



Critical Thinking & Prescribing

NAPICU 18th Annual Conference
September 2013

Caroline Parker
Consultant Pharmacist

● ● ● | Reducing Violence with Medicines

- Medium - Long Term Risk of Violence
 - Poor evidence
 - “High” doses aren’t recommended
 - Non-adherence is a predictor for aggression
 - Clopixol® - related to adherence
 - **Clozapine** – best evidence
 - Effect is independent of antipsychotic effect

Evidence-based guidelines for the pharmacological treatment of schizophrenia: recommendations from the British Association for Psychopharmacology. Barnes T and the Consensus Group. *J Psychopharm.* 2011. DOI: 10.1177/0269881110391123.

Frogley C, et al.. A systematic review of the evidence of clozapine’s anti-aggressive effects. *Int J Neuropsychopharm* 2012; 15: 1351–1371.

Comparative efficacy and tolerability of 15 antipsychotic drugs in schizophrenia: a multiple-treatments meta-analysis

Stefan Leucht, Andrea Cipriani, Loukia Spineli, Dimitris Mavridis, Deniz Örey, Franziska Richter, Myrto Samara, Corrado Barbui, Rolf R Engel, John R Geddes, Werner Kissling, Marko Paul Stapf, Bettina Lässig, Georgia Salanti, John M Davis

www.thelancet.com Published online June 27, 2013 [http://dx.doi.org/10.1016/S0140-6736\(13\)60733-3](http://dx.doi.org/10.1016/S0140-6736(13)60733-3)

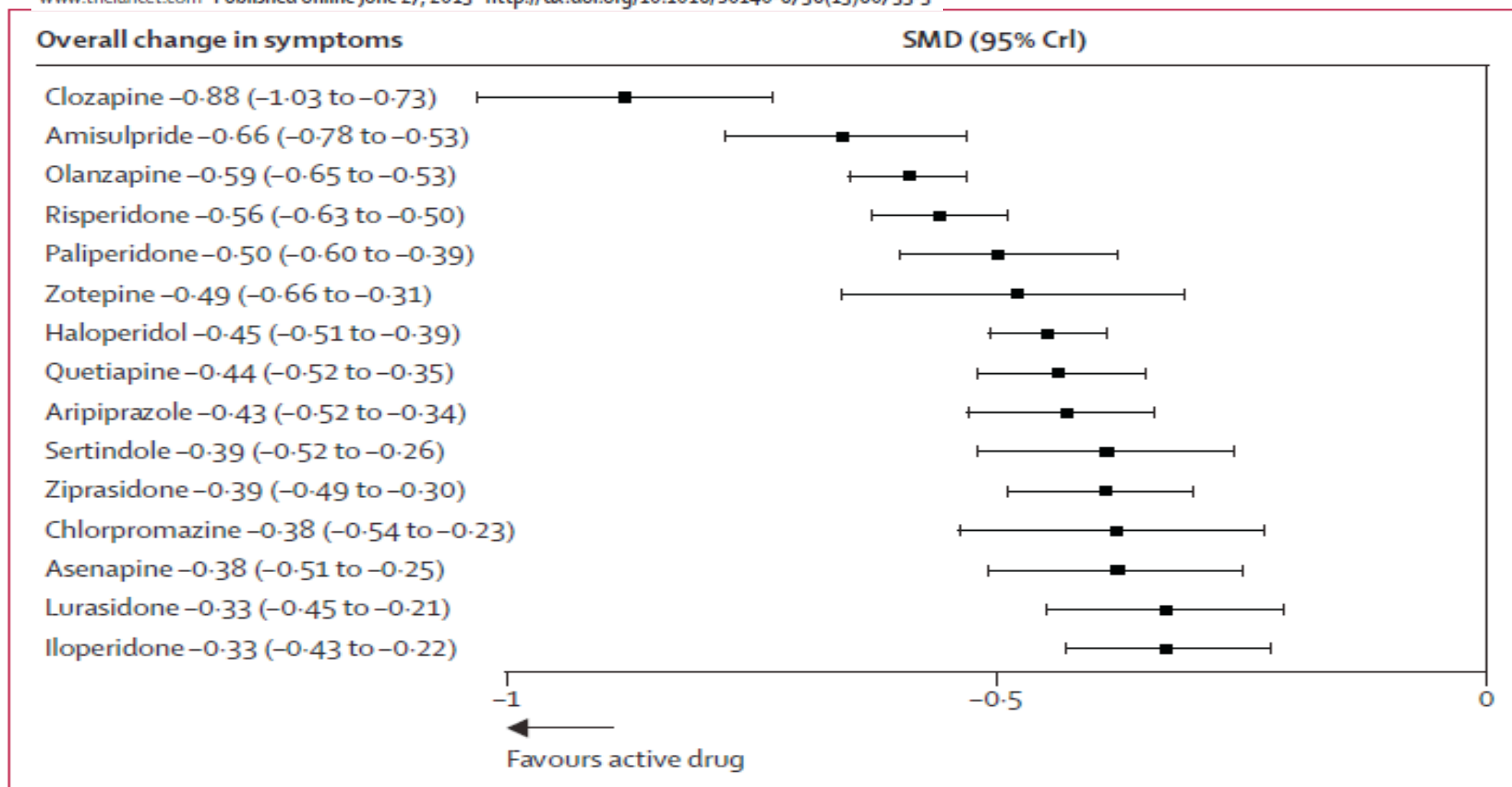


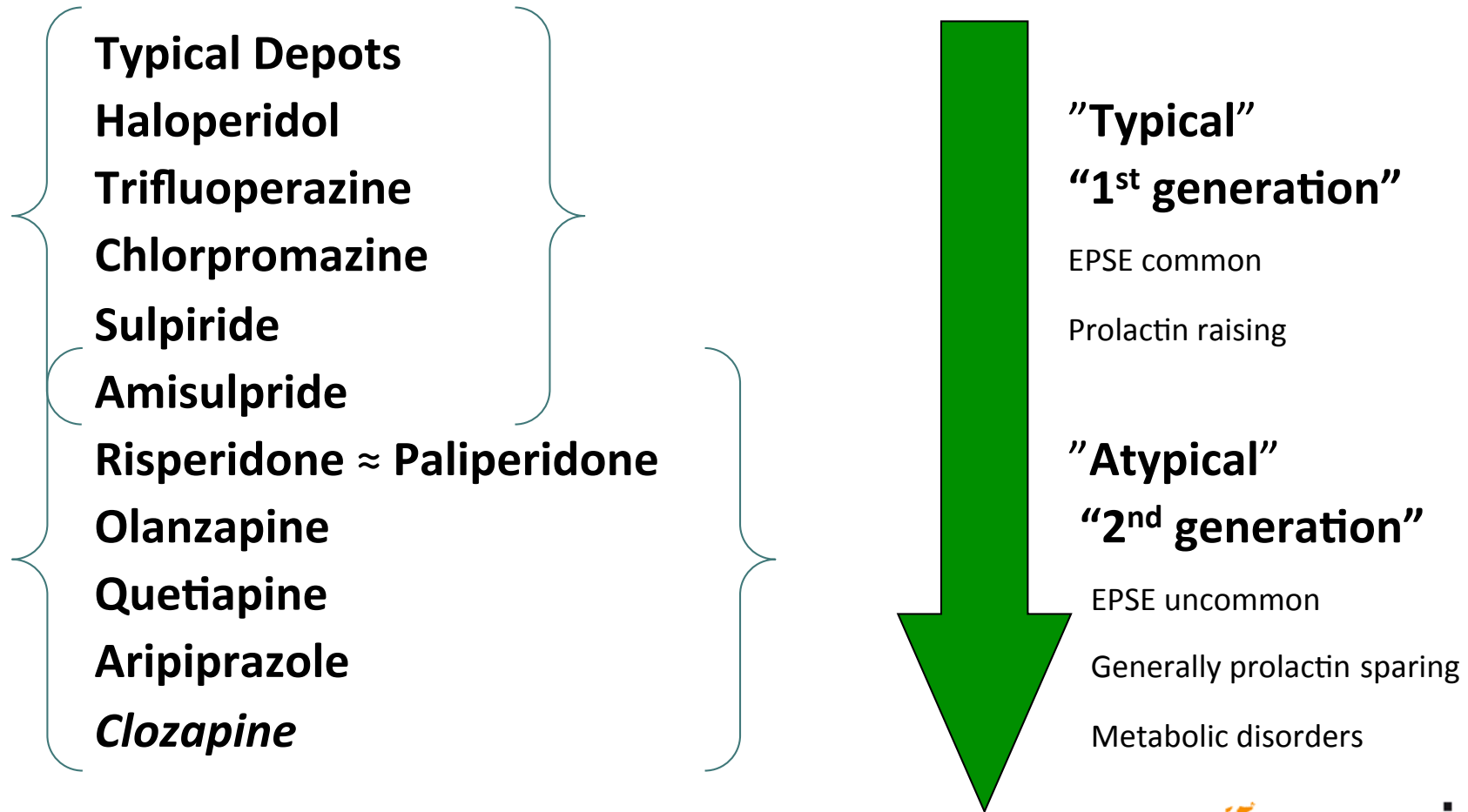
Figure 3: Forest plot for efficacy of antipsychotics drugs compared with placebo

