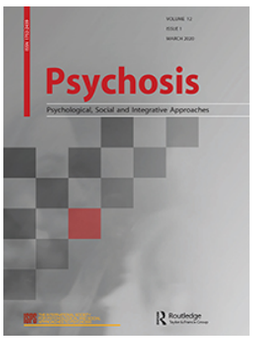

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OPINION PIECE

The case for including antipsychotics in the UK NICE guideline: "Medicines associated with dependence or withdrawal symptoms: safe prescribing and withdrawal management for adults"

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ABSTRACT

The UK's National Institute for Health and Care Excellence (NICE) is in the process of writing guidelines for "Medicines Associated with Dependence or Withdrawal Symptoms: Safe Prescribing and Withdrawal Management for Adults". NICE has excluded antipsychotics, despite inclusion having been requested by all four groups participating in the guideline scoping workshop, as well as the Royal College of Psychiatrists, the All-Party Parliamentary Group for Prescribed Drug Dependence, the International Institute for Psychiatric Drug Withdrawal (IIPDW), Bangor University, Grünenthal Ltd, Pfizer and Mind (the UK's largest mental health non-profit organisation). The IIPDW subsequently submitted the following request, drafted on their behalf by three researchers with expertise in this field, that NICE review its decision to exclude antipsychotics. The request draws on the recently updated German National Guideline for Schizophrenia. Two additional studies published since the submission, adding weight to the case, are also summarised.

ARTICLE HISTORY
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KEYWORDS
NICE guidelines; antipsychotics; withdrawal symptoms

Letter to NICE

To: National Institute for Health and Care Excellence (NICE)

From: International Institute for Psychiatric Drug Withdrawal (IIPDW)

Date: 9 December 2019

The International Institute for Psychiatric Drug Withdrawal request that the decision to not include antipsychotics in the Guideline for "Medicines Associated with Dependence or Withdrawal Symptoms: Safe Prescribing and Withdrawal Management for Adults" be reversed. We detail our objections below and call for antipsychotics to be included in the above named guideline. We look forward to receiving your response,

We object to the failure to include antipsychotics for the following reasons:

1. The justification for not including antipsychotics, copied below, is not satisfactory:

"Thank you for your comment. The views of stakeholders at the workshop, and those submitted (including the information you provide in your associated comments) have been carefully considered, however antipsychotics have not been included within the scope of the guideline. ***These medicines are prescribed for very specific defined conditions by specialists*** *and* ***guidance on their safe***

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prescribing, monitoring and withdrawal is included within the NICE guideline for psychosis and schizophrenia in adults CG178."

We do not feel this justification to be satisfactory for the following reasons:

These medicines are prescribed for very specific defined conditions by specialists:

Antipsychotics are the recommended first-line treatment for schizophrenia and psychosis and are also commonly used for bipolar disorder. However research has shown that only around 50% of people who are prescribed antipsychotics have a psychotic condition or bipolar disorder (Marston, Nazareth, Petersen, Walters, & Osborn, 2014). They are therefore prescribed for a broad range of mental health conditions including those that they are not routinely recommended for: depression, dementia. Or not recommended for (off-licence use): anxiety, insomnia, personality disorders, obsessive compulsive disorders, learning disabilities, ADHD, or even people without a diagnosis. This broad range of prescribing is concerning and contradicts the justification that *"these medicines are prescribed for very specific defined conditions"*. These prescribing patterns were shown through a study which examined all antipsychotic prescriptions in the UK in primary care between 2007 and 2011 (Marston et al., 2014). During this time 47,724 people were prescribed antipsychotics. For those receiving first generation antipsychotics, less than 50% had a diagnosis of a psychotic condition or bipolar disorder. For second generation antipsychotics this was 36–62%. The remaining prescriptions were for people with a diagnosis of anxiety, depression, dementia, sleep, and personality disorders. Up to 17% of people prescribed antipsychotics did not have a primary mental health diagnosis.

This broad range of antipsychotic prescriptions shows that antipsychotics are commonly *not* prescribed and managed by specialist psychiatrists in secondary care. Of those with a psychotic condition or bipolar disorder, approximately 30% are managed by primary care only (Reilly et al., 2012). GPs in primary care are often initiating and managing these prescriptions. A study of prescribing practices across 28.5 million people, 1999–2001 in Germany found that of those prescribed antipsychotics, 60% of these prescriptions were written by non-specialists (Hamann, Ruppert, Auby, Pugner, & Kissling, 2003).

