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Prescribed Medicines Review:
Summary of methods, findings and recommendations

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Contents

Background & scope

- In 2017, the minister for public health and primary care commissioned PHE to identify “the scale, distribution, and causes of prescription drug dependence, and what might be done to address it”.
- Scope: Adults (aged 18 and over) and 5 classes of medicines:
  1. benzodiazepines
  2. z-drugs
  3. gabapentin and pregabalin
  4. opioids for chronic non-cancer pain
  5. antidepressants

Methods

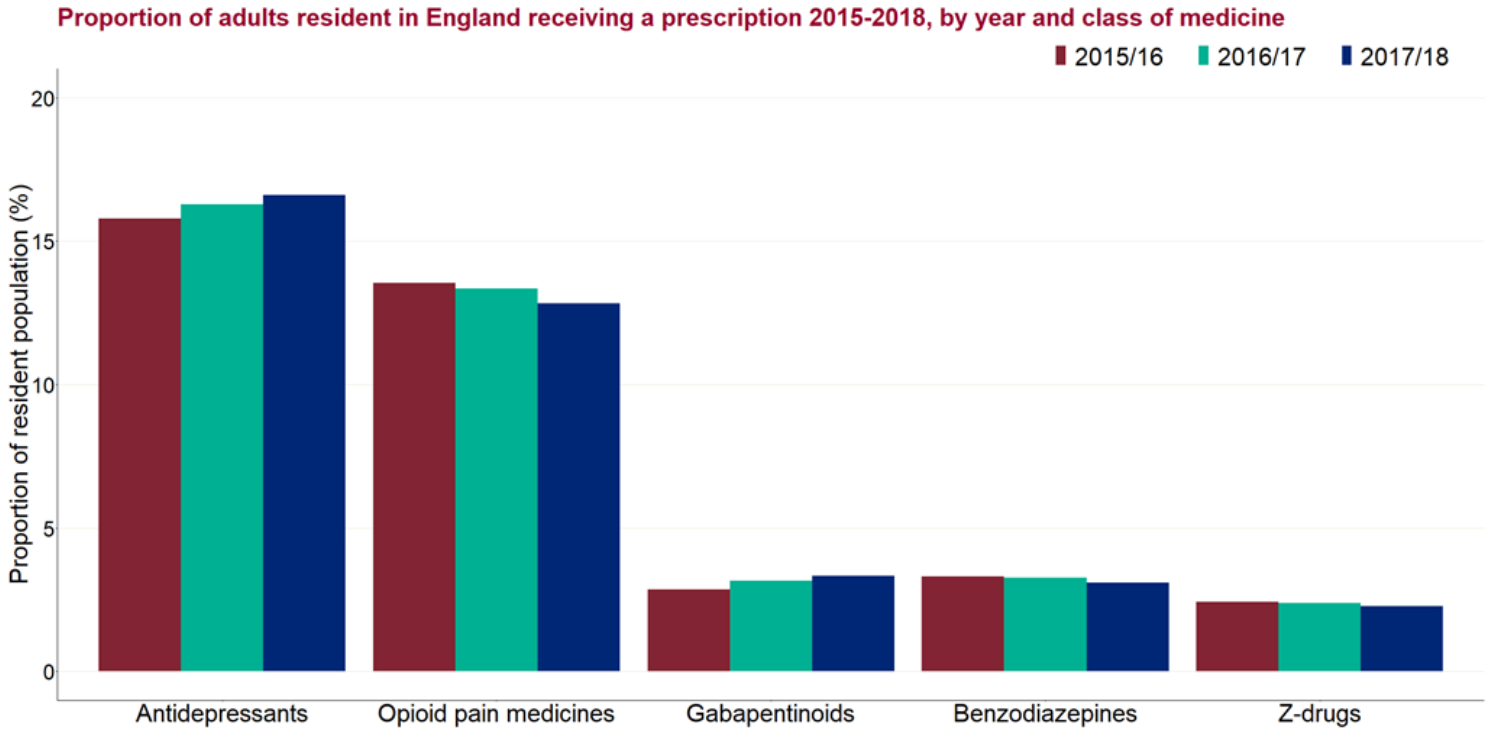
- Mixed-methods public health evidence review comprising:
  - Analysis of all NHS community prescriptions in England reported to the NHS Business Services Authority (2015 to 2018) supplemented by data on longer-term prescriptions to inform trends, and data on medicines supplied in other settings.
  - Rapid evidence assessment (REA) of articles on prescription medicine-associated harms, dependence, withdrawal, risk factors, and service models (published between 2008 and 2018), and a call-for-evidence on patients' experiences and service models.
- An expert reference group advised on methods and discussed findings and recommendations.