Treatments are ranked according to their surface under the cumulative ranking (SUCRA) values (appendix p 98).

SMD=standardised mean difference. CrI=credible interval.



Relative Typical and Atypical Classifications of Antipsychotics





“Depots”

- Definition: Long-acting injection,
–usually IM, not an implant

Doesn't necessarily mean (1st gen) antipsychotics

- Depo-Provera[®] (contraceptive)
- Depo-Medrone[®] (methylprednisolone = steroid)
- No single depot appears superior
- Improves adherence cf. Orals??
 - Real life vs trials?



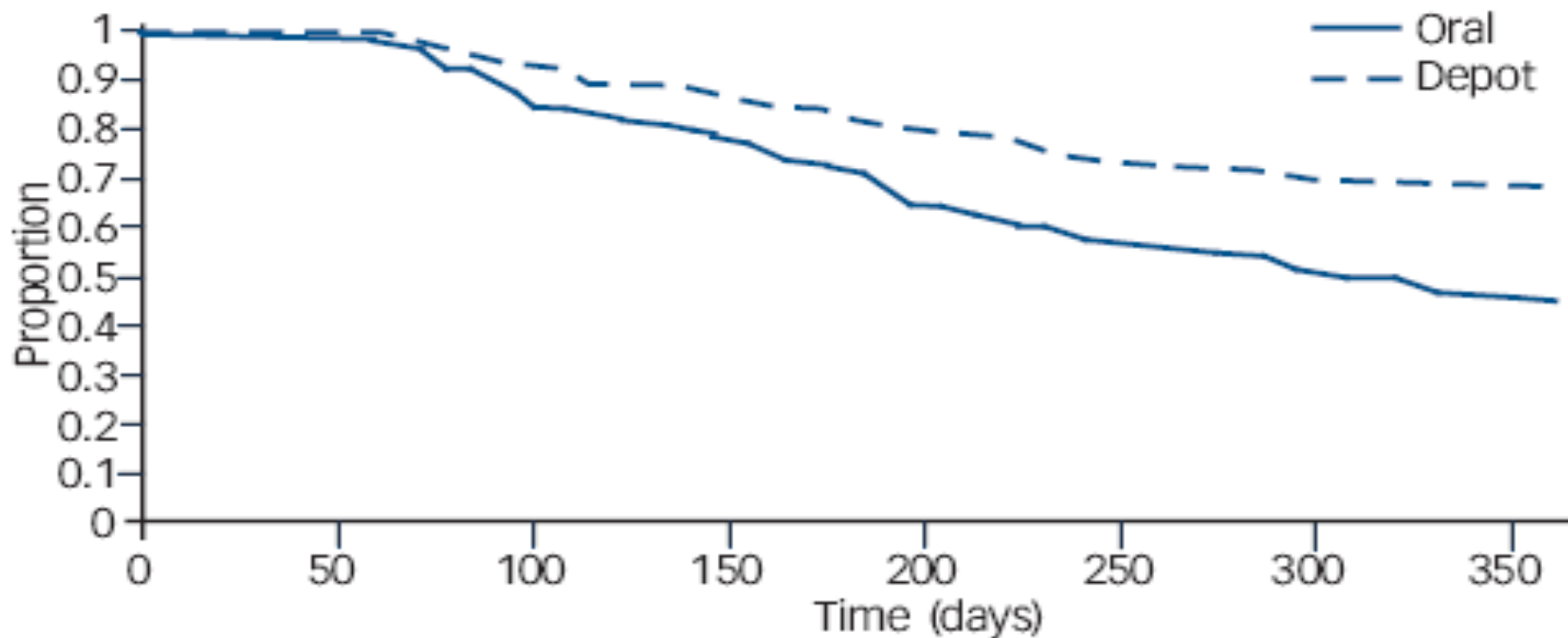


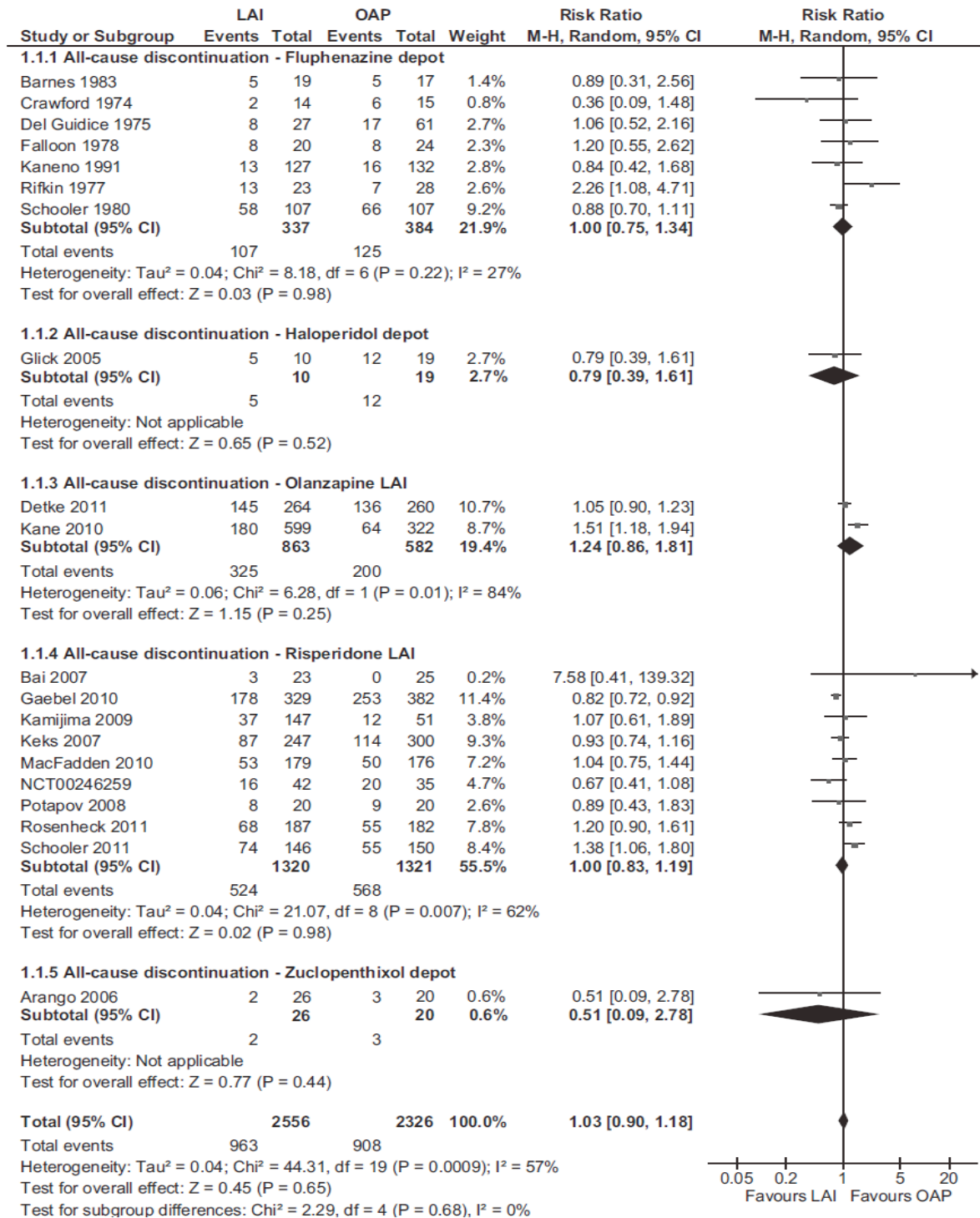
Fig. 3 Survival analysis of time to discontinuation for any reason of first-generation antipsychotics (injected or oral) in the first year after medication initiation. From Zhu *et al.*²⁰ Reprinted with permission from Psychiatric Services (© 2008). American Psychiatric Association.



