Deprescribing antipsychotics in adults with psychotic disorders – a literature review

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ARE ANTIPSYCHOTICS FOR LIFE? PERSPECTIVES ON DEPRESCRIBING ANTIPSYCHOTICS IN ADULTS DIAGNOSED WITH PSYCHOTIC DISORDERS: A REVIEW OF THE LITERATURE

Abstract

Antipsychotic medication is considered one of the first line treatments for psychosis and schizophrenia in adults, however there is also well documented evidence relating to negative impact, and an ongoing conflict between recovery orientated practice that promotes choice and collaboration, and the more traditional notion of promoting adherence over preference.

This review aimed to explore perspectives on deprescribing antipsychotics in this cohort, and to establish whether there is clear guidance to support deprescribing in clinical practice. A structured search was carried out across four databases and the yield filtered according to relevance resulting in 10 papers for appraisal and analysis. A thematic analysis identified three themes that were critically discussed. The review concluded that there is a lack of clear evidence regarding the impact of deprescribing antipsychotics, and no clear guidance on how it should be supported in practice.

Background

The National Institute for Health and Care Excellence (NICE) guidance for the prevention and management of psychosis and schizophrenia in adults (2014), advocates pharmacological first line treatment in the form of antipsychotic medication. Comprehensive guidance for medication initiation and review is provided, and a continuous regimen of antipsychotic maintenance therapy is recommended (NICE, 2014). Guidance on duration of maintenance treatment is less clear, and a lack of consensus is evident in the wider literature on this issue (Emsley, 2020).

Whilst medication is recommended in the context of a broader psychosocial package of interventions, in a recent review of the literature, Cooper et al (2020) identified that the evidence supporting the efficacy of such interventions without adjunctive medication is generally weak. Continuous antipsychotic maintenance treatment is still largely deemed the preferential intervention for those with a long-term psychotic diagnosis (De Hert et al, 2015). Kuipers et al (2014) go further and

describe a secondary care dependence on antipsychotic drugs as a sole treatment for schizophrenia in the longer term.

The long- term adverse effects of antipsychotic treatment are also well documented, including the association of second generation antipsychotics with increased cardio-metabolic risks and reduced mortality (Elkins, 2019) and the long established and disabling extrapyramidal effects that are synonymous with conventional first generation medications (Bahta et al, 2021).

Mental health services have evolved to embed recovery orientated values into clinical practice, including when prescribing medication (Baker et al, 2013). Within this paradigm, individual choice and self-determination are theoretically encouraged, yet individual preferences not to take antipsychotic medication are likely to be seen as a failure to comply over a supported choice, and shared decision making has arguably not transcended policy rhetoric (Morant et al, 2016). This may vary according to profession, with Ross (2015) identifying that mental health nurse prescribers saw reducing or stopping medication as a vital part of their role in supporting improvement in quality of life. Consideration of the potential adverse impact of antipsychotics has also been amplified by current policy on physical health care for those with a serious mental illness (SMI). Nurses are therefore key to identifying medication risk factors (Nash, 2023) and supporting informed choices in response, though a lack of guidance regarding discontinuation may still result in a default to a paternalistic culture of practice (Bladon, 2019).

The term 'deprescribing' refers to the process of withdrawing inappropriate medication with health professional supervision (Reeve et al, 2014). It has evolved partly in response to the growth of polypharmacy which is associated with impairment and poor outcome (Le Couteur et al, 2011).

Deprescribing antipsychotics has been explored in some specialist areas. Antipsychotics that have been initiated to manage behavioural and psychological issues associated with Dementia were the focus of the Halting Antipsychotic Use in Long Term Care (HALT) trial which reported successful reduction in care home settings with a strong emphasis on person centredness as an essential success criterion (Chenoweth et al, 2018).

Similarly, the 'Stopping over medication of people with a learning disability, autism or both' (STOMP) initiative (NHS England, 2019) has sought to address the overuse of psychotropic drugs, including antipsychotics, to manage challenging behaviour, and advocates a multidisciplinary approach to the process of deprescribing where appropriate (Adams, 2019).

In respect of adults with a psychotic disorder, the potential for discontinuation of these medications is less clear. NICE have identified that the treatment and management of psychosis in adults requires ongoing research to understand how those who choose not to take antipsychotic medication are best supported. The guidance also identifies the need to explore the physical health benefits of reduction or discontinuation of such medication (NICE, 2015).

Set parameters for discontinuation are not though fully determined, and standardised deprescribing guidance is not yet developed. This potentially results in a lack of clinical confidence to facilitate patient choice.