Key findings from PHE's analysis of dispensed prescriptions

- In 12 months in 2017-2018, 11.5 million adults in England (26%) received, and had dispensed, one or more prescriptions for any of the medicines within the scope of the review.
- This prescribing rate was similar to 2015/16.
- Breakdown as follows:
  - antidepressants: 7.3 million people (17% of the adult population)
  - opioid pain medicines: 5.6 million (13%)
  - gabapentinoids: 1.5 million (3%)
  - benzodiazepines: 1.4 million (3%)
  - z-drugs: 1.0 million (2%)
- Large variations in the standardised rates of prescribing across clinical commissioning groups (CCGs).

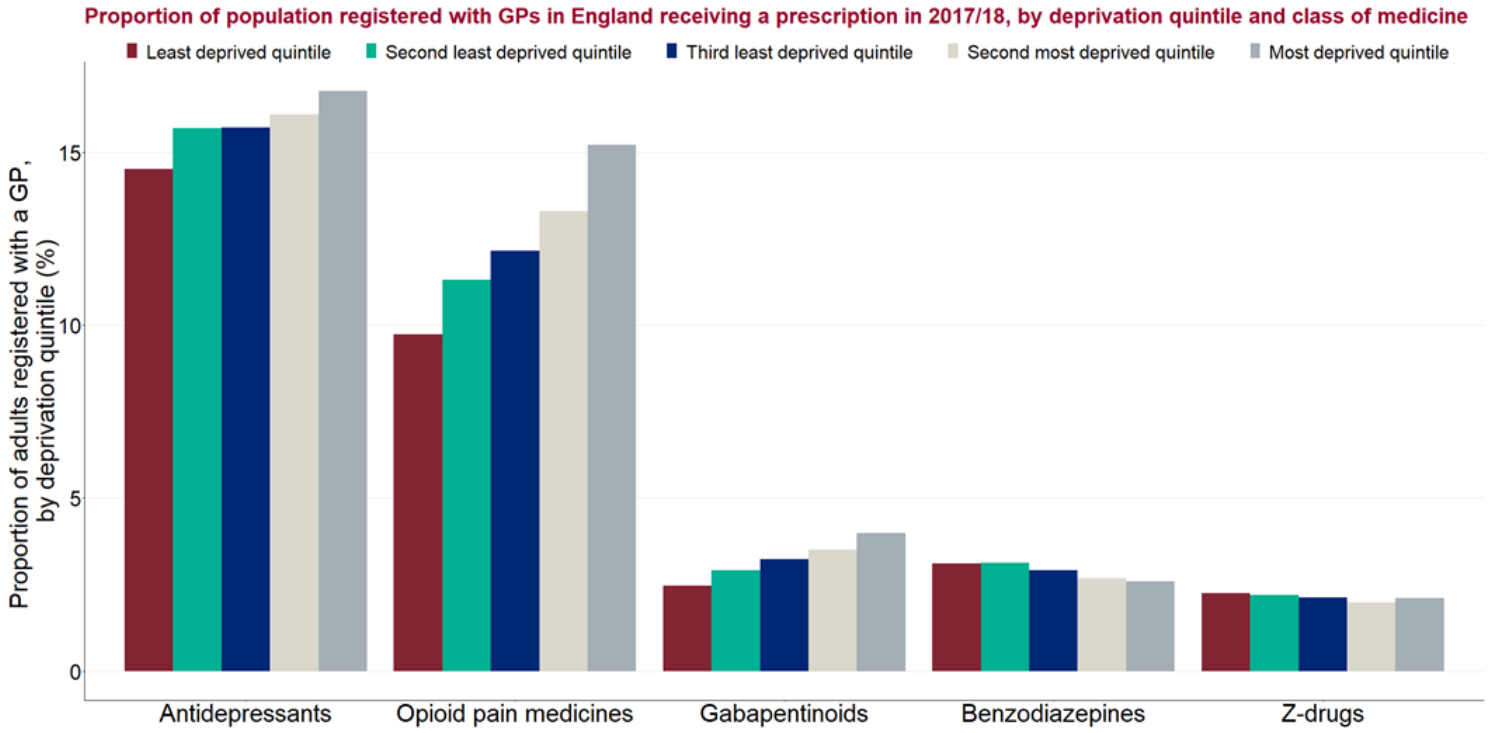
Prescribing rates

- Between 2015/16 and 2017/18 the prescribing rate increased for antidepressants from 15.8% to 16.6% and for gabapentinoids from 2.9% to 3.3%.
- There were small decreases in prescribing rates for the other 3 medicine classes.



