15(1): 45-52	
Oude Voshaar RC, Krabbe PFM, Gorgels WJMJ, et al. (2006) Tapering off benzodiazepines in long-term users: An economic evaluation. Pharmacoeconomics 24(7): 683-94	Not relevant
Polsky D, Glick HA, Yang J et al. (2010) Cost-effectiveness of extended uprenorphine-naloxone treatment for opioid-dependent youth: data from a randomized trial. Addiction 105(9): 1616-24	Not relevant

C.7.2 Obtaining and supplying controlled drugs

Author	Reason for exclusion
Anon (2004) CD registers are to be centralised at Prescription Pricing Authority. Pharmaceutical Journal 273 (7330)	Not an economic analysis
Anon (2005) Hasty approval, more withdrawals Prescrire International 14(78): 144	Not an economic analysis
Burrows D (2005) Towards a regulated market for illicit drugs: Effects of the harm reduction model of controlled drug availability. International Journal of Drug Policy 16(1): 8-9	Not an economic analysis
Duggan AK (1995) The cost of managing post-operative pain - A comparison of tramadol and morphine. British Journal of Medical Economics 9(1): 59-66	Analysis no longer valid due to the controlled drug scheduling of tramadol
Garcia MM, Angelini MC, Thomas T, et al. (2014) Implementation of an opioid management initiative by a state Medicaid program. Journal of Managed Care & Specialty Pharmacy 20(5): 447-54	Not an economic analysis
Koch JV, Grupp SE (1973) Police and illicit drug markets: some economic considerations. British Journal of Addiction to Alcohol & Other Drugs 68(4):351-62	Article not relevant
Mach EP, Venulet J (1975) The economics of adverse reactions to drugs. WHO Chronicle 29 (3): 79-84	Feasibility / methodology paper only
McCarberg B (2012) Early use of adherence tests and recognition of opioid misuse may lower cost of chronic pain treatment. Journal of Pain Conference: 31st Annual Scientific Meeting of the American Pain Society. 16-19 May 2012 . Honolulu, Hawaii, United States Conference Publication: 13 (4 SUPPL.1): S76	Abstract only - no references
McCarberg BH (2011) Chronic pain: reducing costs through early implementation of adherence testing and recognition of opioid misuse. [Review] Postgraduate Medicine 123(6):132-9	Not an economic analysis
McGettrick S, Rodgers J (1996) Cost of administering controlled drugs in a hospice ward. Health Bulletin 54(6) 441-2	Not an economic evaluation
Moore AP (1995) Pharmacy costs associated with handling of controlled drugs. British Journal of Medical Economics 9(1): 69-72	Not an economic analysis
Norvell MJ, McAllister JC, Bailey E (1983) Cost analysis of drug distribution for controlled	US cost-analysis study, no comparator or benefit included

Author	Reason for exclusion
substances. American Journal of Hospital Pharmacy 40(5): 801-7	
Pisano DJ (1996) Controlled substances and pain management: regulatory oversight, formularies, and cost decisions. [Review] [33 refs] Journal of Law, Medicine & Ethics 24(4):310-16	Not an economic analysis
Weigelt JA, Dyke C, Martin RL (1990) Alternative delivery system for controlled drugs in the surgical intensive care unit. Journal of Trauma-Injury Infection & Critical Care 30(9): 1141-6	Not an economic analysis

C.7.3 Administering controlled drugs

Author	Reason for exclusion
Anon (1984) Curtailment of prescribing in the National Health Service. Lancet 2 (8412): 1136-7	Not an economic study
Anon (1996) Drug utilisation Australian Prescriber 19(3):68	Article could not be obtained
Anon (1995) Narcotics are safe for acute and chronic pain. Hospital Peer Review 20(1): 13-15	Not an economic study
Anon (2001) Patient-controlled analgesic infusion pumps. Health Devices 30(5): 157-85	Not an economic study
Asselin WM, Leslie JM (1992) Modification of Emit assay reagents for improved sensitivity and cost effectiveness in the analysis of haemolysed whole blood. Journal of Analytical Toxicology 16(6):381-8	Not relevant
Bloor K, Leese B, Maynard A (1994) The costs of managing severe cancer pain and potential savings from transdermal administration. European Journal of Cancer 30A(4): 463-8	Cost analysis only, not a full economic analysis
Brogan SE, Winter NB, Abiodun A et al. (2013) A cost utilization analysis of intrathecal therapy for refractory cancer pain: identifying factors associated with cost benefit. Pain Medicine 14(4): 478-86	Not a full economic analyses
Byford S, Barrett B, Metrebian N et al. (2013) Cost-effectiveness of injectable opioid treatment v. oral methadone for chronic heroin addiction. British Journal of Psychiatry 203(5):341-9	Not relevant
Dijkgraaf MG, van der Zanden BP, de Borgie CA, et al. (2005) Cost utility analysis of co-prescribed heroin compared with methadone maintenance treatment in heroin addicts in two randomised trials. BMJ 330 (7503):1297	Not relevant
Justad M (148) Continuous subcutaneous infusion: an efficacious, cost-effective analgesia alternative at the end of life. Home Healthcare Nurse 27(3): 140-7	Not an economic analysis
Kumar K, Hunter G, Demeria DD (2002) Treatment of chronic pain by using intrathecal drug therapy compared with conventional pain therapies: a cost-effectiveness analysis. Journal of Neurosurgery 97 (4): 803-10	Not relevant
Lugo RA, Chester EA, Cash J, et al. (1999) A cost analysis of enterally administered lorazepam in the pediatric intensive care unit. Critical Care Medicine 27 (2): 417-21	Cost analysis only, not a full economic analysis

Author	Reason for exclusion
Montesano F, Mellace V (2013) The effects of a novel take-home treatment strategy in patients with opioid-dependence receiving long-term opioid replacement therapy with buprenorphine/naloxone in Italy: A cost analysis. Heroin Addiction and Related Clinical Problems 15(1): 45-52	Cost analysis only, not a full economic analysis
Oude Voshaar RC, Krabbe PFM, Gorgels WJMJ, et al. (2006) Tapering off benzodiazepines in long-term users: An economic evaluation. Pharmacoeconomics 24(7): 683-94	Not relevant
Polsky D, Glick HA, Yang J et al. (2010) Cost-effectiveness of extended uprenorphine-naloxone treatment for opioid-dependent youth: data from a randomized trial. Addiction 105(9): 1616-24	Not relevant

C.7.4 Handling controlled drugs

Author	Reason for exclusion
Anon (2004) CD registers are to be centralised at Prescription Pricing Authority. Pharmaceutical Journal 273 (7330)	Not an economic analysis
Anon (2005) Hasty approval, more withdrawals Prescrire International 14(78): 144	Not an economic analysis
Burrows D (2005) Towards a regulated market for illicit drugs: Effects of the harm reduction model of controlled drug availability. International Journal of Drug Policy 16(1): 8-9	Not an economic analysis
Duggan AK (1995) The cost of managing post-operative pain - A comparison of tramadol and morphine. British Journal of Medical Economics 9(1): 59-66	Analysis no longer valid due to the controlled drug scheduling of tramadol
Garcia MM, Angelini MC, Thomas T, et al. (2014) Implementation of an opioid management initiative by a state Medicaid program. Journal of Managed Care & Specialty Pharmacy 20(5): 447-54	Not an economic analysis
Koch JV, Grupp SE (1973) Police and illicit drug markets: some economic considerations. British Journal of Addiction to Alcohol & Other Drugs 68(4):351-62	Article not relevant
Mach EP, Venulet J (1975) The economics of adverse reactions to drugs. WHO Chronicle 29 (3): 79-84	Feasibility / methodology paper only
McCarberg B (2012) Early use of adherence tests and recognition of opioid misuse may lower cost of chronic pain treatment. Journal of Pain Conference: 31st Annual Scientific Meeting of the American Pain Society. 16-19 May 2012 . Honolulu, Hawaii, United States Conference Publication: 13 (4 SUPPL.1): S76	Abstract only - no references
McCarberg BH (2011) Chronic pain: reducing costs through early implementation of adherence testing and recognition of opioid misuse. [Review] Postgraduate Medicine 123(6):132-9	Not an economic analysis
McGettrick S, Rodgers J (1996) Cost of administering controlled drugs in a hospice ward. Health Bulletin 54(6) 441-2	Not an economic evaluation
Moore AP (1995) Pharmacy costs associated	Not an economic analysis