Guidance on their safe prescribing, monitoring and withdrawal is included within the NICE guideline for psychosis and schizophrenia in adults CG178."

We disagree that NICE provide adequate guidance for the safe withdrawal of antipsychotics. The only guidance provided by NICE (CG178) on withdrawal of antipsychotic medication is as follows:

(1) If withdrawing antipsychotic medication, undertake gradually and monitor regularly for signs and symptoms of relapse.
(2) After withdrawal from antipsychotic medication, continue monitoring for signs and symptoms of relapse for at least 2 years.

This guidance is inadequate, we detail in (2) the significant difficulties incurred by people who are trying to withdraw from antipsychotics. A previous study has highlighted that the lack of guidance for antipsychotic withdrawal is a significant barrier to the reduction and discontinuation of these drugs by mental health professionals (Cooper, Hanratty, Morant, & Moncrieff, 2019). In the absence of formal reduction and discontinuation guidelines, service users report feeling unsupported with antipsychotic withdrawal and will often stop these drugs abruptly, without support, which may be more likely to lead to an adverse outcome (Larsen-Barr, Seymour, Read, & Gibson, 2018). The provision of support through formal guidelines will therefore increase the likelihood of successful antipsychotic discontinuation.

We include, as an attachment and as an appendix, two sets of guidelines that could form the basis for the development of NICE guidelines for antipsychotic withdrawal: The RADAR Study Reduction

Manual (Research into Antipsychotic Discontinuation and Reduction, NIHR Programme Grant[1]); and translated passages from the recently published German National Guidelines for Schizophrenia (DGPPN, n.d.). The RADAR study is a clinical trial based at University College London (UCL) which is assessing the benefits and risks of a flexible, supported strategy for antipsychotic discontinuation and reduction in people with psychotic conditions.

2. The high volume of calls for the inclusion of antipsychotics.

All four groups participating in the guideline scoping workshop proposed extending the scope of the guidelines to include antipsychotics. Alongside this a large number of stakeholders requested the inclusion of antipsychotics during the consultation period. These are: The Royal College of Psychiatrists, The All-Party Parliamentary Group for Prescribed Drug Dependence, Bangor University, Grünenthal Ltd, Mind, and Pfizer.

A brief summary of their reasons for the inclusion of antipsychotics are as follows:

- Antipsychotic reduction and/or discontinuation can cause severe withdrawal effects such as symptomatic relapse, mania, insomnia, anxiety, depression, restlessness, tardive dyskinesia. This may be due to neurotransmitter abnormalities that are caused by antipsychotics. This withdrawal can be interpreted as rebound psychosis leading to termination of the discontinuation attempt (Murray et al., 2016).
- Antipsychotics are associated with dependence, particularly those with sedative properties such as quetiapine and olanzapine.
- Antipsychotics are associated with addictive behaviours.
- Antipsychotics are often prescribed against the person's will under the Mental Health Act. This creates an even stronger duty to consider the impact of withdrawal effects when making treatment decisions.
- One reason why people may not get (or ask for) support to come off antipsychotic medication or mood stabilisers is that the clinician does not agree that they should do so. Inclusion of these drugs in the guideline should support clinicians to work as safely as possible with their patients' choices.

3. In the absence of formal guidelines for antipsychotic withdrawal, long-term prescription of antipsychotics is common and can cause severe and sometimes dangerous adverse effects and medical conditions.

The adverse effects of antipsychotics are well documented, they have been found to cause brain volume reduction which could lead to impaired cognition. They are cardio-toxic and can lead to heart disease and are associated with sudden cardiac death. They can also cause rapid weight gain leading to obesity and the development of type 2 diabetes. Alongside this they can cause movement disorders, sexual dysfunction, sedation, and emotional blunting. An evidence summary for adverse effects is summarised in three papers written by psychiatrists, and academics which have called for a review of the practice of long-term antipsychotic prescription (Moncrieff, 2015; Morrison, Hutton, Shiers, & Turkington, 2012; Murray et al., 2016). The development of formal guidelines for antipsychotic withdrawal will support clinicians in reducing the long-term prescription of these drugs and associated harms.