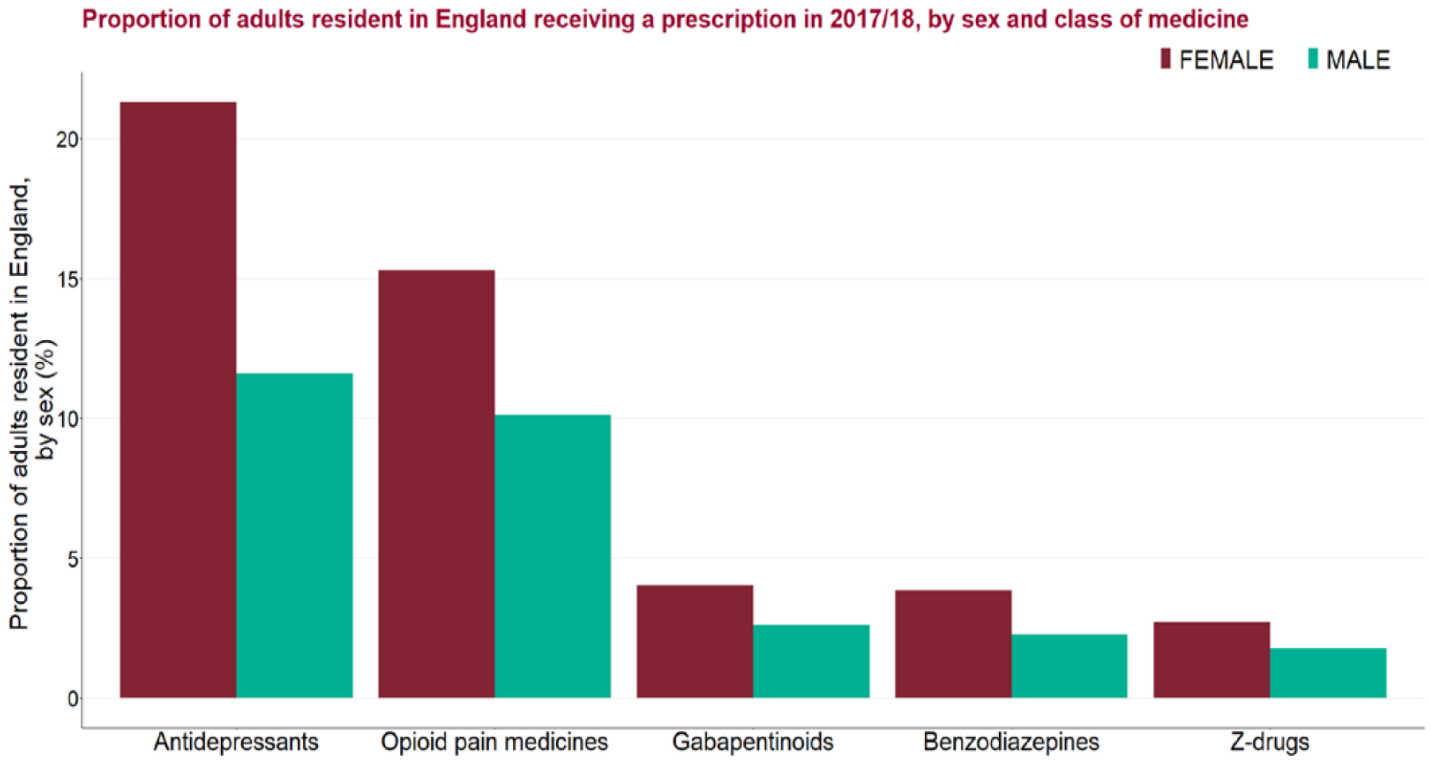
Associations with deprivation

- Prescribing rates for opioids and gabapentinoids were strongly associated with deprivation (1.6 times greater in the most deprived areas compared to the least deprived).
- Antidepressants had a weaker association with deprivation (1.2 times greater in most deprived areas compared to the least deprived).
- For benzodiazepines and z-drugs, prescribing rates slightly *decreased* with higher deprivation.