Author	Reason for exclusion
with handling of controlled drugs. British Journal of Medical Economics 9(1): 69-72	
Norvell MJ, McAllister JC, Bailey E (1983) Cost analysis of drug distribution for controlled substances. American Journal of Hospital Pharmacy 40(5): 801-7	US cost-analysis study, no comparator or benefit included
Pisano DJ (1996) Controlled substances and pain management: regulatory oversight, formularies, and cost decisions. [Review] [33 refs] Journal of Law, Medicine & Ethics 24(4):310-16	Not an economic analysis
Weigelt JA, Dyke C, Martin RL (1990) Alternative delivery system for controlled drugs in the surgical intensive care unit. Journal of Trauma-Injury Infection & Critical Care 30(9): 1141-6	Not an economic analysis

C.7.5 Monitoring controlled drugs

Author	Reason for exclusion
Anon (2004) CD registers are to be centralised at Prescription Pricing Authority. Pharmaceutical Journal 273 (7330)	Not an economic analysis
Anon (2005) Hasty approval, more withdrawals Prescrire International 14(78): 144	Not an economic analysis
Burrows D (2005) Towards a regulated market for illicit drugs: Effects of the harm reduction model of controlled drug availability. International Journal of Drug Policy 16(1): 8-9	Not an economic analysis
Duggan AK (1995) The cost of managing post-operative pain - A comparison of tramadol and morphine. British Journal of Medical Economics 9(1): 59-66	Analysis no longer valid due to the controlled drug scheduling of tramadol
Garcia MM, Angelini MC, Thomas T, et al. (2014) Implementation of an opioid management initiative by a state Medicaid program. Journal of Managed Care & Specialty Pharmacy 20(5): 447-54	Not an economic analysis
Koch JV, Grupp SE (1973) Police and illicit drug markets: some economic considerations. British Journal of Addiction to Alcohol & Other Drugs 68(4):351-62	Article not relevant
Mach EP, Venulet J (1975) The economics of adverse reactions to drugs. WHO Chronicle 29 (3): 79-84	Feasibility / methodology paper only
McCarberg B (2012) Early use of adherence tests and recognition of opioid misuse may lower cost of chronic pain treatment. Journal of Pain Conference: 31st Annual Scientific Meeting of the American Pain Society. 16-19 May 2012 . Honolulu, Hawaii, United States Conference Publication: 13 (4 SUPPL.1): S76	Abstract only - no references
McCarberg BH (2011) Chronic pain: reducing	Not an economic analysis

Author	Reason for exclusion
costs through early implementation of adherence testing and recognition of opioid misuse. [Review] Postgraduate Medicine 123(6):132-9	
McGettrick S, Rodgers J (1996) Cost of administering controlled drugs in a hospice ward. Health Bulletin 54(6) 441-2	Not an economic evaluation
Moore AP (1995) Pharmacy costs associated with handling of controlled drugs. British Journal of Medical Economics 9(1): 69-72	Not an economic analysis
Norvell MJ, McAllister JC, Bailey E (1983) Cost analysis of drug distribution for controlled substances. American Journal of Hospital Pharmacy 40(5): 801-7	US cost-analysis study, no comparator or benefit included
Pisano DJ (1996) Controlled substances and pain management: regulatory oversight, formularies, and cost decisions. [Review] [33 refs] Journal of Law, Medicine & Ethics 24(4):310-16	Not an economic analysis
Weigelt JA, Dyke C, Martin RL (1990) Alternative delivery system for controlled drugs in the surgical intensive care unit. Journal of Trauma-Injury Infection & Critical Care 30(9): 1141-6	Not an economic analysis

Appendix D: Clinical evidence tables and GRADE profiles

D.1 Evidence tables

Evidence table 1: Anonymous 1980

Bibliographic reference	Principles and guidelines for distribution of narcotic and other psychoactive drugs. Canadian pharmaceutical journal 113, 289-292.
Evidence type/ study design	Canadian guidelines.
Quality	AGREE II criteria used for quality assessment. Overall rating of 2 (out of 7) given as very low quality, based on Canadian legislation.
Research parameters	Aim of the guideline is to: • reduce diversion of legal drugs to the illicit market • protect the pharmacist • adhere to legislation and assist enforcement agencies. Guidelines have been prepared by the committee on security in drug distribution, composed of representatives of the bureau of dangerous drugs, bureau of drug surveillance, and the senior consultant in pharmacy, Health Protection Branch, and of representatives from the provincial pharmacy registrars, the Canadian Pharmaceutical

	Association and the Canadian Medical Association.
Population	Pharmacy businesses in Canada.
Themes/Intervention/ System/Process	**Practice points relating to supply:** • The relevant contact details of the person to report to should be known by the pharmacist when forged prescriptions are suspected. • Scrutinise prescriptions that are known to be drugs of abuse. • During dispensing the controlled drug container should not be left on a counter in open public view or reach. • After dispensing the controlled drug, it should be returned to the storage area as soon as possible. **Practice points relating to handling:** • Strict control of prescription pads should be exercised and encouragement should be given to practitioners, hospital, clinics, etc. • Many pharmacies have found that an inventory of narcotics and controlled drugs, renewed at regular intervals, has greatly facilitated the reporting of drug losses.
Limitations	• The guideline is based on Canadian legislation. • This guideline was developed in 1980 by a committee of experts. • The method of guideline development has not been included.
Source of funding	Unknown.
Additional comments	Applicable to the following review questions on: • obtaining and supplying of controlled drugs • handling of controlled drugs. The guidelines is based on Canadian legislation, however, some practice points may be considered for UK practice.

Evidence table 2: Anonymous 1993

Bibliographic reference	American Society of Hospital Pharmacists: Technical assistance bulletin on use of controlled substances in organised health care settings. American journal of hospital Pharmacy 50, 489-501.
Evidence type/ study design	American guidelines.
Quality	AGREE II criteria used for quality assessment. Overall rating of 2 (out of 7) given as very low quality, based on US legislation.
Research parameters	• Guidance has been produced to ensure compliance with American law while still allowing the institution to promote high quality patient care in accordance with acceptable legal and professional standards.
Population	• Organised health care settings, for example hospitals, using controlled drugs in America.
Themes/Intervention/ System/Process	Practice points relating to handling: • Maintenance of accurate records of the receipt and disposition of all controlled drugs according to requirements set out in American legislation. • Physical inventory of all controlled drugs from the date of first receipt should be carried out as specified by American law. Perpetual inventories or periodic audits may be desirable in selected high-risk areas or where diversion is suspected. • In the operating/theatre room there are a number of solutions for the control and security of controlled drugs mentioned in the guideline: ○ Use of a record that identifies the controlled drug, physician/anaesthetist, date, adequate patient information, notation made in patient chart as to medications received.

	○ Maintain no stocks of controlled drugs in the operating/theatre room, but have the anaesthetist bring the assigned stocks for each operation, delivery, or other procedure. The anaesthetist would maintain the stock, all appropriate records for controlled drugs, and the stock would be replenished on an as needed basis. ○ Locate a 'pharmacy annex' in the immediate area of the operating/theatre room. This annex could stock supplies that would routinely be necessary to the anaesthesiologist. Medication could be signed out to the individual anaesthesiologist before each operation or for all procedures scheduled for a given date.
Limitations	• This guideline is based on American law. • This guideline was published in 1987 and developed by the American Society of Hospital Pharmacists and the Drug Enforcement Administration using the Controlled Substances Act and its implementing regulations. • The method of guideline development has not been included.
Source of funding	Unknown.
Additional comments	Applicable to the review question on: • handling of controlled drugs This guideline is based on American law and some practice points have been summarised above that may be considered for UK practice.