Long-Acting Injectable vs Oral Antipsychotics for Relapse Prevention Schizophrenia: A Meta-Analysis of Randomized Trials

Taishiro Kishimoto^{1,2}, Alfred Robenzadeh¹, Claudia Leucht³, Stefan Leucht³, Koichiro Watanabe^{2,4}, Michael Borenstein⁵, John M. Kane^{1,6,7,8}, and Christoph U. Correll^{*,1,6,7,8}

Fig. 2. All-cause discontinuation (safety/efficacy population).





Efficacy and Effectiveness of Depot Versus Oral Antipsychotics in Schizophrenia: Synthesizing Results Across Different Research Designs

Noam Y. Kirson, PhD; Peter J. Weiden, MD; Sander Yermakov, MS; Wayne Huang, MPP; Thomas Samuelson, BA; Steve J. Offord, PhD; Paul E. Greenberg, MS, MA; and Bruce J. O. Wong, MD

DISCUSSION

The effectiveness of long-acting therapies has been debated, in part, because of the inconsistent findings in the clinical literature. However, it appears that study design is an important factor possibly affecting estimates of comparative effectiveness of antipsychotic medications. We find that in a meta-analysis of RCTs, the benefits of depot antipsychotics were not significantly superior to those of oral formulations. In contrast, as study design shifts toward prospective and retrospective observational studies, depot formulations display significant advantage.

Effect of prior treatment with antipsychotic long-acting injection on randomised clinical trial treatment outcomes

Thomas R. E. Barnes, Richard J. Drake, Graham Dunn, Karen P. Hayhurst, Peter B. Jones and Shôn W. Lewis

BJPsych

The British Journal of Psychiatry (2013)
203, 215–220. doi: 10.1192/bjp.bp.113.125807

Method

Analysis of data from two pragmatic 1-year clinical trials in which patients with schizophrenia were randomised to either an oral first-generation antipsychotic (FGA), or a non-clozapine second-generation antipsychotic (SGA, CUTLASS 1 study), or a non-clozapine SGA or clozapine (CUTLASS 2 study).

Results

Across both trials, 43% ($n=155$) of participants were prescribed an FGA-LAI before randomisation. At 1-year follow-up they showed less improvement in quality of life, symptoms and global functioning than those randomised from oral medication. This difference was confined to patients rated as less than consistently adherent pre-randomisation. The relatively poor improvement in

Conclusions

A switch at randomisation from an LAI to an oral antipsychotic was associated with poorer clinical and functional outcomes at 1-year follow-up compared with switching from one oral antipsychotic to another. This effect appears to be moderated by adherence, and may not extend to switching to clozapine. This has implications for clinical

Trade Name	Generic Name	Formulation	Administration (IM)	Since
Clopixol®	Zuclopentixol decanoate	Oily	Gluteal, every 1-4 weeks	1978
Depixol®	Flupentixol decanoate	Oily	Gluteal, every 1-4 weeks	1972
Haldol®	Haloperidol decanoate	Oily	Gluteal, every 4 weeks	1982
Modecate®	Fluphenazine decanoate	Oily	Gluteal, every 2-5 weeks	1968
Piportil®	Pipothiazine palmitate	Oily	Gluteal, every 4 weeks	1983
Risperdal Consta®	Risperidone	Powder for reconstitution with aqueous fluid	Gluteal or Deltoid every 2 weeks (Must be refrigerated)	2002
ZypAdhera®	Olanzapine pamoate	Powder for reconstitution with aqueous fluid	Gluteal, every 2 or 4 weeks	2010
Xeplion®	Paliperidone palmitate	Prefilled syringe of prolonged release suspension	Gluteal or Deltoid every month. (No refrigeration)	2011

Review article

Psychopharmacology and adverse effects
of antipsychotic long-acting injections: a review

David Taylor

Table 1 Pharmacokinetic and pharmacodynamic characteristics of antipsychotic long-acting injections

	Time to peak, days	Plasma half-life, days	Time to steady state, months	Test dose, mg	Typical clinical dose per 2 weeks, mg	Licensed dosing intervals (UK), weeks	Comments
First-generation antipsychotics							
Flupentixol decanoate	3–7	~17	2	20	60	2–4	Available as low-volume injection
Fluphenazine decanoate	1	7–14	2	12.5	50	2–5	Available as concentrate
Haloperidol decanoate	7	~21	2–3	Not stated	100	2–4	
Perphenazine decanoate	1–7	~14	3	Not stated	150	2–4	Not used in UK or USA
Pipotiazine palmitate	7–14	~14	2	25	50	4	
Zuclopentixol decanoate	7	~14	2	100	300	1–4	Available as concentrate
Second-generation antipsychotics							
Olanzapine pamoate	2–4	14–28	2–3	Not recommended	300	2 or 4	Limited clinical experience as recently introduced
Risperidone microspheres	28	4–6	2	Not appropriate	37.5	2	Drug release delayed for 2–3 weeks



Paliperidone palmitate Xeplion®



- Paliperidone is the active metabolite of risperidone
- It has not demonstrated greater efficacy over other antipsychotics
- Risperdal® Consta has been shown to offer no advantage over typical antipsychotic depots
- TWO initial loading doses into *DELTOID muscle*
- Maintenance doses:
 - *Deltoid or gluteal muscle*
 - *(Calendar) Monthly*

Shajahan P, Spence E, Taylor M, Daniel D, Pelosi A. Comparison of the effectiveness of depot antipsychotics on routine clinical practice. *The Psychiatrist* 2010; 3: 273-279