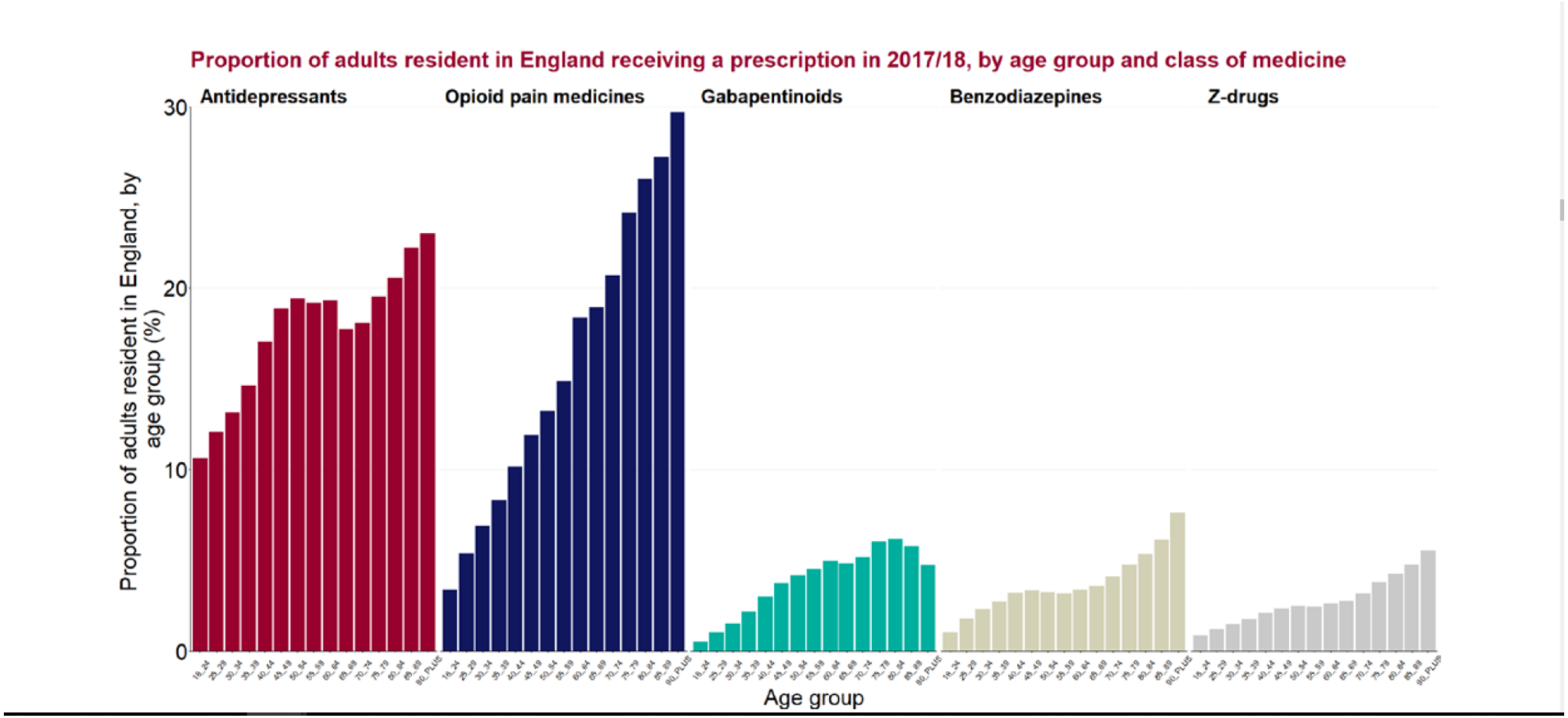


Associations with sex

- Across all groups, the proportion of women receiving a prescription in the year was at least 1.5 times higher than the proportion of men.
- The greatest observed difference by sex was for antidepressants, where 21.3% of women received a prescription compared to 11.6% of men (1.8 times greater).
- The smallest relative difference was for opioid pain medicines (15.3% of women, 10.1% of men).