Evidence table 3: Anonymous 2005

Bibliographic reference	Royal Pharmaceutical Society: Maintaining running balances of stock in controlled drug registers. The Pharmaceutical Journal 274, 663.
Evidence type/ study design	Professional guidance.
Quality	Professional guidance has not been assessed for quality as this is based on legislation and national policy.
Research parameters	• Following the Government's response to the fourth report of the Shipman Inquiry, pharmacists and other health care professionals who supply controlled drugs are being encouraged to maintain a running balance of stock in their controlled drug registers as a matter of good practice.
Population	• Pharmacists and other health professionals who supply controlled drugs in the UK.
Themes/Intervention/ System/Process	• Pharmacists are advised to begin to review their current procedures and develop standard operating procedures to maintain running balances. • Some community pharmacies already record running balances. • Pharmacists who wish to revise their current register layout to incorporate running balances must ensure that they continue to comply with the legislative requirements for registers. • It is the pharmacist's responsibility to ensure that records are made in the controlled drug register and running balances are maintained in line with the pharmacy's standard operating procedures. • The running balance of drug remaining should be calculated and recorded after each transaction and balances should be checked with the physical amount of stock at regular intervals. • When developing standard operating procedures for the reconciliation process, consideration should be given to a number of factors, including the volume and frequency of controlled drug dispensing, dispensary workflow and staffing arrangements.

	• The Society advises that the running balance should normally be checked with the physical amount of drug each week. If discrepancies arise, more frequent reconciliation should be undertaken until the problem is resolved. • Standard operating procedures should clearly define the action that should be taken if a discrepancy between the theoretical and actual balance of stock arises. • Most original packs of liquid preparations have some degree of overage. The Home Office has confirmed that manufacturers' overage can become part of pharmacy stock, provided appropriate records are made to account for this i.e. the overage should be entered in the obtained section of the register. • Whenever possible, spillages should be witnessed and the record initialled by a second person.
Limitations	• Professional guidance only, mainly directed to pharmacists, however it does mention 'other healthcare professionals' at the beginning of the guidance.
Source of funding	Not known.
Additional comments	Applicable to the review question on: • handling of controlled drugs. The guidance also includes legal clarification on the maintenance of running balances and states 'that the Home Office has stated that it is content for persons to include a running balance in a controlled drug register provided that the specific requirements of the Misuse of Drugs Regulations are adhered to'.

Evidence table 4: Ahmed I et al 2007

Bibliographic reference	The safe and responsible disposal of unused controlled drugs. British Journal of Nursing, 16 1318-1322.
Evidence type/ study design	Audit report.
Quality	Very low quality The Health Quality Improvement Partnership (HQIP) 'criteria for high quality clinical audit' tool was used to assess the methodology for this audit. 6 out of 45 individual criteria outlined in the tool were met.
Research parameters	**Aim** To review the current practice of use and disposal of controlled drugs in hospital. **Methods** • The current practice was evaluated by auditing the methods and procedures followed by the staff involved in the use and disposal of controlled drugs. • Awareness about the existence of guidelines governing the disposal of controlled drugs was also assessed. • The study was conducted independently at two sites using a standard questionnaire to collect data. A total of 405 questionnaires were sent to all anaesthetic, midwifery and operating department practitioner (ODP) staff and to nursing staff of preselected, postoperative wards at each site. • Questions asked included: range of controlled drugs encountered, disposal method adopted or practiced, cross-checking with colleague before disposal, keeping record of wasted amount, and awareness

	about existence of guidelines regarding disposal of controlled drugs. • The paper did not list any clinical audit standards that were being measured against however, the following methods of disposal were mentioned: ○ Controlled drugs may be best disposed of by squirting them onto an absorbent material or by using a controlled drug denaturing kit. ○ Alternative suitable methods of denaturing controlled drugs include dissolving into soapy water or adsorbing into cat litter (Royal Pharmaceutical Society of Great Britain 2007). ○ Unused time-expired stock or controlled drugs that are no longer needed from any clinical area or department should be returned to the pharmacy for safe destruction and disposal and a record of these returns should be kept (Department of Health 2007). ○ For patient returned controlled drugs, there are no statutory requirements that destruction need to be witnessed or documented however, the DH recommends that a record of destruction should be made as a matter of good practice and destruction should be witnessed, preferably by a pharmacist or pharmacy technician.
Population	The study was conducted at Birmingham Women's Hospital Trust and University Hospitals of Leicester NHS Trust.
Themes/Intervention/ System/Process	**Results** Main results from the questionnaire included: • 200 (out of 405) completed questionnaires available for analysis. • 74.5% of clinical staff squirted the unused controlled drug out of the syringes, bags or ampoules before discarding them, but 6% admitted that they don't. Squirting is mainly done into the sharps bin (63%) or sink/washbasin (65%). • 4% respondents squirt controlled drug liquid onto some absorbent material. • The majority of those who discard unused drugs in ampoules/syringes without squirting throw them in a sharps bin (24.6%) or yellow bag (2%), whereas 3.5% hand over to a colleague for disposal. • 5% do not do anything to dispose of the controlled drug. • 77% of staff cross-check with another colleague before disposing of the controlled drug. Whereas 78% of staff also record unused discarded drugs, either in the controlled drugs book or in patient notes. • 53.2% of all staff were aware of any guideline or protocol (either local or national) for disposal of controlled drugs, and 60.3% felt there was a need for guidelines in this area.
Limitations	• Small sample and so difficult to extrapolate to all NHS hospitals. • Limited to secondary care only.
Source of funding	Not known.
Additional comments	Applicable to the following review question: • handling of controlled drugs.

Evidence table 5: Baker R et al 2004

Bibliographic reference	Investigation of systems to prevent drug diversion of opiate drugs in general practice in the UK. Qual Saf Health Care 13 21-25.
Evidence type/ study design	Qualitative study
Quality	Very low quality Assessed using qualitative study checklist
Research parameters	**Aim** Study aim was to describe the systems used by GPs and to seek their

	views on how systems could be improved. **Methods** • There were 2 methodological approaches for this study: ○ Semi-structured interviews of lead GPs from a sample of practices to explore range of views of GPs, inform the development of the questionnaire and to enable inspection of records and storage to consider whether the systems were in accordance with regulations. ○ Questionnaire surveys (devised from initial interview findings) sent out to the remaining practices (not selected for interviews) to assess methods used for storage, record keeping, disposal, patient-returns, existing policies and inspection. • The interviews lasted 30-40 minutes and were recorded and transcribed. Responses to closed questions were analysed quantitatively. Responses to open questions were repeatedly studied until the issues of concern to the GPs had been identified. Interpretations of the interviews were agreed between 2 researchers. • Data from the completed questionnaires were entered into a database and descriptive statistics used to identify proportions of practices with different controlled drug storage and register systems, their views on the security of current systems and their ideas on how the system can be improved.
Population	• General practices in 2 counties in the UK from an overall sample of 142. • General practices consisted of dispensing, non-dispensing, single handed and group practices, inner city, suburban and rural practices.
Themes/Intervention/ System/Process	**Results from the interviews** • 14 general practices interviewed in total. • N=6 single handed, N=8 group. • N=5 inner city, N=7 suburban, N=2 rural. • Storage ○ N=4 practices did not keep or store controlled drugs. ○ 3 locations used: N=8 practices used locked cupboard/dedicated drug storage cabinet, N=2 only in doctor's own medical bag and/or practice emergency bag. • Record keeping, drug registers ○ N=7 standard register (from the National Pharmaceutical Association). ○ N=3 notebooks modified for the purpose. ○ Doctors who had drugs in their bags maintained personal registers - the format of these was inconsistent. • Monitoring of practice registers ○ Variable intervals, from daily to annually. ○ None had had external inspection of registers or storage for >10years. • Disposal ○ N=2 practices accepted the return of unused controlled drugs. ○ N=12 left this to pharmacies, 2 practices reported community nurses would collect unused controlled drugs and return them to a pharmacy on behalf of patients/carers. ○ Some GPs reported concerns about arrangements for the disposal of controlled drugs following the death of a patient at home. **Results from the questionnaires** • N=127 practices were sent questionnaires, N=90 responded (response

rate 70.9%) see Table 1 and Table 2 for summary of results.