Aims

This review of the literature sought to:

- gather clinical and academic perspectives on antipsychotic deprescribing for adults with a psychotic disorder in the context of recovery orientated practice.
- establish whether there is sufficient guidance available to support safe deprescribing of antipsychotics in practice.

Method

Literature was sourced, appraised, and analysed to present a qualitative synthesis of critical perspectives on this subject area, an approach congruent with a narrative review methodology (Gregory, 2018).

Search Strategy

A structured electronic search of four health related databases was undertaken: Cumulative Index to Nursing and Allied Health Literature (CINAHL), Medline, Cochrane, and Pubmed.

Search terms and parameters were derived from the research question using the Population Exposure Outcome (PEO) framework.

(Insert Table 1)

Duplicates were removed from 2,382 yielded citations. 792 were then subject to screening guided by the PRISMA tool (Page et al, 2021).

Screening of titles and abstracts excluded 51 papers based on the following:

- The focus was on intellectual disability
- The focus was on deprescribing in dementia

43 articles were read in full and a further 33 excluded for the following reasons:

- The focus was on strategies and guidance to support adherence as opposed to discontinuation.
- The focus was entirely on one drug and/or in relation to one case study without generalisable conclusion.
- The focus was on reduction of regimen from antipsychotic polypharmacy to antipsychotic monotherapy, as opposed to full discontinuation.

The reference lists of the remaining papers were manually searched, but no further papers were identified. This resulted in 10 articles for appraisal and review.

Findings

Of the 10 articles retrieved, two were quantitative studies, two qualitative, and one mixed method.

Five articles did not constitute primary research but have been included given that review's aim was to gather perspectives on an intervention that is still subject to extensive clinical debate amongst a paucity of evidence. These five articles were categorised as practice literature (Aveyard, 2019).

The research papers were appraised via the Mixed Methods Appraisal Tool (MMAT) (Hong et al, 2018). All rated positively in respect of methodological quality and appropriateness, but all had acknowledged limitations, predominantly relative to sampling.

The five practice literature papers were appraised against the 'six questions for critical thinking' (Aveyard et al, 2015) a tool designed to appraise all types of literature focussing on criticality, quality and value. All provided valuable insight, but formal methodology was absent.

Appraisal of all the papers was then summarised in a data extraction table (Table 2) along with the publication details and key findings.

(Insert Table 2 here)

One reviewer analysed the findings and applied codes to key points of each paper before cross comparing and clustering codes into sub-themes and themes (Braun and Clarke, 2021). Three themes were identified and will be discussed in turn.

(Insert Table 3 here)

Discussion

Rationales for Deprescribing

Across the literature reviewed, the premise that indefinite use of antipsychotics should be endorsed without question was universally challenged. Five papers cited flaws in the existing evidence base, with Gupta et al (2018a) asserting that the evidence supporting the long -term benefits of treatment should not be considered robust. Horowitz et al (2021) highlighted the uncertainty across discontinuation studies about the proportion of patients who could potentially stay well without antipsychotics. Moncrieff et al (2020) highlighted that evidence purporting the benefits of long-term treatment which cite discontinuation as a catalyst for relapse, fail to test outcome beyond initial cessation and into the longer term. Gupta et al (2018b) endorsed this view highlighting that discontinuation trials often cease medication abruptly. This could mean that relapse is not distinguishable from withdrawal difficulties (Moncrieff et al, 2020) resulting in unsafe inferences. Le Geyt et al (2017) suggested the dominance of biomedical models of mental ill -health results in a theoretical preference for antipsychotic treatment which in practice implies to patients there is an ongoing need for the medication without question. Cooper et al (2021) argue that the long- term adverse effects of antipsychotic drugs are integral to the desire of many patients to discontinue their medication, and a range of side effects are documented in detail. There is consistent reference to physical health complications and reduced mortality (Gupta et al 2018b; Moncrieff et al, 2020; Cooper et al, 2021). Horowitz et al (2021) described a range of neurological effects and resulting movement disorders, as well as cognitive impacts. All papers identified that these significant impacts inform many individual decisions

to discontinue medication in respect of risk and benefit (Salomon and Hamilton, 2013).