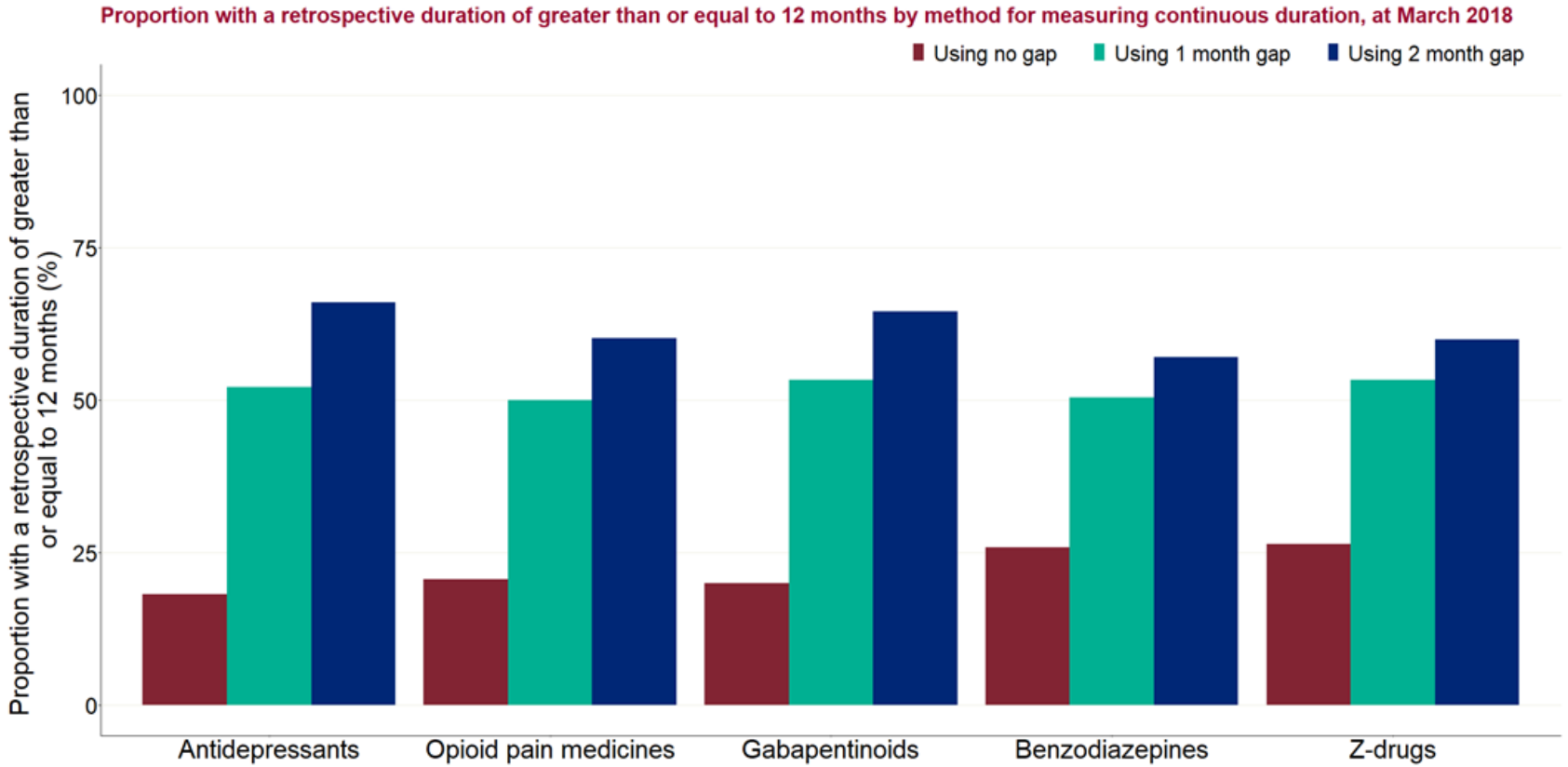


Association with age



Duration – 1 year+

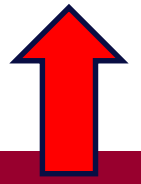
- Of people receiving a prescription in March 2018, around half of patients in each medicine class were estimated to have been receiving a prescription continuously for at least 12 months at that point (allowing for a one month gap in prescribing – green columns).



Duration – 3 years+

Number and proportion of individuals in each medicine class in receipt of a prescription in April 2015 who received a prescription continuously up to March 2018

Medicine class	Number of individuals in receipt of prescription April 2015 (millions, rounded to 10,000)	Of which, those continuously receiving a prescription March 2018 (millions, rounded to 10,000)	Proportion still in receipt of prescription (%)
Antidepressants	3.14	0.93	30
Opioid pain medicines	1.98	0.54	27
Gabapentinoids	0.53	0.16	31
Benzodiazepines	0.40	0.12	29
Z-drugs	0.33	0.10	31