- N=59 (65.5%) reported they held a supply of controlled drugs.
- All practices used some form of register, 20 of these practices had more than 1 register.
- Practices reported a variety of policies on the destruction of controlled drugs.
- Of the practices that held controlled drugs, more than half had not been inspected in the previous 10 years, see Table 2.

Table 1: Results from questionnaire.

N=59 practices	N	%
Storage of controlled drugs		
Doctor's bag	36	61.0
Locked cabinet/safe	46	78.0
Emergency practice bag	9	15.3
Locked case	1	1.7
Registers		
Standard register only	11	18.6
Practice notebook only	15	25.4
Doctor's notebook only	13	22.0
Standard register plus doctor's notebook	12	20.3
Practice notebook plus doctor's notebook	8	13.6
Disposal of outdated stock		
Destroyed at practice by an individual	5	8.5
Destroyed at practice by another member of staff	11	18.6
Destroyed at practice before an authorised witness	15	25.4
Returned to a pharmacy	20	33.9
Destroyed by police	6	10.2
Other	2	3.4

Table 2: Time since last inspection of controlled drug registers and views on regular external scrutiny of registers (N=59 practices)

	N	%
Last external inspection of register;		
Within the last 12months	6	10.2
1-5years	12	20.3
5-10years	9	15.3
>10years	31	52.5
Would welcome independent scrutiny;		
Very much	5	8.5
Yes	37	62.7
Rather not	14	23.7
Absolutely not	3	5.1
Would welcome independent unannounced scrutiny;		
Very much	2	3.4
Yes	31	52.5
Rather not	20	33.9
Absolutely not	5	8.5

The results show that there is:

- Variation in how controlled drugs are stored, recorded and disposed.
- Controlled drugs registers do not comply with the regulations in some practices.
- There is some confusion among GPs about the details of the regulations.
- Anxiety about the systems in use.

	• Dissatisfaction with the availability of advice and support.
Limitations	• This study is based on regulations dated back in 2004. There have been changes to regulations since then. • The study was undertaken in one health district and so may not be representative of all practices in England. • Small sample size. • Findings based on self-reports. • Interview schedule not piloted and developed during the course of the interviews, no detailed description of the selection of the practices to be included in the interviews. • No methodology described for identifying the issues from open questions.
Source of funding	Commissioned by Leicester, Leicestershire and Rutland Drug Action Teams.
Additional comments	• The study found that both standard registered and modified notebooks had been altered by some practices to enable recording of batch numbers and total amount of drug in stock. • One GP devised a computerised system incorporating a permanent audit trail. Note that at the time of this study regulations did not allow the use of electronic registers. • Out of the 127 practices included in the survey, the study reported that 59 practices held controlled drugs, it is not clear from the study whether or not the other 68 practices not accounted for held controlled drugs as stock or not. • Applicable to the following review questions: ○ handling of controlled drugs ○ monitoring of controlled drugs.

Evidence table 6: Bell J et al 2007

Bibliographic reference	A randomised controlled trial of effectiveness and cost-effectiveness of observed versus unobserved administration of buprenorphine-naloxone for heroin dependence. Addiction 102, 1899-1907
Evidence type/ study design	Randomised controlled trial
Quality	Low quality assessed using NICE methodology checklist for randomised controlled trials.
Research parameters	This study aimed to compare the effectiveness of treatment with observation of dosing by randomising heroin users seeking treatment to either usual care (regular attendance for observed dosing) versus picking up the controlled drug medicine once per week for administration at home (unobserved doing). Inclusion criteria included: • aged over 18 years • opioid-dependent with a history of at least 12 months' opioid use Participants who chose maintenance treatment with buprenorphine with naloxone were invited to take part in the trial and were allocated randomly either observed or unobserved dosing. Observed dosing group could attend daily, second-daily or thrice-weekly (using 2-day or 3-day dosing schedules) depending on their stability Unobserved dosing group had their medicine dispensed weekly then taken home

	Participants were advised that after 3 months treatment, their treatment allocation to observed or unobserved dosing would be revised based on a case conference between the doctor and case manager. Each participant remaining in treatment would be allowed access to unobserved dosing at that point, unless during weeks 9 to 13 they met specified criteria of instability (predominately, continued injecting drug use). Participants who met the criteria of instability could remain in treatment for daily observed administration. Treatment effectiveness was measured by: • retention in treatment at 3 months • heroin use at 3 months measured by the change in the number of self-reported days of heroin use and the drug scale of the Opiate Treatment Index (OTI). Quality of life (QOL) was measured by World Health Organisation QoL BREF – self-report inventory. 4 domains were assessed: physical, psychological, social and environmental. Each participating clinic kept a log of all reports of trial medicines being diverted or injected by trial participants and a record of adverse drug reactions. Outcomes were assessed at research interview by blinded research assistants who administered questionnaires to the participants.
Population	Heroin users (seeking maintenance treatment in specialist outpatient treatment centre in Australia.
Themes/Intervention/ System/Process	The intervention involved allocating 119 heroin users to observed or unobserved doing for 3 months where all the participants received buprenorphine-naloxone and weekly clinical reviews. Analysis was performed on an intention-to-treat basis. **Primary outcomes** • Retention to treatment at 3 months: ○ Observed (n=61): 37/61, 61% ○ Unobserved (n=58): 33/58, 57% ○ Log-rank χ^2 = 0.04, df=1, P=0.84 ○ No significant difference • Self-reported heroin use at 3 months mean reported reduction was: ○ Observed: 22.0 days (95% CI 24.3−19.7) ○ Unobserved: 18.5 days (95%CI 21.8−15.3) ○ Mann-Whitney U=807.5, P=0.13 ○ No significant difference **Secondary outcomes** • Quality of Life ○ Intention-to-treat analysis comparing observed and unobserved dosing showed no significant difference. ○ Baseline to 3 months reported significant improvements in the following domains for the WHOQoL BREF: ○ Physical: (t=5.4, df=91 P<0.001) ○ Psychological: (t=3.5, df=92 P<0.001) ○ Environmental: t=3.6, df=92 P<0.001)

	○ No differences in the social domain. ○ The reported data was for the entire analysed sample, there was no significant difference between the groups and only the total data was presented. • One serious adverse event was reported in the unobserved group related to injection of buprenorphine-naloxone and associated cellulitis. • There were 18 reports of diversion of trial medicines. The number reported from each group was not specified in the paper.
Limitations	• All participants were aware that at the end of the trial they could gain access to unobserved administration, and the incentive of unobserved doses may have enhanced retention in the observed group. • Only 131/591 heroin users were recruited and a total of 119 participants actually enrolled therefore small sample size limiting the generalisability of the results. • Follow up study was underpowered to demonstrate clinically important difference at 6 months.
Source of funding	NSW Health Centre for Drugs and Alcohol (Government Department) ReckittBenckiser P/L (manufacturers of buprenorphine-naloxone)
Additional comments	• Urine analysis for opioids at 3 months showed that 29/36 participants who reported no heroin use submitted urine tests consistently negative for opioids. When a requested sample was not provided this was counted as positive and the number of negative tests fell to 22/36 of those reporting abstinence. Observed: 60%, unobserved: 62%. • Applicable to the following review question: ○ administration of controlled drugs.
Abbreviations CI confidence interval; df degrees of freedom.	