Moncrieff et al (2020) suggested that reducing the symptom burden may not be a sufficient benefit if functional capacity is reduced, and Gupta et al (2018b) concurred, asserting that considering risk and benefit from within a recovery paradigm increases the value placed on quality of life goals over symptom reduction. Across the papers, focus on recovery over remission (Gupta et al, 2018a) creates an opposition between the biomedical and the psychosocial, perhaps in response to the traditional paternal nature of mental health care often associated with pharmacological treatment. The need to empower patients in respect of choice and address traditional power dynamics is championed by Larsson- Barr et al (2018) who assert that patients should have all the information available to make an informed choice about antipsychotic medication. This is endorsed by Le Geyt et al (2017) who highlighted the need to undermine long standing power imbalances in mental health services that result in a culture of coercion. Whilst expressed less strongly elsewhere, there is consensus that given the challenging impact of long -term antipsychotic use, individual choice to discontinue should be supported, and not deemed irrational or lacking in insight (Le Geyt et al, 2017 ; Moncrieff et al, 2020; Cooper et al, 2021) given the extensive and well documented adverse effects.

Risk and Clinical Anxiety

All of the literature reviewed addressed the risks associated with discontinuation of antipsychotic medication, with the issue of relapse being cited as a key barrier to deprescribing in practice (Gupta et al 2018b). The issue of relapse is pivotal as it is a universal concern for clinicians and patients alike, with Moncrieff et al (2020) asserting that societal and economic pressures to avoid relapse short term take priority over the longer-term functional benefits of discontinuation.

Many of the papers highlighted the difference between short and long-term outcomes in respect of relapse with tentative suggestions that whilst relapse rates might increase on discontinuation in the short term, poorer outcome in the long term is not necessarily a given (Cooper et al, 2021). Indeed, Landolt et al (2016) in their analysis of the European First Episode Schizophrenia Trial (EUFEST) data found that after 12 months, those individuals who had stopped taking antipsychotic

medication, did not experience relapse more often than those who remained on maintenance therapy.

This short term and long- term differential was discussed extensively across the papers in respect of the impact of withdrawal, with Horowitz et al (2021) highlighting the difficulty in distinguishing endogenous relapses, from those that might be associated with withdrawal or discontinuation symptoms.

Whilst there is broad acknowledgement that withdrawal/discontinuation syndromes have not been formally characterised or indeed recognised (Salomon and Hamilton, 2013) there are multiple references to symptoms that can occur as antipsychotics are deprescribed. Horowitz et al (2021) refers to the proposed contribution of dopaminergic hypersensitivity, to the development of withdrawal symptoms particularly in relation to 'rebound' psychosis , and several other effects are cited across the papers including heightened emotions and anxiety (Moncrieff et al, 2020), difficulty with sleep (Gupta et al, 2018b) , and a full range of cross domain effects physically, emotionally, cognitively and functionally, as described by research participants surveyed by Larsen-Barr et al (2017).

Whilst there seems to be an acknowledged conflation of the experiences of rebound and relapse at discontinuation, and a clear call for further research, there was also agreement that concern over the negative impact of either is a source of significant clinical reticence when it comes to deprescribing antipsychotics. This is compounded by the fact that there is no official guidance to support the process (Salomon and Hamilton, 2013; Cooper et al, 2021; Horowitz et al, 2021). Gupta et al (2018a) suggested that clinicians lack training and peer support to deprescribe, and consequently Le Geyt et al (2017) asserted that in relation to discontinuation patients encounter risk aversity within health services, creating a barrier to collaborative care and decision making.

Safe Deprescribing in Practice

Actual and perceived risks of deprescribing were consistently referenced across the papers, and strategies for risk mitigation and supportive deprescribing were also well addressed.

A dominant area of discussion was the rate of discontinuation in terms of timescales and dosing increments. Horowitz et al (2021) made the case for prolonged tapering, proposing that this reduces the likelihood and intensity of withdrawal symptoms. This view is endorsed by several other papers which concur that there is some

evidence that gradual reduction reduces the risk of relapse (Gupta et al, 2018a; Moncrieff et al, 2020; Cooper et al, 2021), although Gupta et al (2018b) also cited a recent metanalysis that suggests there is not a clear link. There are though no set timescales or formulas, and Horowitz et al (2021) were clear that the process is subject to huge interindividual variability. Horowitz et al (2021) suggested that the process of a tapered discontinuation could be conceptualised as a method of ascertaining a new minimum effective dose, and Cooper et al (2021) agreed that for some patients this dose optimisation process might be more conceivable than full discontinuation.