The German national guidelines for schizophrenia

In March 2019 the German Association for Psychiatry, Psychotherapy and Psychosomatics (DGPPN) published new guidelines for the treatment of schizophrenia (DGPPN, 2019a). In December the DGPPN published an abbreviated English translation (DGPPN, 2019b). We recommend that NICE guidelines should be at least as thorough as their German equivalent, and certainly should not avoid the important issues addressed by the DGPPN about antipsychotic reduction/discontinuation by

failing to include antipsychotics in their forthcoming withdrawal guidelines. The sections relevant to the issues at hand include:

> We recommend embedding pharmacotherapy in a holistic treatment concept that includes general and specific psychotherapeutic and psychosocial measures and psychiatric treatment, depending on the differential indication. (p.24)
>
> We recommend telling the patient at the start of pharmacotherapy about the acute and long-term effects and adverse effects of the drugs (risk-benefit evaluation) and actively involving patients in the decision-making process (shared decision making, see Module 3). We also recommend presenting the advantages and disadvantages of the treatment and possible alternatives in clear language and explaining technical terms. (p. 24)
>
> If the patient is stable and there are reasons why continuous long-term medication cannot be continued (e.g. lack of acceptance), we suggest offering stepwise dose reduction. (p. 29).
>
> After a decision has been made that the dose of antipsychotics can be reduced, we suggest offering a dose reduction, taking into account the recommended treatment duration. We suggest reducing the dose in very small steps at intervals of 6 to 12 weeks, depending on the patient's preferences. Furthermore, we suggest involving the patient's family and close confidants and taking into consideration the overall treatment plan, course of treatment to date and tolerability of the existing antipsychotic medication. (p. 29)
>
> We recommend offering a reduction and possible discontinuation of antipsychotics at any stage of the illness in terms of shared decision-making between the patient and the treating doctor, as long as sufficient stability and psychosocial support and regular, ongoing monitoring of symptoms are guaranteed and there are no indications that the patient is a danger to self or others. (p. 30).

The unabbreviated, untranslated German version (Deutsche Gesellschaft für Psychiatrie und Psychotherapie, Psychosomatik und Nervenheilkunde (DGPPN), 2019a) includes a detailed list of the withdrawal symptoms of antipsychotics (p. 62), including difficulties with concentration and memory, gastrointestinal disturbances, sweating, dizziness, tachycardia, hypertension, tremor, collapse, flu-like symptoms, excessive sensitivity to pain, headache, delirium, abnormal involuntary movements, and emotional disturbances. This is followed by guidance on how to withdraw slowly, safely and with professional and personal support systems in place (pp. 63, 64). It also clearly states that patients and other involved people should be informed about withdrawal symptoms: "Patienten sowie deren Umfeld sollten über Absetzphänomene [. . .] aufgeklärt werden" (p. 64).

Additional research

Since writing this submission results from the largest international online survey of antipsychotic users to date has come to our attention. The survey included 832 antipsychotic users across 30 countries, predominantly USA, UK, and Australia (Read & Sacia, 2020; Read & Williams, 2019). The survey found that although 41% experienced their antipsychotics as 'helpful' an equivalent number (43%) found then unhelpful. Alongside this many people wanted to stop their antipsychotics (70%). The most common reasons for wanting to stop were side-effects and concerns about effects on long-term physical health. However 65% reported withdrawal effects when trying to stop their antipsychotics and 51% of these described the withdrawal effects as severe. The survey also asked people to describe their experience of taking antipsychotics in their own words. Of the 650 people who completed this section 14.3% of participants were categorised as reporting purely positive experiences, 27.9% had mixed experiences, and 57.7% reported only negative ones. One of the main negative experiences of taking antipsychotics was the difficulty withdrawing from these drugs, with respondents stating: *"Withdrawal from the anti-psychotic was torturous and took a very long time. I would never choose to take them again, ever"; "Withdrawal symptoms were always blamed on relapse of my 'disease'"; "I suffered hallucinations, and headaches during withdrawal even from stopping a low dosage"* (Read & Sacia, 2020). This survey reinforces the significant need for the development of UK guidelines for withdrawal from antipsychotic medication.

Note

1. The RADAR study reduction manual is unable to be published with this article, however an overview is provided in the RADAR published protocol (Moncrieff et al., 2019).

Disclosure statements

No potential conflict of interest was reported by the authors. The journal Editor is member of the Board of IIPDW and invited the authors to submit this paper.

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