Evidence table 7: Flood C et al 2015

Bibliographic reference	Reducing risk of overdose with midazolam injection in adults: an evaluation of change in clinical practice to improve patient safety in England. Journal of Evaluation in Clinical Practice 21 57-66
Evidence type/ study design	Qualitative study
Quality	Low quality Assessed using qualitative study checklist.
Research parameters	**Aim** This study aimed to find out if the UK national patient safety alert 'reducing risk of overdose with midazolam injection in adults' resulted in a reduction in reports of severe harm and death caused by midazolam use and also to see if there was any change in practice for handling midazolam. **Method** To measure change in actual clinical practice a number of approaches were used. There was a survey of clinicians, audit of clinical areas and evidence of change in purchasing behaviour. Measurements identified as potential markers of success for the rapid response report (RRR) were: • A reduction in incidents involving serious harm or death reported to the National Learning and Reporting System (NRLS) post-implementation of the RRR compared with pre-issue. • A self-reported compliance rate of over 90% for NHS organisations implementing the recommendations where the RRR is deemed

	relevant. • A change in purchasing patterns for high-strength and low-strength midazolam injections ampoules where use of high-strength midazolam decreases and low-strength increases post-implementation compared with pre-issue. • Feedback in the form of survey returns from clinicians and implementation leads (who use midazolam for conscious sedation) on awareness of the issue and RRR, compliance and a change in local practice as a result of implementation. The National Patient Safety Agency (NPSA) was an Arms Length Body that was authorised to self-regulate and assess their national communications which included surveys and audits against the standard criteria in accordance with the Department of Health gateway principals. As an additional measure, all NPSA released surveys and communications were reviewed by a Department of Health Gateway team before they were issued, against a set of standard criteria informed by Department of Health policy and approved by Ministers. **Data analysis** • NRLS was searched for patient safety incidents resulting in death or severe harm related to midazolam use. Data was collected (before the RRR) between October 2003 and November 2008 and compared with data collected between June 2009 and August 2010 (after RRR issue). • Organisational compliance was assessed by analysing the data from the Central Alert System (CAS) that reports actions taken by the organisation in respect of issued patient safety alerts. • Data on purchasing of midazolam and flumazenil medicines for injection was provided by the NHS Purchasing and Supply Agency. Data was available from 12 months before the release of RRR and for 8 months after the implementation deadline. • Gastroenterologists were selected to take part in an online survey where 100 from a UK total of 903 responded. Implementation leads were also asked to complete an online survey. • Audits which identified the actions in the original RRR were distributed to all acute organisation chief pharmacists.
Population	All 333 health care trusts that provide acute care in England.
Themes/Intervention/ System/Process	**Results** • Reporting and learning system incident review October 2003 and November 2008: 498 incidents received (severity not specified in the study), including 3 deaths June 2009 and August 2010: no incidents resulting in death or severe harm. • CAS results December 2010 96% (321/333) NHS organisations reported completing all actions arising from the RRR December 2011, CAS was rechecked and all organisations reported having completing all actions arising from RRR. • Changes in purchasing patterns within the NHS in England Mean difference between pre-and post-RRR purchasing ampoule quantities: ○ Flumazenil 500micrograms/5mL: 43 (95% CI, -723.4, 809.7, P value 0.9016). ○ Midazolam 10mg/2mL (HS): -12 061 (95% CI -23 793.1, -329.9, P

	value 0.0603). ○ Midazolam 10mg/5mL (HS): -31 681 (95% CI -45 934.4, -17 428.1, P value 0.0002). ○ Midazolam 2mg/2mL (LS): 10 021 (95% CI 6625.9, 13 415.7, P value 3.32E-06). ○ Midazolam 5mg/2mL (LS): 43 179 (95% CI 24 878.7, 61.478.8, P value 2.54E-05). A two-sample t-test was used to test significant difference. • Survey results (100 responses) from gastroenterologists ○ 4/15 qualitative free text reponses:1mg/1mL midazolam availability was a wide spread recent change. ○ 63% were aware that NPSA had issued a RRR. ○ 49% knew the lead responsible for implementing. ○ 4 clinicians expressed concerns about use of low strength relating to possible inadequate sedation. • Survey results from implementation leads (133 responses from 37 NHS organisations) ○ 65% changed their midazolam purchasing habits. ○ 86% developed a communication plan of arrangements. ○ 51% developed an evaluation plan. ○ 30% stated that the timeframe to implement the RRR was not appropriate. • Audit results ○ >99% compliance rates to restricting access to HS midazolam. ○ 58% auditing of flumazenil to check for overuse.
Limitations	• This study focusses on the results of an evaluation of one single alert and national policy initiative. • Revisit of NRLS between September 2010 and September 2013, 2 cases of overdose that were classified as serious harm have been highlighted. • Some effects post RRR may be mistaken for the intervention (in this case the RRR) when this may not be the case. • Individual clinicians self-selecting in responding to the survey. • CAS requires self-reported organisational compliance. • No methodology described for identifying the issues from the survey.
Source of funding	Unknown.
Additional comments	• In June 2012, the key functions and expertise for patient safety developed by the National Patient Safety Agency (NPSA) transferred to NHS England. • Applicable to the following review question: ○ monitoring of controlled drugs.
Abbreviations CI confidence intervals; HS sigh strength; LS low strength.	

Evidence table 8: Humphries DJ et al 1997

<table>
<tr><td>Bibliographic reference</td><td>Audit of opioid prescribing: the effect of hospital guidelines. Anaesthesia 52 745-749.</td></tr>
<tr><td>Evidence type/ study design</td><td>Audit</td></tr>
<tr><td>Quality</td><td>Very low quality
The Health Quality Improvement Partnership (HQIP) ‘criteria for high quality clinical audit’ tool was used to assess the methodology for this audit. 11 out of 45 individual criteria outlined in the tool were met.</td></tr>
<tr><td>Research parameters</td><td>The aim of this audit was to assess intramuscular opioid analgesic prescribing habits in a large district general hospital before and after the introduction of prescribing guidelines.

The prescribing of 3 opioid medicines (morphine, papaveretum and pethidine) was recorded by the ward pharmacists on 6 wards (2 general, 2 general surgical and 2 orthopaedic wards) over a 2 week period in November 1994.
• Information collected included:
• name of the opioid prescribed
• age, sex and weight of the patient
• dose of analgesic
• frequency of analgesic administration.

The information collected was compared to dose and frequency as recommended by the BNF and against prescribing guidelines set by the Acute Pain Service (APS). The prescriptions were then categorised according to correct dose/frequency or inadequate dose/frequency to the BNF and/or prescribing guidelines.

Following the initial survey, the guidelines for prescribing analgesia was introduced via posters, pocket sized guides and addition to junior doctor’s handbook.

A re-audit was carried out a year later in 1995 on the same 6 wards. The data collected was analysed using Chi-squared test and significance was determined at a P value of <0.05.</td></tr>
<tr><td>Population</td><td>Doctors prescribing opioid analgesics in a district general hospital in Blackpool, England.</td></tr>
<tr><td>Themes/Intervention/ System/Process</td><td>The intervention was the introduction of prescribing guidelines for analgesia for prescribers to use.