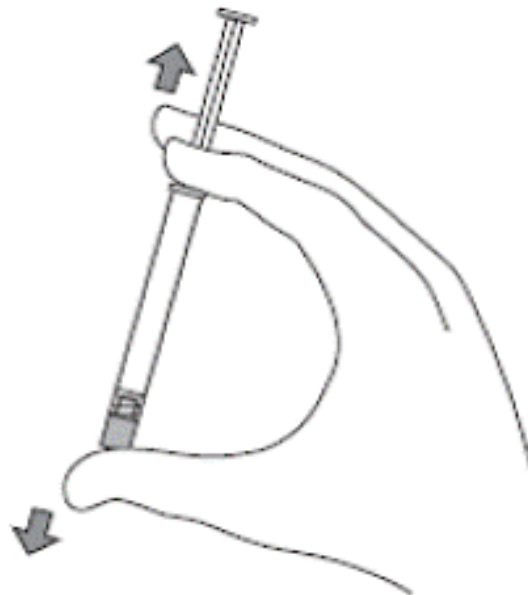
Administration

Aqueous suspension

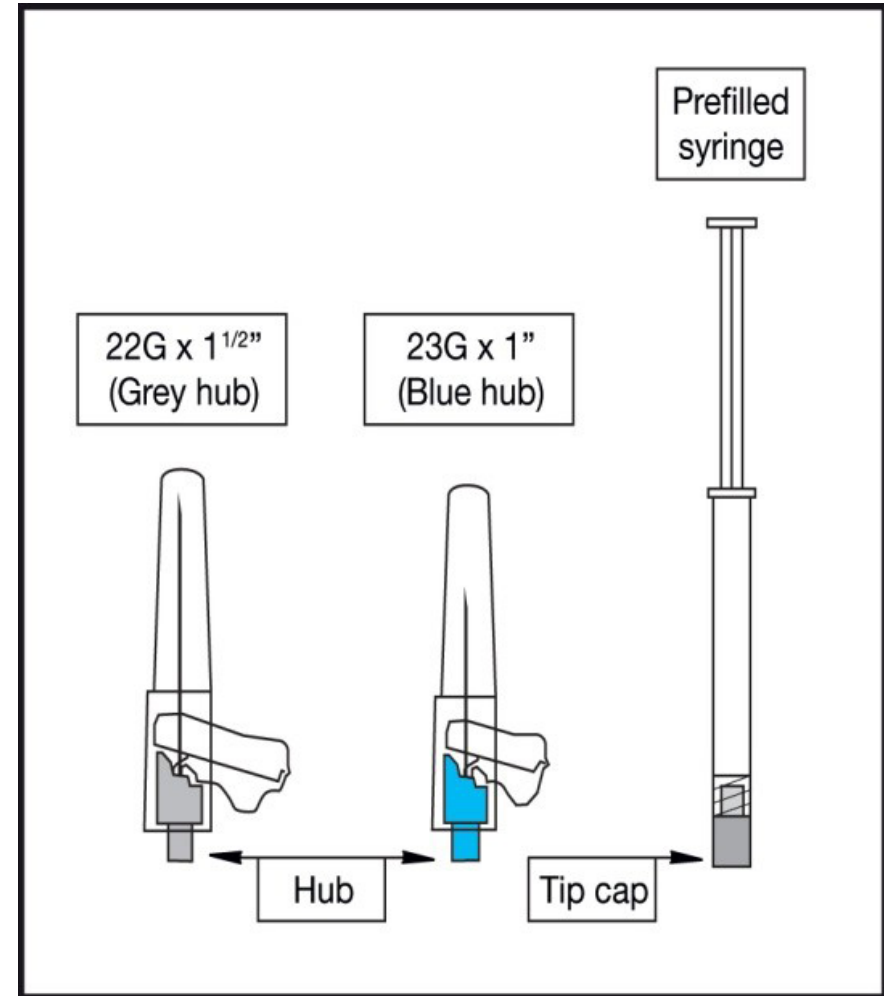
Pre-filled syringe

Shake 10 seconds

Select correct needle



Central anc



● ● ● | Paliperidone - Place in Therapy

- **EXPENSIVE!** (as per Risperdal[®] Consta)
- Consider typical depots first
- Not test dose, so must have tried oral risperidone (or paliperidone) first
- Risperdal[®] Consta vs paliperidone palmitate
 - Several practical advantages
 - monthly dosing
 - immediate drug release (no 3-wk lag)
 - no refrigeration



Olanzapine depot - ZypAdhera ▼

- Trials were to establish pharmacokinetics and safety of the formulation (since 1996)
- “Post-injection syndrome”
 - Unpredictable: 1.4% of during trials (29 events in 28 patients patients) = “common”
 - not related to dose or frequency or patient
 - Symptoms = “overdose”, ranging from mild (e.g. sedation) to serious
 - e.g. unconscious or comatosed, 2 patients were intubated, 20/24 patients were hospitalised
 - Onset: all began with milder symptoms which progressed
 - No fatalities, most recovered within 24-72 hours
 - Not changed by systematic re-training of nurses administering
 - All coincide with high peak olanzapine serum concentrations
 - Not thought to be due to inadvertent intravascular injection (due to inset of symptoms).
- Observe for 3 hours in a “healthcare setting” - most initial symptoms appeared within 1 hr
 - should not drive home, and will need to be accompanied home
- Marketed to LSU (“forensic” settings)
 - Patient (informed) consent?