The issue of abrupt cessation of antipsychotics was also addressed in relation to the quality of clinical support provided to individuals who want to stop taking medication. Salomon et al (2014) identified that clinical support is associated with a gradual withdrawal regimen whereby individuals who discontinue medication covertly in isolation, are more prone to abrupt cessation, and increased risk (Moncrieff et al, 2020; Horowitz et al, 2021). Larsen-Barr et al (2018) cited a significant association between effective support and successful deprescribing that is maintained in the longer term. Salomon et al (2014) asserted the need for clinicians to be trusted partners in the deprescribing process to play a key part in harm minimisation, and Gupta et al (2018b) suggested that involving clinical and wider support sources such as family, lays a foundation for successful deprescribing. Le Geyt et al (2017) suggested that a shared understanding with treating clinicians serves to undermine the perception that mental health services have a bias towards adherence, and this would support Salomon et al's (2014) view that an increased emphasis on engagement is essential. Salomon and Hamilton (2013) asserted the need for a more person centred and transparent approach to deprescribing, and in the interests of harm minimisation, Moncrieff et al (2020) suggested that helping people to stop medication can be considered a legitimate treatment option.

In addition to a need for intensified support during the process of deprescribing (Cooper et al, 2021), there are other conditions and interventions that contribute to a successful outcome as described in the reviewed literature.

Landolt et al (2016) identified that social circumstances, in particular education, increased the likelihood of successful discontinuation, and acquired knowledge was also deemed an important prerequisite by Le Geyt et al (2017).

Beyond this, there is a call for further research into how established non-pharmacological interventions can support individuals to cope with the impact of discontinuation, and indeed manage any risk of destabilisation with enhanced coping strategies (Gupta et al, 2018a; Moncrieff et al, 2020; Cooper et al, 2021). Le Geyt et al (2017) described the concept of 'safety nets' – nonpharmacological elements that can cushion the challenges of withdrawal such as networks of support, practical resources and talking therapy.

There was a consistent view that successful deprescribing requires a context of support and non-pharmacological intervention to mitigate risk, but Salomon and Hamilton (2013) concluded that for some, the process of deprescribing itself, can be a significant therapeutic step as opposed to a cause of harm; and for some it could be lifesaving.

Limitations of this review

Only a small amount of literature that addressed the specifics of this review was available, and only half constituted primary research. Many of the authors have contributed to multiple papers, indicating that this is a narrow field of interest, but one that demands a wider body of evidence.

Conclusion

When considering recovery orientated practice, the literature was clear that adverse effects of long-term antipsychotic therapy are such that indefinite use should be reviewed collaboratively with individuals in the context of a risk benefit appraisal. Whilst the process of deprescribing is not without risk, there was agreement that mitigation can be achieved by increased support, strong therapeutic alliance, and a gradual tapering of dose over time.

However, despite the clear emphasis in the literature on therapeutic consideration of risk, benefit, and choice; existing guidance for the safe discontinuation of antipsychotic medication is extremely limited. Improved understanding of the impact of withdrawal is particularly essential to guide safe and effective best practice.

Deprescribing antipsychotic medication therefore has therapeutic, educational, and resourcing implications, and requires more extensive research. The challenge for

nurses is to balance support of patient autonomy with risk mitigation to ensure a safe but supportive culture of practice.

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TABLE ONE: SEARCH TERMS AND PARAMETERS

	QUESTION KEY WORDS	SEARCH TERMS	PARAMETER
POPULATION	Adults with a Diagnosed Psychotic Disorder		18+ cohort age limiters applied to exclude literature pertaining to children Literature related to non-psychotic disorders excluded from yield
EXPOSURE	Antipsychotic Medication	Antipsychotic* Neuroleptic*	
BOOLEAN OPERATOR	**AND**		
OUTCOME	Deprescribing	Deprescribing Discont* Withdraw* Reduc*	

TABLE TWO: DATA EXTRACTION TABLE

AUTHOR/DATE/ LOCATION	TITLE	TYPE OF LITERATURE	MAIN FINDINGS	STRENGTHS/LIMITATIONS
Salomon,C, Hamilton, B (2013): Australia	"All Roads Lead to Medication?" Qualitative Responses from an Australian First-Person Survey of Antipsychotic Discontinuation	Primary Qualitative Research	Importance of context and relationships in the consideration of discontinuation. Experiences of withdrawal hugely variable	Small non-randomised sample (98) Convenience sampling– issue with representativeness and potential bias. Non-generalisable results Primary and secondary researcher coding of themes robust and supported by Dedoose software.
Salomon C, Hamilton, B & Elsom, S (2014): Austrailia	Experiencing antipsychotic discontinuation: results from a survey of Australian consumers	Primary Quantitative	Collaboration and effective information sharing regarding withdrawal syndrome and/or treatment duration are essential.	Same data set and sample as previous study – non-probability and unrandomised. Issues with representativeness Range of uncontrolled variables– results in fragile correlation.
Landolt, K et al -.(2016) EUFEST Study Group - cross EU trial	Predictors of discontinuation of antipsychotic medication and subsequent outcomes in the European First Episode Schizophrenia Trial (EUFEST)	Secondary Quantitative Analysis of RCT Data	Successful discontinuation differed with the outcome definition used . Correlation between discontinuation and better quality of life. Further studies are needed	Data from a large RCT was used but sample for secondary analysis was non-randomised. Patients who discontinued medication were extracted as a cohort and compared with the rest of the initial RCT sample. Researcher acknowledges potential bias resulting. Analysis robust. Cox regression highlighted statistically significant characteristics/predictors relative to discontinuation – however 12 mth trial duration limiting in terms of long-term outcome.
Le Geyt,G, Awenat,Y Tai,S Haddock,G (2017) UK	Personal Accounts of Discontinuing Neuroleptic	Primary Qualitative Research	There is a need to develop resources for	Rigorous attempts to be reflexive and minimise influence of researcher