Prescribing trends
Table showing prescribing trends by dose and frequency. n=prescriptions
<table>
<tr><td></td><td colspan="2">1994 survey n=120</td><td colspan="2">1995 survey n=122</td></tr>
<tr><td></td><td>BNF</td><td>APS</td><td>BNF</td><td>APS</td></tr>
<tr><td>Correct dose & frequency</td><td>40% (48)</td><td>16% (19)</td><td>61% (75)**</td><td>26% (32)*</td></tr>
<tr><td>Total inadequate by dose</td><td>36% (43)</td><td>36% (43)</td><td>26% (32)</td><td>26% (32)</td></tr>
<tr><td>Total inadequate by</td><td>43% (51)</td><td>84% (101)</td><td>16% (19)**</td><td>65% (79)**</td></tr>
</table></td></tr>
</table>

	<table><tr><td>frequency</td><td></td><td></td><td></td><td></td></tr><tr><td>Inadequate dose and frequency</td><td>18% (22)</td><td>36% (43)</td><td>3% (4)**</td><td>17% (21)**</td></tr><tr><td colspan="5">*p<0.05 **p=0.001</td></tr></table> • There was a statistically significant increase in the number of prescriptions that were correct for both dose and frequency according to the BNF and APS. • There was a statistically significant decrease in the: ○ number of prescriptions that were inadequate for dose and frequency ○ number of prescriptions with inadequate frequency of prescribing. • The prescribing of all 3 opioids improved over the study period in respect to both the BNF and the APS recommendations.
Limitations	• Only 6 wards audited to be a representative of prescribing across the major acute specialities. • This papers mentions looking at junior doctor's prescribing and no mention o other senior doctors or non-medical prescribers. • Only audited intramuscular injections for 3 opioids. • Methods used to develop the APS guideline unclear.
Source of funding	Unknown.
Additional comments	• Applicable to the following review question: ○ prescribing of controlled drugs.
Abbreviations BNF British National Formulary; APS Acute Pain Service.	

D.2 GRADE profiles

D.2.1 Administering controlled drugs

GRADE profile 1:

Author(s): Goldman 2005; Revankar 1998
Date: 2014-08-20
Question: Continuous versus intermittent (episodes) fluconazole for candida
Settings: Community

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Continuous prophylaxis	Control	Relative (95% CI)	Absolute		
Emergence of resistance (follow-up 3 - 24 months; assessed with: Proportion of people in whom the final isolate was resistant)												
2[1]	randomised trials	very serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	52/126 (41.3%)	84/246 (34.1%)	RR 1.22 (0.93 to 1.59)	75 more per 1000 (from 24 fewer to 201 more)	⊕OOO VERY LOW	CRITICAL
								0%		-		
Fungal infection (follow-up 3 - 24 months; assessed with: Number of individuals with candida infections)												
2[1]	randomised trials	very serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	15/126 (11.9%)	39/246 (15.9%)	RR 0.66 (0.15 to 2.85)	54 fewer per 1000 (from 135 fewer to 293 more)	⊕OOO VERY LOW	CRITICAL
								0%		-		
Mortality related to fungal infection (follow-up median 24 years; assessed with: Number of deaths in each group)												
1[4]	randomised trials	serious[5]	no serious inconsistency	no serious indirectness	no serious imprecision	none	3/413 (0.73%)	1/416 (0.24%)	RR 3.02 (0.32 to 28.93)	5 more per 1000 (from 2 fewer to 67 more)	⊕⊕⊕O MODERATE	CRITICAL
								0%		-		
CD4*T cell count at last study measurement (follow-up median 24 years; assessed with: Median cells/mm^3)												
1[4]	randomised trials	serious[5]	no serious inconsistency	no serious indirectness	no serious imprecision	none	108/329 (32.8%)	151/333 (45.3%)	RR 0.72 (0.6 to 0.88)	127 fewer per 1000 (from 54 fewer to 181 fewer)	⊕⊕⊕O MODERATE	CRITICAL
								0%		-		
Laboratory anomalies (follow-up median 24 years; assessed with: Number of individuals with a platelet count <50,000 platelets/mm^3)												
1[4]	randomised trials	serious[5]	no serious inconsistency	no serious indirectness	no serious imprecision	none	8/327 (2.4%)	1/334 (0.3%)	RR 8.17 (1.03 to 64.97)	21 more per 1000 (from 0 more to 192 more)	⊕⊕⊕O MODERATE	CRITICAL
								0%		-		

[1] Goldman 2005; Revankar 1998
[2] High risk of performance and attrition bias, unknown /unclear risk of selection and detection bias in Goldman study; Unknown/unclear risk of performance, attrition, selection and detection bias in Revankar study.
[3] Low even in pooled analysis
[4] High risk of performance and attrition bias, unknown /unclear risk of selection and detection bias

[b] High risk of performance and attrition bias, unknown/unclear risk of selection and detection bias in Goldman study

D.3 Relevant national alerts and reports

Table 9: Summary of safety alerts and reports

Source of evidence	Title	Reason for alert/report	Actions outlined in the alert/report
NHS England	Reducing risk of overdose with midazolam injection in adults – Rapid Response Report. (December 2008)	• The National Reporting and Learning Service (NRLS) received 498 patient safety incidents between November 2004 and November 2008 where the dose prescribed or administered to the patient was inappropriate. There were 3 deaths reported. • Some adult patients are being overdosed with midazolam injection when used for conscious sedation.	• Healthcare organisations should: ○ assign overall responsibility to a senior clinician. ○ restrict the storage and use of high strength midazolam to clinical areas/situations where its use has been risk-assessed. ○ replace the storage and use of high-strength midazolam with low-strength midazolam in other clinical areas. ○ clarify guidance on the use of midazolam. ○ ensure that the risks are fully assessed and that staff involved in sedation techniques have the necessary skills. ○ ensure that flumazenil is available where midazolam is used and audit the use of flumazenil as a marker of excessive dosing of midazolam. ○ ensure that sedation is covered by organisational policy.
	Reducing dosing errors with opioid medicines - Rapid Response Report. (July 2008)	• The NRLS received reports of 5 deaths and over 4,200 dose-related patient safety incidents concerning opioid medicines up to June 2008. • This applies to the prescription,	• When prescribing, dispensing or administering these medicines the health professional or their clinical supervisor should: ○ confirm any recent opioid dose, formulation, frequency of administration and any other

Source of evidence	Title	Reason for alert/report	Actions outlined in the alert/report
		dispensation or administration of buprenorphine, diamorphine, dipipanone, fentanyl, hydromorphone, meptazinol, methadone, morphine, oxycodone, papaveretum and pethidine. • This is to alert all health professionals prescribing, dispensing or administering opioid medicines to the risks of patients receiving unsafe doses. • Every member of the team has a responsibility to check that the intended dose is safe for the individual patient.	analgesic medicines prescribed for the patient. ○ ensure where a dose increase is intended, that the calculated dose is safe for the patient. ○ check the usual starting dose, frequency of administration, standard dosing increments, symptoms of overdose, and common side effects of that medicine and formulation. • Healthcare organisations should review local medicines and prescribing policies, including standard operating procedures, to reflect the guidance in the alert.
	Ensuring safer practice with high dose ampoules of diamorphine and morphine - Safer Practice Notice. (May 2006)	• There have been a number of reports of deaths and harm due to the administration of high dose (30mg or greater) diamorphine or morphine injections to patients who had not previously received doses of opiates. • The main risks identified include: lookalike or similar packaging for different strengths of diamorphine and morphine ampoules; poorly differentiated outer cartons and ampoules; higher and lower strength ampoules of diamorphine and morphine stored together in clinical areas in both primary and secondary care. • Understanding by healthcare staff of the risks and precautions when prescribing, dispensing and administering higher doses of	• This document alerts the NHS in England and Wales to review and improve measures for safer practice in prescribing, storing, administering and identifying high dose morphine and diamorphine injections. • It advises all NHS organisations to put measures in place to protect patients from simple but potentially fatal mistakes.