Central and North West London 

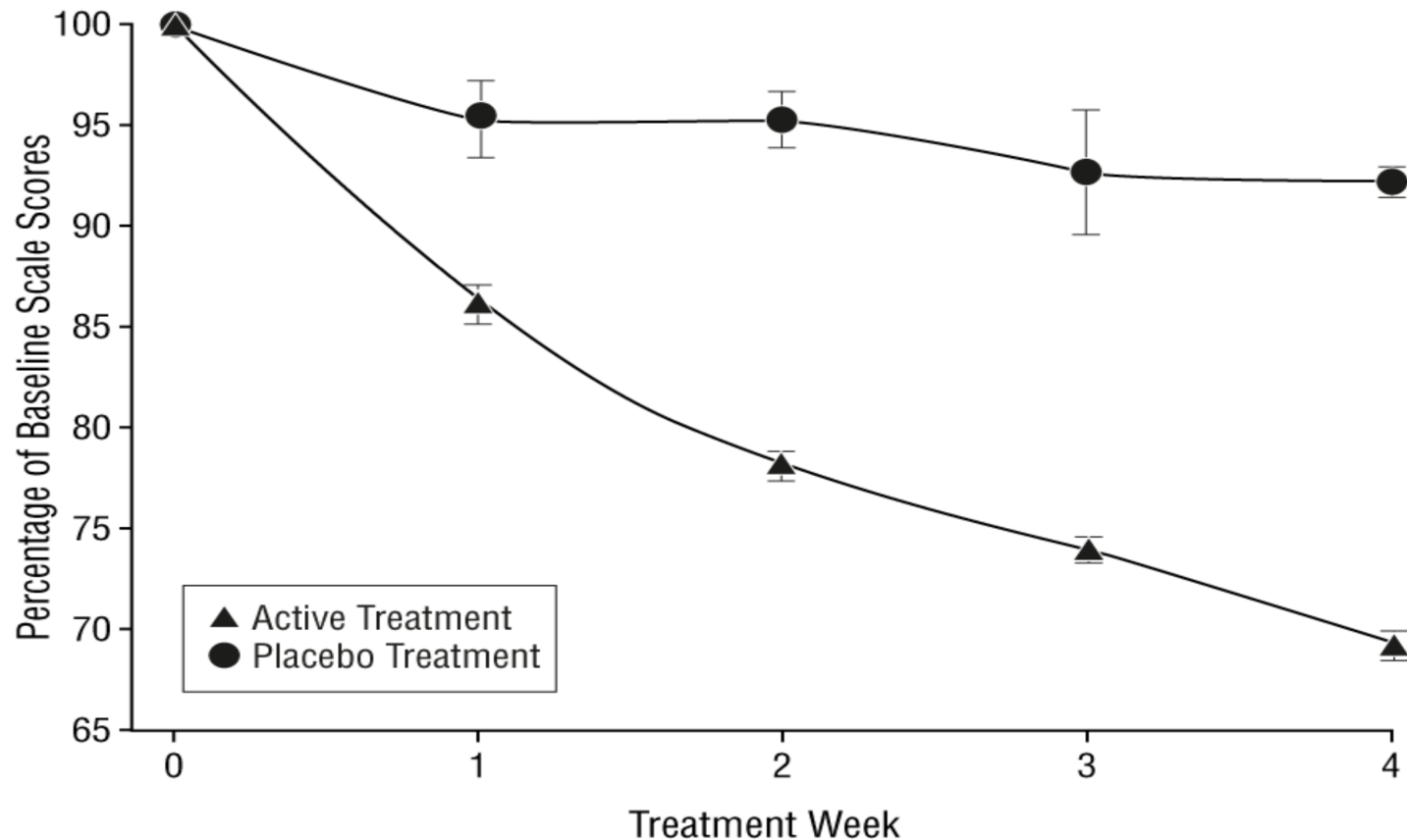
NHS Foundation Trust

 **napicu**
national association of psychiatric intensive care & low secure units

Antipsychotics – Onset of Action

Arch Gen Psychiatry. 2003;60(12):1228-1235. doi:10.1001/archpsyc.60.12.1228

From: **Delayed-Onset Hypothesis of Antipsychotic Action: A Hypothesis Tested and Rejected**



Mean improvement in standardized baseline scores in patients taking antipsychotic drugs vs placebo over time.
Error bars represent SE.

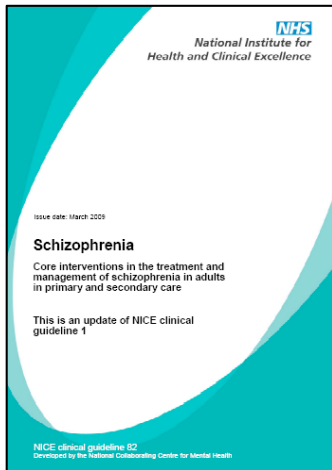


Antipsychotics - Risks



ECGs

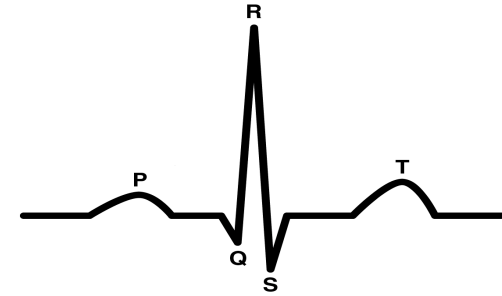
- “Before starting antipsychotic medication, **offer** the person with *[FEP]* schizophrenia an electrocardiogram (ECG) if:




- specified in the SPC
- a physical examination has identified specific cardiovascular risk (such as diagnosis of high blood pressure)
- there is personal history of cardiovascular disease, or
- *the service user is being admitted as an inpatient*”



Haloperidol



-  ECG monitoring requirements
- SPC: “Baseline ECG is **recommended** prior to treatment in all patients, especially in the elderly and patients with a positive personal or family history of cardiac disease or abnormal findings on cardiac clinical examination..... discontinue if the QTc exceeds 500ms.”
- Very rare reports of QT prolongation +/- ventricular arrhythmias
- Maybe more frequent with high doses & in predisposed patients
- Dose related
- Alcohol abuse may ↑ risk
- Concomitant use of other drugs that ↑QT interval may ↑risk
- Doses: max 30mg/d po, 18mg/d IM
- No longer licensed for IV use

QTc-interval abnormalities and psychotropic drug therapy in psychiatric patients

J G Reilly, S A Ayis, I N Ferrier, S J Jones, S H L Thomas

Summary

Background Sudden unexplained death in psychiatric patients may be due to drug-induced arrhythmia, of which lengthening of the rate-corrected QT interval (QTc) on the electrocardiogram is a predictive marker. We estimated the point prevalence of QTc lengthening in psychiatric patients and the effects of various psychotropic drugs.

Methods Electrocardiograms were obtained from 101 healthy reference individuals and 495 psychiatric patients in various inpatient and community settings and were analysed with a previously validated digitiser technique. Patients with and without QTc lengthening, QTc dispersion, and T-wave abnormality were compared by logistic regression to calculate odds ratios for predictive variables.

Findings Abnormal QTc was defined from the healthy reference group as more than 456 ms and was present in 8% (40 of 495) of patients. Age over 65 years (odds ratio 3.0 [95% CI 1.1–8.3]), use of tricyclic antidepressants (4.4 [1.6–12.1]), thioridazine (5.4 [2.0–13.7]), and droperidol (6.7 [1.8–24.8]) were robust predictors of QTc lengthening, as was antipsychotic dose (high dose 5.3 [1.2–24.4]; very high dose 8.2 [1.5–43.6]). Abnormal QT dispersion or T-wave abnormalities were not significantly associated with antipsychotic treatment, but were associated with lithium therapy.

Interpretation Antipsychotic drugs cause QTc lengthening in a dose-related manner. Risks are substantially higher for thioridazine and droperidol. These drugs may therefore confer an increased risk of drug-induced arrhythmia.

Lancet 2000; **355**: 1048–52

Introduction

Cardiovascular mortality in psychiatric patients is high.¹ Reports of sudden unexplained death in those taking antipsychotic drugs^{2,3} have raised the concern that part of this excess may be due to drug-induced arrhythmias, since many of these drugs have cardiac electrophysiological effects similar to those of quinidine.² The polymorphic ventricular arrhythmia known as torsade de pointes has been recorded in patients with psychotropic drug overdose⁴ and provides a plausible mechanism for sudden unexplained death associated with drug therapy.⁵

Several psychotropic drugs are associated with lengthening of the rate-corrected QT interval (QTc) on the electrocardiogram,² which often precedes torsade.⁶ There is no direct evidence linking the extent of drug-induced QTc lengthening with the risk of torsade or sudden death. However, QTc-interval lengthening is a predictor of sudden death in patients with cardiac disease⁷ and the extent of drug-induced QTc-interval lengthening is thought to be an important marker of arrhythmia risk by drug regulatory authorities (see website: www.emeasearch.is.eudra.org/humandocs/PDFs/SWP/098696en.pdf). Risk of arrhythmia with drugs that lengthen ventricular repolarisation may also be indicated by the dispersion of repolarisation, which can be assessed by measuring QT dispersion.⁸ Abnormal repolarisation may also cause non-specific abnormalities of the T wave, although there is no direct evidence to link such changes with arrhythmia.

Clinical guidelines advise caution in the use of high-dose antipsychotic therapy with special reference to the risk of sudden death, as well as regular monitoring of the QTc interval,⁹ but evidence for this change in practice is



Sudden cardiac death

- Association with antipsychotics may be over estimated¹
 - Physical health co-morbidities more of a concern
- Case control studies: some antipsychotics (mainly haloperidol) are associated with ↑ sudden cardiac death
- Risk factors:
 - Epidemiological studies: indicated high doses²
 - Antipsychotic polypharmacy: independent risk factor
 - for death in a 10-year prospective study of a cohort of 88 psychiatric patients with schizophrenia (mean age of 63 years)²
- A retrospective cohort study³ compared the risk between typical (n=44,218) & atypicals (n=46,089) and matched non users (n=186,600)
 - Typical: adjusted rate of sudden cardiac death rate x2 that of nonusers
 - Atypicals: similar, rate was slightly more than x2 that for nonusers
 - Rates did not differ significantly between 1st and 2nd generation

1. Manu P et al. *J Clin Psychiatry* 2011; 72(2): 936-941.

2. Haddad PM, Anderson IM. *Drugs* 2002;62:1649-71.

3. Ray W et al. Atypical antipsychotic drugs and the risk of sudden cardiac death. *NEJM* 2009;360(3):225-35



NMS

- Reported with both 1st and 2nd generation
 - Probably less often with 2nd generation
 - Use lower doses than decades ago
 - NMS presentation different with 2nd generation? (or just clozapine)
 - Less rigidity
 - Lower mortality

