Pharmacological management and treatment of First Episode Psychosis

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A little bit about me

- Brighton Pharmacy Graduate
- Worked across multiple clinical settings
- Worked in Dublin for 2 years
- Calling for Early Intervention in Psychosis
- First qualified Mental Health Pharmacist Advanced Clinical Practitioner
- Special interest in co-morbid CUD and FEP
- Advocate for improving access to clozapine in FEP
- Language is very important to me

Overview

1. Recommendations and current evidence on the pharmacological management and treatment psychosis
2. Working in partnership with service users to identify the appropriate medication for them and ensuring the side effects are understood
3. Optimising treatment outcomes
4. Novel medications and treatments

NICE Guidelines

Two important guidelines

1. Psychosis and schizophrenia in adults: prevention and management (CG178)

Published February 2014 and Updated in March 2014

2. Psychosis and schizophrenia in children and young people: recognition and management (CG155)

Published January 2013 and Updated in October 2016

NICE Guidelines

June 2020:

Prescribing guidelines for patients with a first episode psychosis

By Dr L. Ewins (consultant psychiatrist EIP)

At Avon and Wiltshire Partnership Mental Health Trust

Key questions:

When should antipsychotics be started?

Which one? How long for?

Is there an order in which to prescribe?

NICE FEP continued

1. Assessment may/ should include medication free period
2. a) When appropriate, low dose 2nd generation antipsychotic

   b) Always include client in choice of medication
3. Move away from olanzapine, cardiometabolic risk highest

Each Trust different 1st choice

Aripiprazole most common amongst 1st line

All are as effective apart from clozapine

Unanswered questions

What is low dose:*
Aripiprazole 10mg OD effective
Lurasidone 37mg OD effective
Risperidone 2mg OD effective
Olanzapine 5mg OD effective
How long for before switching?
Consensus is 6 weeks, but is this realistic on the shop floor?

*Maudsley Prescribing Guidelines

Unanswered questions

How long to be on treatment?

Consensus 1-2 years

"… individuals receiving antipsychotic medications for ⩾5 years had less than half the cumulative incidence of hospitalization at all times between one and four years after treatment cessation. In all groups, hospitalization rate was most rapid in the first six months after treatment cessation."

Psychiatric hospitalization following antipsychotic medication cessation in first episode psychosis

Joseph F Hayes, David PJ Osborn, [...], and Christina Dalman +1 View all authors and affiliations

Volume 33, Issue 4 | https://doi.org/10.1177/0269881119827883

Unanswered questions

Effect of discontinuation *v.* maintenance of antipsychotic medication on relapse rates in patients with remitted/stable first-episode psychosis: a meta-analysis

Published online by Cambridge University Press: **18 June 2018**

Taro Kishi, Toshikazu Ikuta, Yuki Matsui, Ken Inada, Yuki Matsuda, Kazuo Mishima and Nakao Iwata

Show author details

How long to be on treatment?

"…maintenance of antipsychotic treatment is beneficial for preventing relapse for 18–24 months in remitted/stable FEP patients…

…discontinuation of antipsychotics was associated with a significant risk of relapse in a period as short as 2 months…

…?difference between abrupt and tapered discontinuation in the impact on the primary outcome (the relapse rate at 12 months) and found no significant difference…

…45.7% of the patients whose antipsychotics were discontinued for 12 months (39.4% after 18–24 months) did not experience a relapse…"

Unanswered questions

Real-world effectiveness of antipsychotic doses for relapse prevention in patients with first-episode schizophrenia in Finland: a nationwide, register-based cohort study

Heidi Taipale, PhD • Antti Tanskanen, PhD • Prof Christoph U Correll, PhD • Prof Jari Tiihonen, PhD

Published: February 16, 2022 • DOI: https://doi.org/10.1016/S2215-0366(22)00015-3 •

How long to be on treatment?

"Standard dose was associated with the best outcome until the second relapse, but after that, all doses had markedly lower effectiveness for relapse prevention.

The first relapse should be considered as the first marker of a more severe and potentially chronic course of schizophrenia needing enhanced interventions to prevent subsequent relapses.

All patients after their first relapse should receive a sufficient antipsychotic dose and enhanced efforts to prevent relapses, including psychoeducation and long-acting antipsychotic injections."

Unanswered questions

What order?

2 antipsychotics.

Then, clozapine.

Early access to clozapine in Early Intervention in Psychosis: Hope vs reality. A mixed method service analysis

Nikola Nikolić [1,2], Katherine Hill [1,3], Emogen Campbell [4], Vijitha Wickramasinghe [5], Richard Whale [1,3]

Affiliations + expand

PMID: 32281741 DOI: 10.1111/eip.12962

Why is clozapine so underused?