Source of evidence	Title	Reason for alert/report	Actions outlined in the alert/report
		these medicines.	
Medicines Healthcare products and Regulatory Agency (MHRA)	Drugs and driving: blood concentration limits to be set for certain controlled drugs in a new legal offence (July 2014)	• The Department for Transport has introduced an offence of driving with certain controlled drugs above specified limits in the blood. • Came into force on 2nd March 2015.	• Advice for health professionals: ○ Any condition that requires medicinal treatment may itself pose a risk to driving ability if left untreated. Therefore it is important to advise patients to continue their treatment. • Advice to give to patients taking any medicine: ○ Continue taking your medicine as prescribed. ○ Check the leaflet that comes with your medicine for information on how your medicine may affect your driving ability. ○ It is against the law to drive if your driving ability is impaired by this medicine. ○ Do not drive while taking this medicine until you know how it affects you (especially just after starting or changing the dose of the medicine). ○ Do not drive if you feel sleepy, dizzy, unable to concentrate or make decisions, or if you have blurred or double vision.
	Codeine for analgesia: restricted use in children because of reports of morphine toxicity (July 2013) Codeine: restricted use as analgesic in children and adolescents after European safety review (June 2013)	• A European review was triggered by concerns of an increased risk of morphine toxicity when susceptible children receive codeine for pain after surgery. • The review highlighted that despite the established use of codeine,	• A list of factors to consider has been provided for health professionals when prescribing codeine. These include: ○ Only to prescribe codeine for acute moderate pain in children older than 12 years and if it

Source of evidence	Title	Reason for alert/report	Actions outlined in the alert/report
	Codeine-containing pain relief in children (December 2012)	there remains substantial lack of knowledge about its safety and efficacy, particularly in the paediatric population. • The review concluded that codeine should only be used to relieve acute moderate pain in children older than 12 years and only if it cannot be relieved by other painkillers such as paracetamol or ibuprofen alone.	cannot be relieved by other painkillers such as paracetamol or ibuprofen alone. ○ In children age 12–18 years, the maximum daily dose should not exceed 240 mg. ○ Codeine is contraindicated in all children (younger than 18 years) who undergo tonsillectomy or adenoidectomy (or both) for obstructive sleep apnoea. It is not recommended for use in children whose breathing might be compromised. ○ Information should be given to parents and carers on how to recognise the signs of morphine toxicity, and advice should be given to stop giving the child codeine and to seek medical attention immediately if their child is showing these signs or symptoms. Additional details can be found on the hyperlinks provided for each drug safety update.
	Buccal midazolam (Buccolam▼): new authorised medicine for paediatric use (October 2011)	• Information provided for health professionals to take care when transferring from unlicensed formulations of midazolam to the licensed formulation of midazolam (Buccolam).	• Health professionals should consider several factors when transferring patients to the authorised Buccolam product when an unlicensed medicine other than Buccolam has been used previously. This includes: ○ Buccolam is half the strength of some other unlicensed preparations. It contains the hydrochloride salt, whereas

Source of evidence	Title	Reason for alert/report	Actions outlined in the alert/report
			some other preparations contain the maleate salt of midazolam.
	Addiction to benzodiazepines and codeine (July 2011)	• Drug safety update based on findings from 2 reports commissioned by the Department of Health on addiction to prescribed and over-the-counter medicines. • Use of anxiolytic benzodiazepines increased between 1991 and 2009. • The data also showed a gradual increase in sales of over-the-counter codeine-containing medicines since these were placed on the market in 2006. • Regional breakdown of long-term prescribing of benzodiazepines data showed very large variations in prescribing practice across England.	• Reminder for health professionals: ○ given the risks associated with the use of benzodiazepines, patients should be prescribed the lowest effective dose for the shortest time possible. Maximum duration of treatment should be 4 weeks, including the dose-tapering phase. ○ over-the-counter codeine-containing medicines should be used for the short-term (3 days) treatment of acute, moderate pain which is not relieved by paracetamol, ibuprofen, or aspirin alone (see also drug safety update: over-the-counter painkillers containing codeine or dihydrocodeine, September 2009).
	Codeine-containing liquid over-the-counter medicines (October 2010)	• The Commission on Human Medicines and its Paediatric Medicines Expert Advisory Group have advised that codeine-containing over-the-counter liquid medicines should not be used for cough suppression in children and young people younger than age 18 years.	• Health professionals who can supply codeine-containing over-the-counter liquid should take this advice into account when requests for supply are made.
	Over-the-counter painkillers containing codeine or dihydrocodeine (September 2009)	• The Commission on Human Medicines have advised to introduce additional warnings and tighter controls on the sales of over-the-counter medicines	• Pharmacists asked to support the public health measures taken by: ○ recommending codeine or dihydrocodeine containing products appropriately within the

Source of evidence	Title	Reason for alert/report	Actions outlined in the alert/report
		containing codeine or dihydrocodeine to minimise the risk of overuse and addiction to these medicines.	over-the-counter analgesic range ○ giving key safety messages regarding short-term use and avoidance of addiction if taken as recommended ○ noting that packs of more than 32 tablets are for dispensing use only.
	Methylphenidate: safe and effective use to treat attention deficit/hyperactivity disorder (ADHD) (March 2009)	• A review was completed by the European Medicines Agency (EMA) on the benefits and risks of methylphenidate after concerns about its cardiovascular, cerebrovascular, and psychiatric safety and its long-term effects. • Based on the availability of data at that time, the EMA concluded that the benefits of methylphenidate continue to outweigh the risks when used in its licensed indication.	• Health professionals prescribing and monitoring people who require treatment with methylphenidate should: ○ take in to consideration contraindications, ○ carry out pre-treatment screening, and ○ carry out on-going monitoring. Additional details can be found on the hyperlink provided for the drug safety update.
	Serious and fatal overdose of fentanyl patches (September 2008)	• MHRA has received reports of unintentional overdose of fentanyl due to dosing errors, accidental exposure, and exposure of the patch to a heat source.	• Advice for health professionals, particularly those who prescribe and dispense fentanyl patches includes: ○ fully inform patients and carers about directions for safe use ○ Use the information provided in the summary of product characteristics and in the package insert for patients. ○ Ensure that patients and carers are aware of the signs and symptoms of fentanyl overdose. Additional details can be found on the hyperlink provided for the drug safety update.

Source of evidence	Title	Reason for alert/report	Actions outlined in the alert/report
	Codeine: very rare risk of side-effects in breastfed babies (November 2007)	• Drug safety update based on a Canadian case report that described a breastfed neonate who died from morphine poisoning associated with maternal codeine used for episiotomy pain. The mother was an ultra-rapid codeine metaboliser as a result of CYP2D6 polymorphisms • In the UK, only 1–2% of people are CYP2D6 ultra-rapid metabolisers and only the breastfed babies of these mothers may be more prone to these adverse effects. • Breastfed babies might very rarely develop side-effects due to the presence of morphine in breast milk.	• Advice for health professionals includes: ○ All patients should be advised about the typical side-effects of opioids because most patients are not aware of their CYP2D6 status ○ If any symptoms of opioid toxicity develop in the mother or baby, the person should stop taking all codeine-containing medicines, and alternative analgesics should be prescribed. ○ These side-effects are very rare and most women will be able to use medicines that contain codeine to obtain adequate analgesia when needed after labour without any problems for them or their baby. Additional details can be found on the hyperlink provided for the drug safety update.
Care Quality Commission (CQC)	Safer Use of Controlled Drugs – Preventing harms from the use of methadone	• Large numbers of patient safety incidents involving methadone have been reported to the NRLS under the category 'medication error'.	• A list of recommendations for clinical practitioners who prescribe, dispense or administer methadone has been provided which covers: ○ competence ○ dosage and formulation ○ potential harms ○ co-prescribing with other opioids ○ supervised consumption. Additional details can be found on the hyperlink provided for the document.
	Safer Use of Controlled Drugs -	• Large numbers of patient safety	• A checklist has been provided for