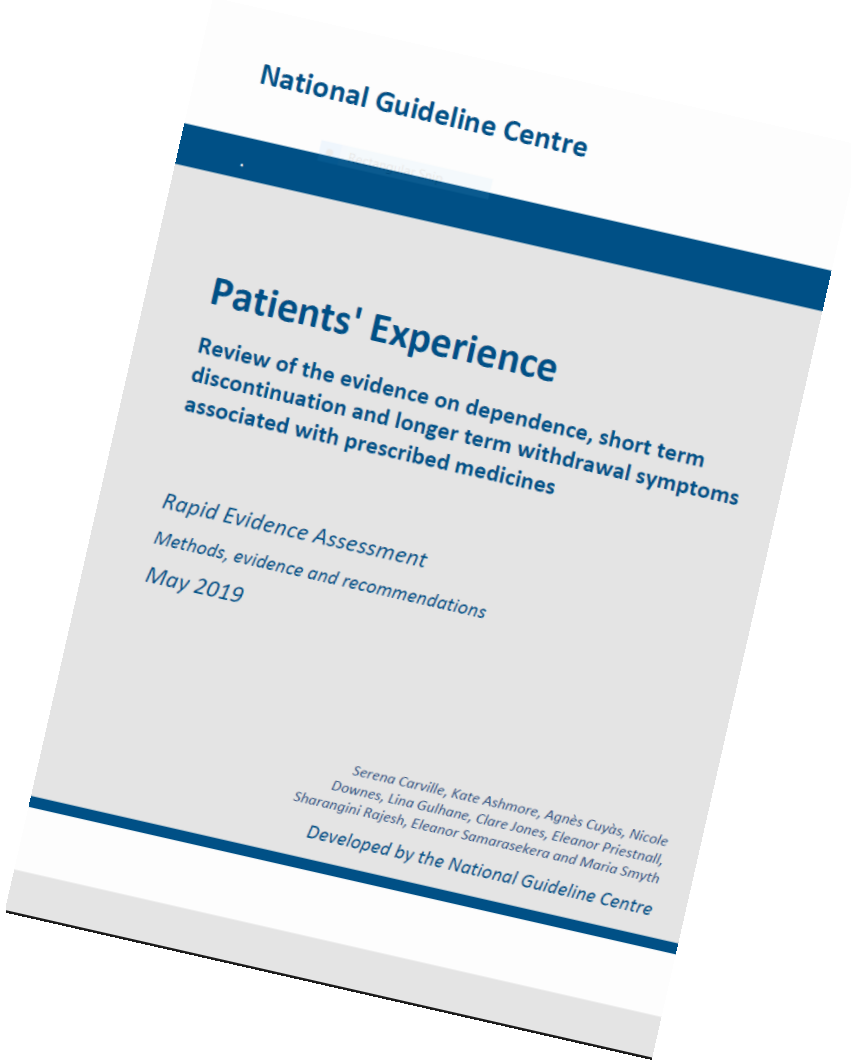
Evidence review and call for papers

1. Dependence, withdrawal & interventions

- Benzodiazepines, z-drugs, opioid pain medicines and gabapentinoids are associated with a risk of dependence and withdrawal.
- Antidepressants are associated with withdrawal. Symptoms include insomnia, depression, suicidal ideation, and physical symptoms on cessation of medication.
- Interventions for treating dependence and managing withdrawal varied widely and meta-analysis, or combining data from the studies, was not feasible.

2. Patients' experiences

- Some patients report harmful effects and withdrawal symptoms on stopping benzodiazepines, z-drugs, opioids and antidepressants.
- Symptoms affect well-being, personal, social and occupational functioning and could last many months.
- Patients experienced barriers to accessing and engaging in treatment services.
- Lack of information on the risks of medication.
- Doctors did not acknowledge or recognise withdrawal symptoms.
- Patients not being offered non-medicinal options, lack of review, and a lack of support services.



3. Risk factors

- Higher initial opioid doses and prior mental health problems were associated with long-term use of opioids and opioid dependence, respectively.
- Prescribing opioid pain medicines for longer than 90 days was associated with opioid overdose and dependence.
- Low income and use of shorter-acting benzodiazepines are associated with long-term benzodiazepine use.

4. Service models

- There was insufficient evidence to draw firm conclusions on the effectiveness/cost effectiveness of service models.
- However some common features were identified of service models submitted:
  - Involvement of GPs and other primary care services