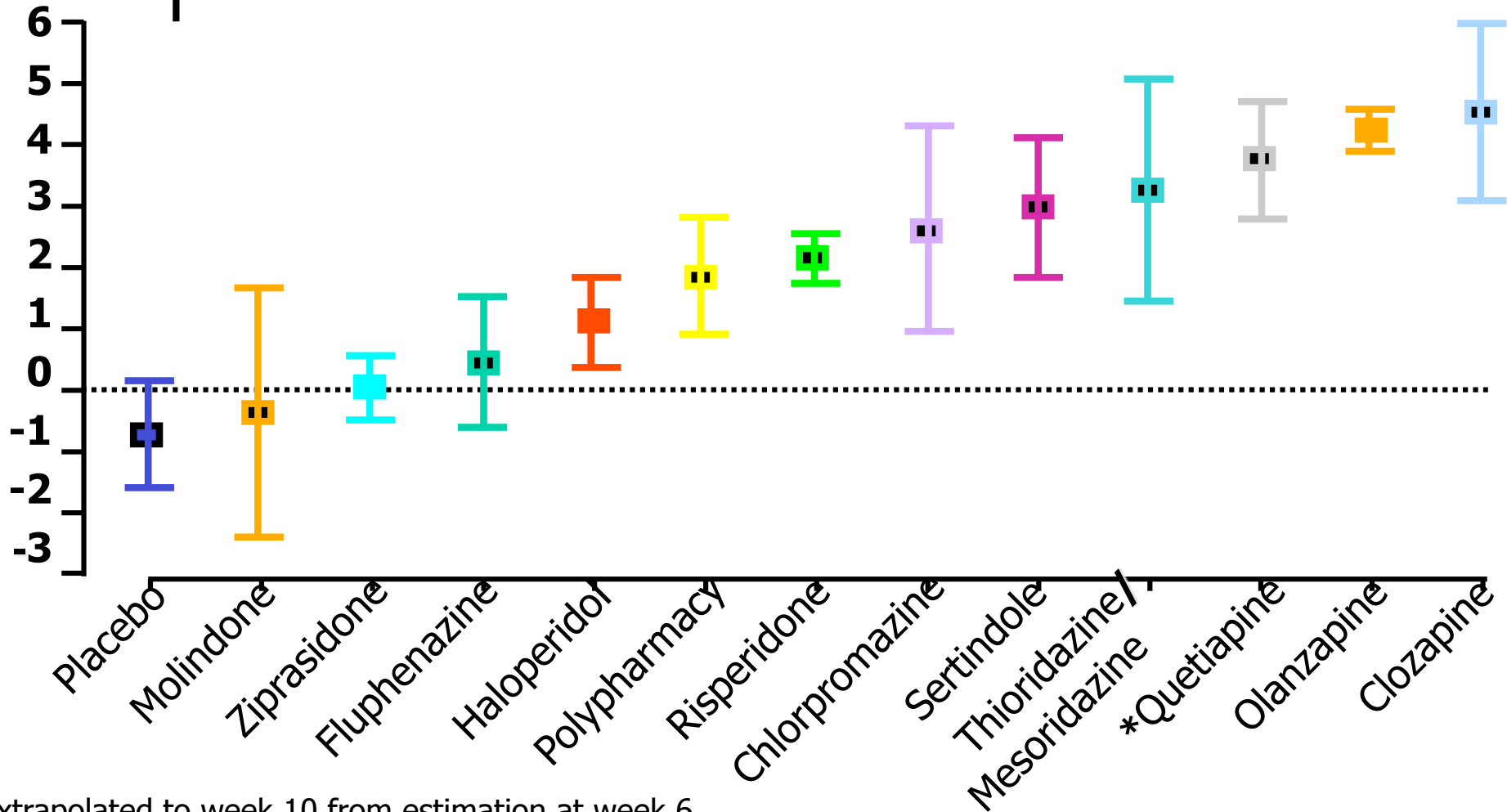
Trollor JN et al. *CNS Drugs* 2009; 23(6):477-492.