Source of evidence	Title	Reason for alert/report	Actions outlined in the alert/report
	Preventing harms from fentanyl and buprenorphine transdermal patches	incidents involving fentanyl and buprenorphine transdermal patches have been reported to the NRLS.	health professionals who prescribe, dispense and administer fentanyl and buprenorphine transdermal patches. This list includes: ○ co-prescribing with regular opioid doses ○ dosing and double checking of calculations ○ recording anatomical position of currently applied patches ○ prescribing by brand and giving adequate amount ○ provision of advice in accordance with the summary of product characteristics ○ considering that patients may exhibit symptoms of opioid withdrawal when a controlled drug transdermal patch has been omitted. Additional details can be found on the hyperlink provided for the document.
	Safer use of oral oxycodone medicines	• Large numbers of patient safety incidents involving oral oxycodone medicines have been reported to the NRLS.	• A checklist has been provided for health professionals who prescribe, dispense and administer oxycodone medicines. This list includes: ○ second-line use if morphine is not suitable or cannot be tolerated. ○ obtaining information of previous analgesics used ○ checking formulation, for example short-acting or long-acting

Source of evidence	Title	Reason for alert/report	Actions outlined in the alert/report
			○ prescribing by brand and checking therapeutic duplication. Additional details can be found on the hyperlink provided for the document.
	Safer use of MS syringe drivers	• In December 2010 the National Patient Safety Agency[1] issued: 'Safer Use of Ambulatory Syringe Drivers'. • This identified 8 deaths and 167 non-fatal that were reported the NRLS. • The NRLS is still receiving reports of incident involving MS Syringe Drivers, usually involving Controlled Drugs, where patients are being harmed.	• It is recommended that no MS syringe drivers are used in NHS and independent healthcare providers providing NHS funded care, by December 2015 at the latest. • A checklist has been provided for health professionals to ensure safe use of ambulatory syringe drivers. Additional details can be found on the hyperlink provided for the document.
1 The key responsibilities for patient safety developed by the National Patient Safety Agency (NPSA) transferred to NHS England in 2012			

Appendix E: Economic evidence tables

E.1.1 Administering controlled drugs

Evidence Table 10: Bell et al 2007 A randomized trial of effectiveness and cost-effectiveness of observed versus unobserved administration of buprenorphine–naloxone for heroin dependence

Bell, J; Shanahan, M; Mutch, C *et al* 2007 A randomized trial of effectiveness and cost-effectiveness of observed versus unobserved administration of buprenorphine–naloxone for heroin dependence. Addiction, 102, pp1899–1907				
Study details	**Population and interventions**	**Costs**	**Health outcomes**	**Cost effectiveness**
Economic analysis: Cost effectiveness analysis **Study design:** Randomised trial data informed	**Population:** The analysis accompanied a randomised trial which recruited 119 predominantly male (75%) adult individuals (mean age 34.7 years ± 8.8 [SD]) seeking	**Total cost:** Unobserved group: AU$2385 (95% CI 2079–2539) Observed group:	The primary measure of effectiveness was retention in treatment at 3 months and heroin use at 3 months. Retention (NS[3]):	**ICER:** Once all the costs and outcomes were combined, it cost (on average) an additional AU$1477 (95% CI 736.41, 2006.52) to achieve an equivalent change in

Bell, J; Shanahan, M; Mutch, C *et al* 2007 A randomized trial of effectiveness and cost-effectiveness of observed versus unobserved administration of buprenorphine–naloxone for heroin dependence. Addiction, 102, pp1899–1907				
an economic analysis[1] **Approach to analysis:** The perspective taken for this economic evaluation was that of the health care sector. **Time horizon:** No specific time horizon for the economic model was stated. However, the ICER in this study was the incremental cost per additional day free of opioid use from baseline to *3-month follow-up*. **Discounting:** Discounting was not discussed.	treatment for heroin use from 4 specialist out-patient drug treatment centres in Australia. Treatment was for 13 weeks, and all subjects received combination buprenorphine–naloxone. **Intervention:** Participants picking up medication once per week, for administration at home (unobserved dosing). **Usual care:** Subjects in the observed group could attend daily, second-daily or thrice-weekly (using 2- or 3-day dosing schedules) depending on their stability.	AU$3862 (95% CI 3509–4127) **Currency & cost year:** Australian dollars (AU$), 2005. **Cost components incorporated:** Medication, medical, counselling and dispensing costs. Hospital admissions, ambulance service, dental services, emergency visits, allied health professionals, pathology tests and prescription costs. A separate cost analysis including travel costs was also presented[2].	Unobserved:57% Observed: 61% Heroin use in past month (NS[4]): Unobserved:61% Observed: 45% **Secondary outcomes:** Non-significant differences were found for non-opioid drug use, psychological symptoms and quality of life scores. Also reported were serious adverse events and diversion and injection of medication.	heroin-free days in the observed compared to unobserved subjects. **Analysis of uncertainty:** No sensitivity analyses were reported.

[1] It is unclear what form of economic model was used in this study
[2] Mean treatment cost in unobserved group: AU$1796 (95% CI 1422–2169) versus observed group: AU$2589 (95% CI 1829–2777)
[3] Non-statistically significant finding P=0.84
[4] Non-statistically significant finding P=0.14

Appendix F:Summary of the legal framework associated with controlled drugs

Legislation	Summary
Medicines Act 1968	• Sets out the requirements for the legal sale, supply and administration of medicines. • Allows certain exemptions from general restrictions on the sale, supply and administration.
Misuse of Drugs Act 1971 (and associated regulations)	• Sets out the provisions for the export, import, supply and possession of dangerous or otherwise harmful drugs. • In addition to the provisions, there are 6 Schedules of the Act. Controlled drugs are listed in schedule 2 of the Act. • Specifies drugs into 3 parts: Part 1 (Class A drugs), Part 2 (Class B drugs) or Part 3 (Class C drugs).The specification of each drug is 'set with reference to the harm a drug has or is capable of having when misused' and the type of illegal activity undertaken in regard to that drug.
Misuse of Drugs (Safe Custody) Regulations 1973, and subsequent amendments)	• Sets out the provisions for the storage of controlled drugs. The degree of control depends on the premises within which the controlled drugs are being stored. • There are 2 Schedules to the Regulations. Schedule 1 lists controlled drugs that are exempt from safe custody requirements. Schedule 2 sets out the structural requirements for cabinets and rooms uses for keeping controlled drugs.
Misuse of Drugs (Supply to Addicts) Regulations1997, and subsequent amendments)	• Requires doctors who prescribe, administer or supply diamorphine, cocaine or dipipanone for the treatment of addiction to have a General License to carry out this activity. This is issued by the Home Office Drugs Licensing and Compliance Unit.
Misuse of Drugs Regulations 2001, and subsequent amendments), MDR	• Defines classes of people who are authorised to supply and possess controlled drugs while acting in their professional capacities and lay down the conditions under which these activities may be carried out. • Divides controlled drugs into 5 Schedules, which dictate the degree to which a controlled drug use is regulated. The Schedule in which a controlled drug is placed and depends upon its medicinal or therapeutic benefit balanced against its harm when misused. Schedule 1 controlled drugs are subject to the highest level of control, whereas Schedule 5 controlled drugs are subject to a much lower level of control.

	• Sets out the Schedules that detail the conditions under which activities such as the import, export, production, supply, possession, prescribing, destruction and record keeping of a drug may be carried out. • The MDR are periodically amended and revised. The MDR currently in force and its amendments can be found on the government website.
The Human Medicines Regulations 2012	• The regulations are the result of the Medicines and Healthcare Products Regulatory Agency's consolidation and review of UK medicines legislation. • Replaces much of the Medicines Act 1968 and around 200 statutory instruments. • Introduces some small policy changes to help ensure that the legislation remains fit for purpose and reflects modern practice. • Sets out a comprehensive regime for the authorisation of medicinal products for human use; for the manufacture, import, distribution, sale and supply of those products; for their labelling and advertising; and for pharmacovigilance.
The Controlled Drugs (Supervision of Management and Use) Regulations 2013	• Sets out the requirements for NHS England to ensure systems are in place and working effectively for the safe use and management of controlled drugs. • Sets out the appointment, registration requirements and the core duties and functions of controlled drugs accountable officers (CD AO). • Requires NHS England CD AOs to be the assigned lead CD AOs for establishing local intelligence networks (LINs) in England for a particular area.