The best way to answer (the unanswered questions)

In true **EIP ethos** and alignment to our **values**

Embrace the uncertainty

Be curious

Be humble

Empower by choice

Focus on the strengths

Positive risk taking

Holistic means not just you, and not just medication

Partnership. Triangle of care. Recovery Model.

My clinic:

We are working together, all of us.

I happen to try to oversee it all.

I am not shy to talk about it.

I try my best to not be risk-averse.

I badger about physical health. A lot.

We are learning and getting to know each other.

Recovery: not characterised by **my definition** of **your clinical outcomes**. Its about your goals, your strengths, your hopes.

Are you accountable? Who is?

Physical health assessments: are we performing well enough for our clients?

Its not just about the cardiometabolic syndrome!

As a service we have identified issues with testosterone, thyroid function, but even cancers (cervical and colon).

"Our findings indicate that there are robust alterations in non-CNS systems in psychosis, and that these are broadly similar in magnitude to a range of CNS alterations."

Mol Psychiatry. 2019; 24(6): 776–794.
Published online 2018 May 9. doi: 10.1038/s41380-018-0058-9
PMCID: PMC6124651
EMSID: EMS76319
PMID: 29743584

Is psychosis a multisystem disorder? A meta-review of central nervous system, immune, cardiometabolic, and endocrine alterations in first-episode psychosis and perspective on potential models

Toby Pillinger,[1] Enrico D'Ambrosio,[1] Robert McCutcheon,[1] and Oliver D. Howes[1,2,3]

Thank you Steve!

A handy chart to help you compare the medicines to help the symptoms of a first episode of psychosis (page 2 of 2)

Medicine	Available as	Usual dose for a first episode	Some of the main side effects *								
			Feeling sleepy	Stiff muscles	Feeling restless	Weight gain	Dry mouth	Sexual problems	Hormone upset	Low bp	Risk of diabetes
Dopamine partial agonists (regulate dopamine receptors)											
Aripiprazole	Tablets, liquid, melt-in-the-mouth tablets	5-10mg a day a day	●	●	●●●	○	○	○	○	○	○
	Abilify Maintena LAI (Long-Acting Injection or 'Depot')	300(-400)mg once a month									
Cariprazine	Tablets	1.5-6mg a day	●	●●	●●	●	○	○	○	○	○
Serotonin-dopamine receptor blockers											
Risperidone	Tablets, liquid, melt-in-the-mouth tablets	1-2mg a day	●	●●	●●	●●	●	●●	●●	●	●
	LAI (Risperdal Consta®)	25-50mg every 2 weeks									
	LAI (Okedi®)	75-100mg every 4 weeks									
Paliperidone	Tablets (Invega®)	6mg a day	●	●●	●●	●●	●	●●	●●	●	●
	LAI (Xeplion®)	50-150mg once a month									
	LAI (Trevicta®)	175-525mg every 3 months									
	LAI (Byannli®)	700-1000mg every 6 months									
Olanzapine	Tablets, melt-in-the-mouth tablets	5-10mg a day	●●●	●	●●	●●●	●	●	●	●	●●
	LAI (Zypadhera®)	150-405mg every 2-4 weeks									
Quetiapine	Tablets (liquid)	Up to 300-400mg a day	●●●	●	●	●●	●	●	○	●●	●
Lurasidone	Tablets	37-148mg a day	●	●	○	○	○	○	○	○	○
Dopamine-serotonin receptor blockers											
Zuclopenthixol	Tablets	10-25mg a day	●●	●●	●●	●●●	●●	●●●	●●	●	○
	LAI (Clopixol®)	200-500mg every 2 weeks									
Dopamine receptor blockers											
Haloperidol	LAI (Haldol Decanoate®)	25-200mg every 4 weeks	●	●●●	●●●	●●	●	●●●	●●●	●	○
	Tablets, liquid	2.5-10mg a day									
Amisulpride	Tablets, liquid	200-400mg a day	●	●●	●●	●	●	●●●	●●	○	○
Sulpiride	Tablets, liquid	400-1600mg a day	●	●●	●●	●●	●	●●●	●●	○	○

V08.07 [EE/SRB 05-2022] ©2022 Mistura™ Enterprise Ltd (www.choiceandmedication.org). Choice and Medication™ indemnity applies only to licensed subscribing organisations or individuals. *This Handy Chart is to help you know about your medicine options and help you to make any choices. A healthcare professional should help you with this and explain what it all means. We can't include everything that could be important to you on one sheet.*

https://www.choiceandmedication.org/sussex/

Although the information here may help you choose a medication, please remember that local (e.g. your GP practices) and national (e.g. NICE) guidance and rules may also affect the final decision.

* See first page for more information about these side effects.

Steve again, but, I helped.