Trollor JN et al. *BJPsych* 2012



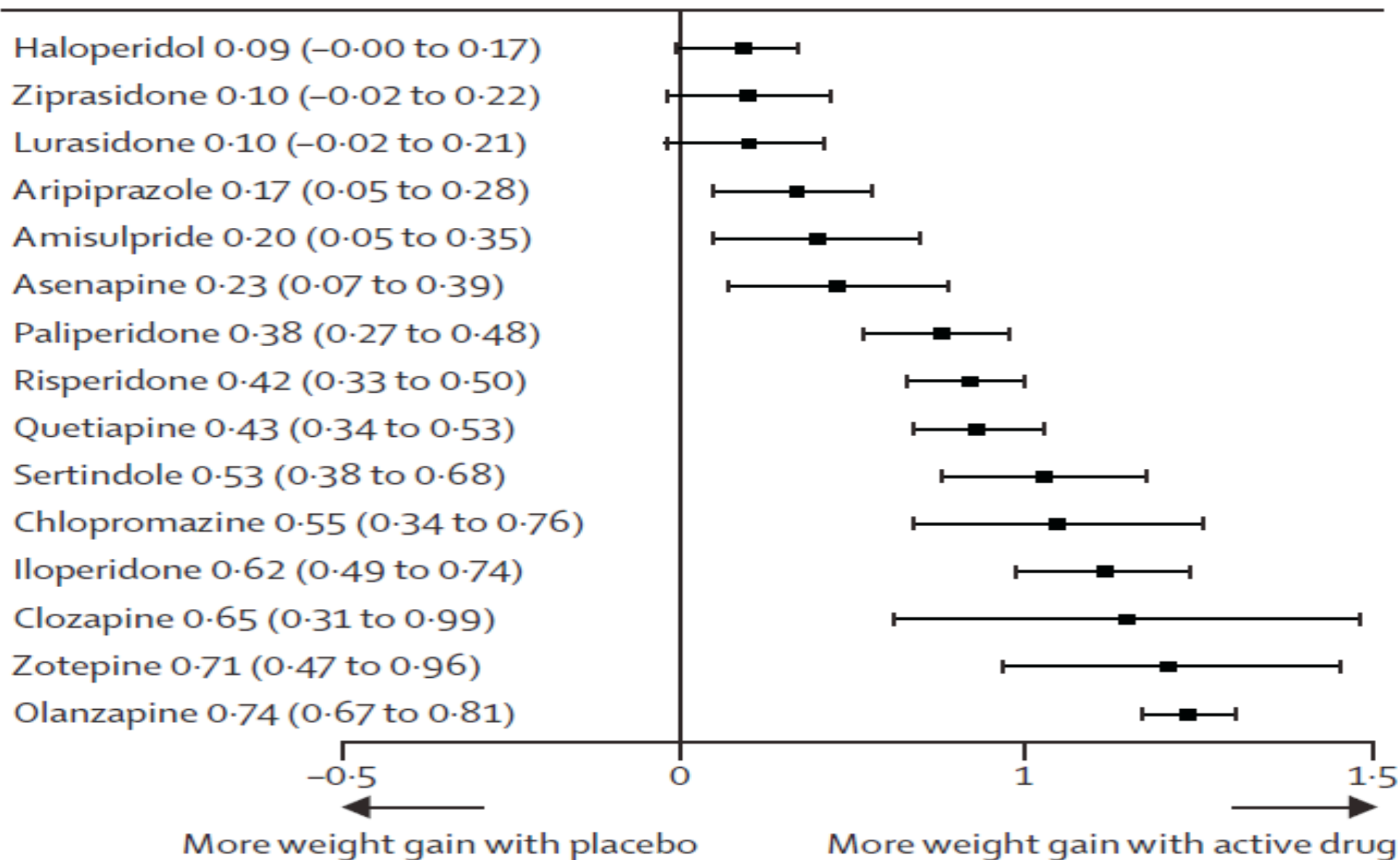
Antipsychotics and weight gain

95% CI for estimated weight gain at week 10



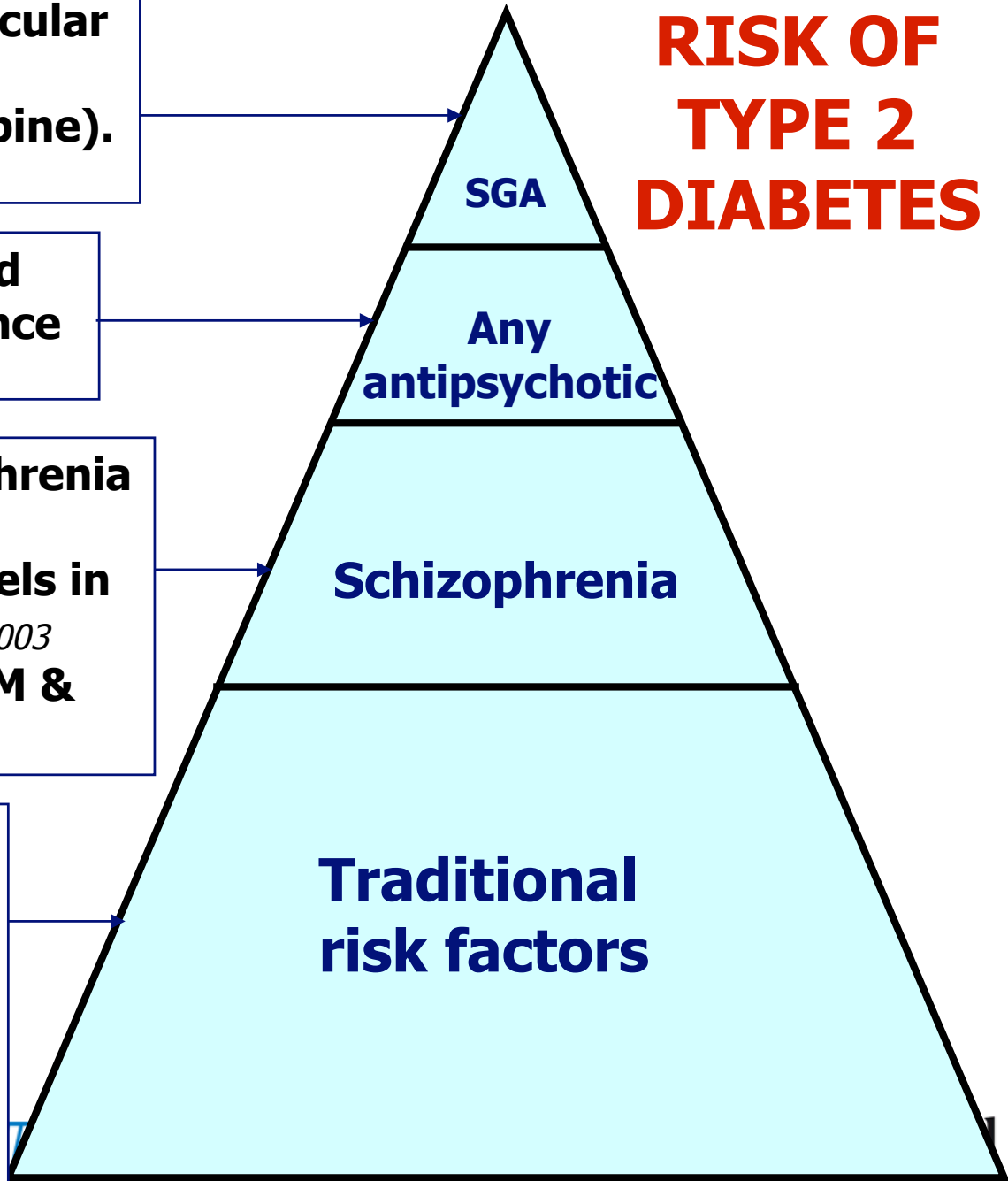
*Extrapolated to week 10 from estimation at week 6

B Weight gain SMD (95% CrI)



Leucht S et al. Comparative efficacy and tolerability of 15 antipsychotic drugs in schizophrenia: a multiple-treatments meta-analysis. *The Lancet*. Published Online June 27, 2013. [http://dx.doi.org/10.1016/S0140-6736\(13\)60733-3](http://dx.doi.org/10.1016/S0140-6736(13)60733-3).

RISK OF TYPE 2 DIABETES



Attributable risk due to particular SGAs is small, from 0.05% (risperidone) to 2% (olanzapine).

Leslie & Rosenheck 2005

FGAs associated with 2-3 fold increase in diabetes prevalence

Lambert et al 2004

DM risk increased in schizophrenia before SGAs. *Dixon et al 2000*

Impaired fasting glucose levels in drug-naïve patients *Ryan et al 2003*

?Genetic overlap between DM & schizophrenia. *Stone et al 2004*

**Older age
Family history**

Poor diet

Obesity

Lack of exercise

Ethnic predisposition

Cardiovascular disease, etc.



Lithium liquid



One 200mg tablet
(carbonate)

One 5ml spoonful liquid
(citrate)

“Clear, colourless, pineapple flavoured, sugar free syrup containing 520mg lithium citrate equivalent to 200mg lithium carbonate per 5ml.”



<http://www.nrls.npsa.nhs.uk/resources/?EntryId45=65426>

Central and North West London
NHS Foundation Trust



NHS
National Patient
Safety Agency
National Reporting
and Learning Service

Lithium Therapy

**Important information
for patients**

CCQI
COLLEGE CENTRE FOR QUALITY IMPROVEMENT

NPA
National Pharmacy
Association

POMH UK
PRESCRIBING OBSERVATORY
FOR MENTAL HEALTH



Valproate and loading doses

- **Depakote** (semi-sodium valp): initial recommended daily dose is 750mg daily in 2–3 divided doses
- **Valproate M/R** (sodium valp + valproic acid): start at 600mg daily increase by 200mg at 3-day intervals until control is achieved
- Mean daily dose usually: 1–2g daily valproate i.e. 20-30mg/kg/day
 - Maximum 2.5g per day
- A starting dose of 20mg valproate/kg - also acceptably safe in trials
- Dose should be increased as rapidly as possible
- > 45mg/kg/day (e.g. >3g) - careful monitoring
- “Toxicity”: plasma concs up to 5 to 6 times max. therapeutic levels - unlikely to be any symptoms other than nausea, vomiting & dizziness.
- Plasma-valproate concentrations are not a useful index of efficacy, therefore routine monitoring is unhelpful (BNF re epilepsy)



Oral Benzodiazepines

Diazepam

- “Long acting”
- Active metabolites including N-desmethyldiazepam with a half-life of 30 - 100 hours
- Terminal elimination phase of 1-2 days
- Licensed for anxiety & insomnia
- BNF 4.2.1 – anxiolytics (T2/3)
- Tabs & liquid
- Max. 30mg/day

Clonazepam

- “Long acting”
- Active metabolites
- Terminal elimination half-life of 20 - 60 hours (mean 30 hrs)
- Greater inter-individual variation in response
- Unlicensed indication
- BNF 4.8.1 – antiepileptic (T2/3)
- Tabs & liquid (liq = £++)
- Max. 8mg/day

Equivalent doses – **no consensus:**

Approximately Diazepam 5mg = Clonazepam 0.5mg
Ranges quoted: 0.5 – 1mg, 0.5mg (0.25 -4mg), 0.25mg



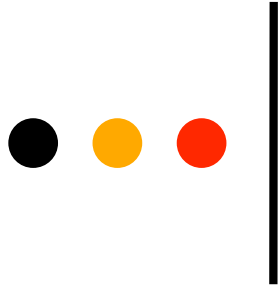
Clopixol Acuphase[®]

Role?