  - Helplines and telephone support
  - Counselling and support groups

The review's conclusions (1/2)

- 1 in 4 adults in England in 2017/18 were prescribed one or more of the medicines covered by the review.
- Prescribing rates for antidepressants and gabapentinoids are increasing.
- Opioid pain medicine prescribing is slightly decreasing (after increasing for many years).
- Benzodiazepine prescribing continues to decrease (a long-term trend), as does prescribing for z-drugs, but this was increasing until relatively recently.
- Women have a higher prescribing rate than men.
- Older people have a higher prescribing rate.
- There are wide variations in prescribing rates at CCG level.
- Rate and duration of prescribing are generally associated with deprivation, particularly for opioids, gabapentinoids and antidepressants.

The review's conclusions (2/2)

- Longer term prescribing is widespread – this may be contrary to some guidelines, but with the exception of antidepressants.
- There is a lack of recent high-quality research studies on medicine dependence and withdrawal, and prevention and treatment.
- Effective, personalised care should include shared decision making with patients and regular reviews of whether treatment is working.
- Patients who want to stop using a medicine must be able to access appropriate advice, treatment and support, and must never be stigmatised.
- Inappropriate limiting of medicines may increase harm, including the risk of suicide, and lead some people to seek medicines from illicit or less-regulated sources, such as online pharmacies.
- There needs to be increased public and clinical awareness of other interventions, such as cognitive behavioural therapy and exercise.