Handy fact sheet (highlights)
Taking an antipsychotic for the first time for psychosis

The problem:	Why it is important:	How to help yourself:
• You may be worried about taking an antipsychotic for the first time	• Psychosis can be really scary • Antipsychotics can help reduce the symptoms and help keep you well • But taking them for too long might not be best for you	• Find out about antipsychotics • Remember they do help with the symptoms and are not addictive • Make decisions that give you the best chance of getting on with your life

People stop their medication!

50% of people with chronic illness do not take their medication as prescribed. (WHO **2003**)

How is FEP any different?

The norm should be: Most clients discontinue their first antipsychotic medication (for a variety of reasons) in the first year of treatment

Long-acting antipsychotic (LAI) preparations may have a role in enhancing effectiveness.

Common adverse effects associated with discontinuing specific medications should be a focus of discussion.

BJPsych Open. 2016 Sep; 2(5): 323–329.
PMCID: PMC5056529
Published online 2016 Oct 10. doi: 10.1192/bjpo.bp.116.002766
PMID: 27733935

Effectiveness of antipsychotics used in first-episode psychosis: a naturalistic cohort study

Richard Whale, Michael Harris, Gail Kavanagh, Vijitha Wickramasinghe, Christopher I. Jones, Steven Marwaha, Ketan Jethwa, Nirmalan Ayadurai, and Andrew Thompson

What variety of reasons?

Aripiprazole, poor efficacy and **agitation/restlessness**, then **extrapyramidal side-effects.**

Olanzapine, **weight gain** and poor adherence, **sedation** and then poor efficacy.

Quetiapine, **sedation**, poor efficacy and then **weight gain.**

Risperidone, poor efficacy, **raised prolactin**, **sedation** and then **weight gain**. (Whale et al 2016)

What about cannabis, the most commonly used illicit drug in FEP?

Up to 50% reporting use cannabis at the onset of FEP.

Lancet. 2015 Feb 26;385 Suppl 1:S79. doi: 10.1016/S0140-6736(15)60394-4.

Cannabis use and treatment resistance in first episode psychosis: a natural language processing study

Rashmi Patel [1], Robin Wilson [2], Richard Jackson [3], Michael Ball [3], Hitesh Shetty [4], Matthew Broadbent [4], Robert Stewart [3], Philip McGuire [2], Sagnik Bhattacharyya [2]

Affiliations + expand

PMID: 26312901 DOI: 10.1016/S0140-6736(15)60394-4

Up to 35% of people continue to use cannabis after the onset of FEP.

Review Lancet Psychiatry. 2016 Mar;3(3):215-25. doi: 10.1016/S2215-0366(15)00363-6. Epub 2016 Jan 15.

Continued versus discontinued cannabis use in patients with psychosis: a systematic review and meta-analysis

Tabea Schoeler [1], Anna Monk [1], Musa B Sami [1], Ewa Klamerus [1], Enrico Foglia [1], Ruth Brown [1], Giulia Camuri [1], A Carlo Altamura [2], Robin Murray [1], Sagnik Bhattacharyya [3]

Affiliations + expand

PMID: 26777297 DOI: 10.1016/S2215-0366(15)00363-6

Optimising treatment outcomes

LAIs were associated with about a 50%–65% lower risk of rehospitalization than oral formulations of the same compounds. Clozapine and olanzapine were associated with the lowest all-cause discontinuation and rehospitalization rates.

Clinical Trial > Am J Psychiatry. 2011 Jun;168(6):603-9. doi: 10.1176/appi.ajp.2011.10081224. Epub 2011 Mar 1.

A nationwide cohort study of oral and depot antipsychotics after first hospitalization for schizophrenia

Jari Tiihonen [1], Jari Haukka, Mark Taylor, Peter M Haddad, Maxine X Patel, Pasi Korhonen

Affiliations + expand

PMID: 21362741 DOI: 10.1176/appi.ajp.2011.10081224

The use of an LAI in this population produced a significant 44% reduction in the incidence rate of first hospitalization.

> JAMA Psychiatry. 2020 Dec 1;77(12):1217-1224. doi: 10.1001/jamapsychiatry.2020.2076.

Effect of Long-Acting Injectable Antipsychotics vs Usual Care on Time to First Hospitalization in Early-Phase Schizophrenia: A Randomized Clinical Trial

John M Kane [1 2 3], Nina R Schooler [4], Patricia Marcy [5], Christoph U Correll [1 2 3 6], Eric D Achtyes [7 8], Robert D Gibbons [9], Delbert G Robinson [1 2 3]

Optimising treatment outcomes

Hyperbolic tapering:

Aripiprazole dose (mg)	D2 occupancy (%)
30	86.2
20	85.8
15	85.5
10	84.8
5	82.8
2.5	79
1.25	72.4
0	0

> JAMA Psychiatry. 2021 Feb 1;78(2):125-126. doi: 10.1001/jamapsychiatry.2020.2166.