	Medication for Psychosis		staff to facilitate service user choice.	perspectives – acknowledgement that this cannot be fully avoided. Small sample – but emphasis on narrative content not generalisable significance. No consistent timeframes for discontinuation amongst participants.
Larsen-Barr,M, Seymour,F, Read, J, Gibson K (2018) New Zealand	Attempting to stop antipsychotic medication: success, supports and efforts to cope	Primary Mixed Methods Research	A wide range of coping strategies can be used to support the process. Supported withdrawal may be more successful and less prone to relapse. There is a need for more research.	Significant sample size of 105 compared to other studies, but still small. Content analysis of short answer responses was robust with 96.7% agreement rate. Variation and limitations associated with categories of coping strategies problematic as 'no strategies' and 'no strategies described' were grouped together. Potential false negatives acknowledged.
Gupta,S, Cahill, JD, Miller,R (2018) USA	Deprescribing antipsychotics: a guide for clinicians	Practice Literature	Alludes to the evolution of deprescribing in psychiatry and the need to focus on quality of life not just symptom management.	Detailed reference to range of evidence in relation to risk, benefit and ethics of prescribing and deprescribing. No formal methodology.
Gupta,S, Steingard,S, Aracena, EFG, Fathy, H (2018) USA	Deprescribing Antipsychotic Medications in Psychotic Disorders: How and Why?	Practice Literature	Cites that studies that report high risk of relapse as linked to discontinuation are flawed due to non-individualised approaches to withdrawal. Effort is needed to address consideration of discontinuation due	No formal methodology, but includes brief meta-analysis of studies examining relapse rates post antipsychotic discontinuation. Also includes brief summary of evidence re non-pharmacological interventions, and withdrawal symptoms.

			to long term questions about efficacy and side-effects.	
Moncrieff; Gupta,S; and Horowitz, MA (2020). UK	Barriers to stopping neuroleptic (antipsychotic) treatment in people with schizophrenia, psychosis or bipolar disorder	Practice Literature	Patients should have the right to make their own decisions about neuroleptic medication in most scenarios. The risk of relapse may be mitigated by supported gradual reductions.	Draws on wide ranging evidence, but has no formal methodology
Horowitz,M; Jauhar,S; Sridihar, N; Murray, RM; and Taylor,D (2021) UK	A Method for Tapering Antipsychotic Treatment That May Minimise the Risk of Relapse	Practice Literature	Establishment of formal guidelines for tapering antipsychotics is required. Argument is made for slower tapering to avoid withdrawal. Hypothesis for tapering presented should be tested in further trials.	No formal methodology documented, but clear evidence of scrutiny and consideration of a range of neuropharmacological data to make a strong case for slow tapering of antipsychotic dosing in order to mitigate relapse.
Cooper, RE; Mason, JP; Calton,T; Richardson,J; and Moncrieff (2021) UK	Opinion Piece: The case for establishing a minimal medication alternative for psychosis and schizophrenia	Practice Literature	Further research is needed to establish the effectiveness of alternative treatments/ psychosocial interventions to cater for those who wish to avoid antipsychotics long term.	No formal methodology Draws on existing and evidenced examples of practice in other countries that is rooted in a minimal medication ideology.

TABLE THREE: IDENTIFIED THEMES

MAIN THEME	SUB-THEMES
Rationales for Deprescribing	- Unwanted side effects - Uncertainty over maintenance therapy - Recovery v Remission - Choice v Paternalism
Risk and Clinical Anxiety	- Lack of clear guidance - Withdrawal Syndrome - Relapse - Clinical Reticence
Safe Deprescribing in Practice	- Tapering - Collaboration and Therapeutic alliance - Effective intervention - Individual pre-requisites