Summary of review's recommendations

- PHE's recommendations from the review are grouped in 5 areas:
  1. Increasing the availability and use of data on the prescribing of medicines to help ensure practice is in line with guidance.
  2. Enhancing clinical guidance and the likelihood it will be followed.
  3. Improving information for patients and carers, increasing informed choice and shared decision making between clinicians and patients.
  4. Improving support available.
  5. Further research on the prevention and treatment of dependence on, and withdrawal from, prescribed medicines.
- Local strategic leadership of CCGs, sustainability and transformation partnerships and integrated care systems will be vital.
- In total there are 41 detailed recommendations, which are summarised below.

5 key messages

1. Data and the patient experience evidence suggest that dependence on prescribed medication is a significant issue, particularly in relation opioids for chronic non-cancer pain which is not effective for most patients, and benzodiazepines which should not usually be used for longer than 28 days
2. Health and social inequalities are an important factor and addressing them needs to part of the solution
3. Long-term prescribing, in some circumstances and for some patients, may be clinically appropriate and helpful, particularly for antidepressants, and it is vital that care is taken not to generate any unintended negative consequences by stigmatising, curtailing or limiting the appropriate and safe use of potentially helpful medicines
4. Personalised care, shared decision making with patients and regular/purposeful prescribing reviews are an important part of the prevention and treatment response, alongside enhanced options for meeting need in relation to underlying conditions and better support for patents experiencing problems
5. A lot of activity is already in train or planned and there is some evidence that aspects of practice are improving but this is a complex and multifaceted issue which will require on-going attention

Medicines associated with dependence or withdrawal: a mixed-methods public health review and national database study in England

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Summary

Background Antidepressants, opioids for non-cancer pain, gabapentinoids (gabapentin and pregabalin), benzodiazepines, and Z-drugs (zopiclone, zaleplon, and zolpidem) are commonly prescribed medicine classes associated with a risk of dependence or withdrawal. We aimed to review the evidence for these harms and estimate the prevalence of dispensed prescriptions, their geographical distribution, and duration of continuous receipt using all patient-linked prescription data in England.

Methods This was a mixed-methods public health review, comprising a rapid evidence assessment of articles (Jan 1, 2008, to Oct 3, 2018; with searches of MEDLINE, Embase, and PsycINFO, and the Cochrane and King's Fund libraries), an open call-for-evidence on patient experience and service evaluations, and a retrospective, patient-linked analysis of the National Health Service (NHS) Business Services Authority prescription database (April 1, 2015, to March 30, 2018) for all adults aged 18 years and over. Indirectly (sex and age) standardised rates (ISRs) were computed for all 195 NHS Clinical Commissioning Groups in England, containing 7821 general practices for the geographical analysis. We used publicly available mid-year (June 30) data on the resident adult population and investigated deprivation using the English Indices of Multiple Deprivation (IMD) quintiles (quintile 1 least deprived, quintile 5 most deprived), with each patient assigned to the IMD quintile score of their general practitioner's practice for each year. Statistical modelling (adjusted incident rate ratios [IRRs]) of the number of patients who had a prescription dispensed for each medicine class, and the number of patients in receipt of a prescription for at least 12 months, was done by sex, age group, and IMD quintile.

Findings 77 articles on the five medicine classes were identified from the literature search and call-for-evidence. 17 randomised placebo-controlled trials (6729 participants) reported antidepressant-associated withdrawal symptoms. Almost all studies were rated of very low, low, or moderate quality. The focus of qualitative and other reports was on patients' experiences of long-term antidepressant use, and typically sudden onset, severe, and protracted withdrawal symptoms when medication was stopped. Between April 1, 2017, and March 31, 2018, 11·53 million individuals (26·3% of residents in England) had a prescription dispensed for at least one medicine class: antidepressants (7·26 million [16·6%]), opioids (5·61 million [12·8%]), gabapentinoids (1·46 million [3·3%]), benzodiazepines

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Dependence and withdrawal associated with some prescribed medicines

An evidence review

https://www.gov.uk/government/publications/prescribed-medicines-review-report