Tapering Antipsychotic Treatment

Mark Abie Horowitz [1, 2], Robin M Murray [3], David Taylor [3, 4]

Affiliations + expand

PMID: 32777027 DOI: 10.1001/jamapsychiatry.2020.2166

Review > J Clin Psychopharmacol. 2013 Oct;33(5):675-81. doi: 10.1097/JCP.0b013e3182983ffa.

Estimating dopamine D_2 receptor occupancy for doses of 8 antipsychotics: a meta-analysis

Irene M Lako [1], Edwin R van den Heuvel, Henrikus Knegtering, Richard Bruggeman, Katja Taxis

Affiliations + expand

PMID: 23948784 DOI: 10.1097/JCP.0b013e3182983ffa

Commonly used doses of aripiprazole and their D2 occupancy. Based on an Emax equation derived from data in Lako et al(2013)

Optimising treatment outcomes

The algorithm recommends only a fraction (no more than 25%) of the dosage to be reduced at a time, with at least a 6-month stabilization period required before reducing another 25% of the dose.

How does this fit with half lives, and steady states? Or the D2 occupancy?

Aripiprazole PO:

t1/2 = 75-146 hours, time to steady state = 14 days

Achieving the Lowest Effective Antipsychotic Dose for Patients with Remitted Psychosis: A Proposed Guided Dose-Reduction Algorithm

Chen-Chung Liu & Hiroyoshi Takeuchi

CNS Drugs **34**, 117–126 (2020) | Cite this article

394 Accesses | **6** Citations | **1** Altmetric | Metrics

Novel medications and treatments

Cariprazine? 2017 is not novel!

Indicated for schizophrenia. Min dose 1.5mg OD. Max 6mg OD.

Long half life, and >3 weeks to steady state.

Partial agonist activity at dopamine $D_{3,}$ D_2 and serotonin 5-HT_{1A} receptors

Antagonist activity at serotonin 5-HT_{2B}, 5-HT_{2A} and histamine H_1 receptors

Low affinity for serotonin 5-HT_{2C} and adrenergic α1 receptors

No appreciable affinity for cholinergic muscarinic receptors

In other words: no sedation, no weight gain, some akathisia, no hypotension

Cariprazine v risperidone

Total of 461 people randomised to either treatment.

Mean daily doses were 4·2 mg (SD 0·6) for cariprazine and 3·8 mg (0·4) for risperidone.

After 26 weeks, greater changes in blunted affect, emotional withdrawal, poor rapport, passive/apathetic social withdrawal, lack of spontaneity/flow of conversation, motor retardation, and active social avoidance, in **favour of cariprazine.**

ARTICLES | VOLUME 389, ISSUE 10074, P1103-1113, MARCH 18, 2017

Purchase

Cariprazine versus risperidone monotherapy for treatment of predominant negative symptoms in patients with schizophrenia: a randomised, double-blind, controlled trial

Dr György Németh, MD • István Laszlovszky, PharmD • Pál Czobor, PhD • Erzsébet Szalai, MD • Balázs Szatmári, MD • Judit Harsányi, MD • et al. Show all authors

Published: February 06, 2017 • DOI: https://doi.org/10.1016/S0140-6736(17)30060-0 • Check for updates

Open Dialogue (Rutledge 2021)

Developed during the 1980s in Finland’s Western Lapland region.

An integrated approach involving systemic family therapy and incorporating some psychodynamic principles.

Bringing together both social and professional networks to provide continuity of psychological care across the boundaries of (traditional) services.

Aims to promote respect for the decisions, values and priorities of the person involved.

Self-exploration, self-explanation and self-determination.

Open Dialogue: Development and Evaluation of a Social Network Intervention for Severe Mental Illness (ODDESSI)

Open Dialogue

29% of people were using medication (in this 5 year period), benzodiazepines and/ or antipsychotics.

“The aim was to find ways to integrate the medication as a part of a psychosocial treatment as any other treatment methods that are used according to a specified need.”

Five-year experience of first-episode nonaffective psychosis in open-dialogue approach: Treatment principles, follow-up outcomes, and two case studies

Jaakko Seikkula, Jukka Aaltonen, Birgittu Alakare, Kauko Haarakangas, Jyrki Keränen & Klaus Lehtinen

Pages 214-228 | Received 18 Jan 2004, Published online: 22 Feb 2007

Download citation https://doi.org/10.1080/10503300500268490

Summary

1. Recommendations and current evidence on the pharmacological management and treatment psychosis
2. Working in partnership with service users to identify the appropriate medication for them and ensuring the side effects are understood
3. Optimising treatment outcomes
4. Novel medications and treatments

Thank you for listening.