Clopixol Acuphase[®]

- Zuclopenthixol acetate (Clopixol Acuphase[®]) injection is indicated for the short-term management of acute psychosis, mania, or exacerbations of chronic psychosis
- Zuclopenthixol acetate injection **cannot** be “*Rapid Tranquillisation*”
 - It acts too slowly
 - It lasts for 3 days
- Will not ‘hasten’ antipsychotic effect



RT Alternatives



Olanzapine IM injection ▼

- Still licensed in EU
- Not marketed or distributed by Lilly
 - Financial reasons (not clinical)
 - Can be imported to UK
 - ↑ Cost
 - “Simultaneous injection of IM olanzapine and parenteral benzodiazepine is not recommended. If the patient is considered to need parenteral benzodiazepine treatment, this should not be given until at least 1 hour after IM olanzapine administration.”





Lorazepam

- National shortages since 2005
- Trusts buying unlicensed version from abroad
 - Legal implications
- Short acting, no active metabolite, po = IM
 - low risk of accumulation
- Maximum dose IM?



Lorazepam

- National shortages since 2005
- Trusts buying unlicensed version from abroad
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- Short acting, no active metabolite, po = IM
 - low risk of accumulation
- Maximum dose IM?

“Acute Anxiety

Adults: 0.025-0.03mg/kg (1.75-2.1mg for an average 70kg man). Repeat 6 hourly”



Midazolam IM

- Unlicensed indication: medico-legal implications
- Quick onset of action^{1,2} rapid & complete absorption
- Short duration of action
- 7.5-15mg, max. 15mg/day
- Risks – **respiratory depression** (> lorazepam)
- Flumazenil (Dr to administer)
- CQC advice to SOADs
- Practicalities: Controlled Drug (Schedule 4)

1. Huf G *et al.* Rapid tranquillisation for agitated patients in psychiatric rooms: a randomised trial of midazolam versus haloperidol plus promethazine. *British Medical Journal* 2003; 327 (7417): 708-711
2. Martel M., Sterzinger A, Miner J, *et al.* Management of acute undifferentiated agitation in the emergency department: A randomized double-blind trial of droperidol, ziprasidone, and midazolam. *Academic Emergency Medicine*. 2005; 12 (12): 1167-1172.

● ● ● | Midazolam – buccal & sublingual

- Studied in paediatrics and learning disabilities
 - emergency antiepileptic as alternative to rectal diazepam¹
- Sublingual: high bioavailability (about 75%) and reliable plasma concentrations²
- Buccolam ▼ (2011) for oromucosal administration, a pre-filled oral syringe.
 - Only licensed for the treatment of seizures in patients aged under 18 years.
 - Not licensed for use in RT, or for any indication in adults
 - Solution should be slowly inserted into the space between the cheek and gum, approximately half the solution on each side of the mouth
- UK: Minimal role in RT, as preferable oral formulations
- A small study (n=27)³ in x2 English male PICUs, instead of routine IM, for 6/12
 - Sedative effects at the first time point (15 minutes) peaking at 30minutes, and lasted at least 1 hour (no further measures taken)
 - >1/3 further doses of RT were required within 24 hours
 - One case of over sedation

1. Sweetman S. Martindale: The complete drug reference (2013). The Pharmaceutical Press.

2. Schwagmeier R, et al. *Br J Clin Pharmacol* 1998; 46: 203–6

3. Taylor D, Okocha C, Paton C, Smith S, Connolly A. *Int J Psych Clin Prac.* 2008; **12** (4): 309-311



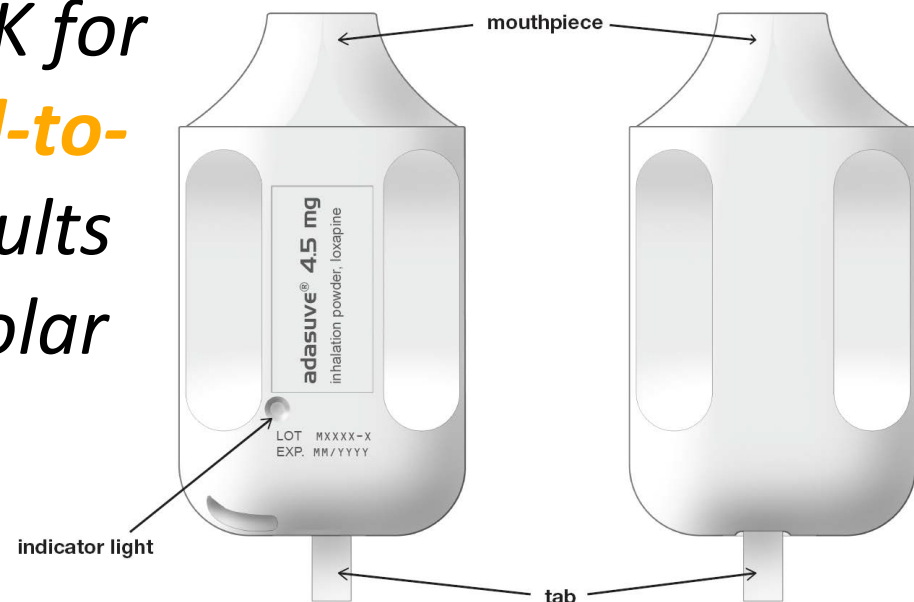
Emergency treatment for excess benzodiazepines

- **Flumazenil** - benzodiazepine antagonist
- Give if respiratory rate drops <10/min after administration of benzodiazepines
- IV administration = Drs to administer
- Shorter $t_{1/2}$ than lorazepam
 - repeat doses needed
- NPSA alert on midazolam inj. Re flumazenil

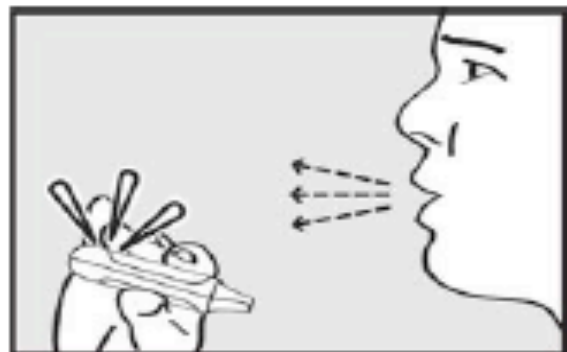


Loxapine - Inhalation

- *Recently licensed in the UK for “the management of **mild-to-moderate agitation** in adults with schizophrenia or bipolar affective disorder.”*
- *Typical antipsychotic*
 - *Used orally & IM in some countries for many years*

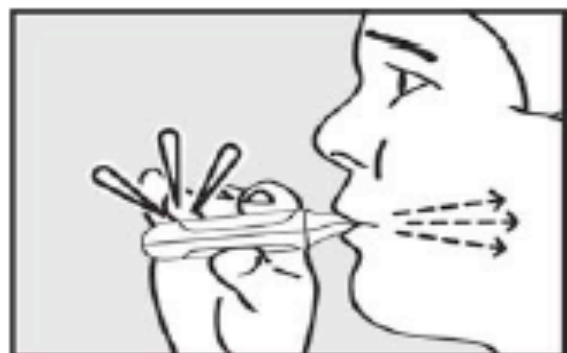


Instruct the patient to:



3. Exhale

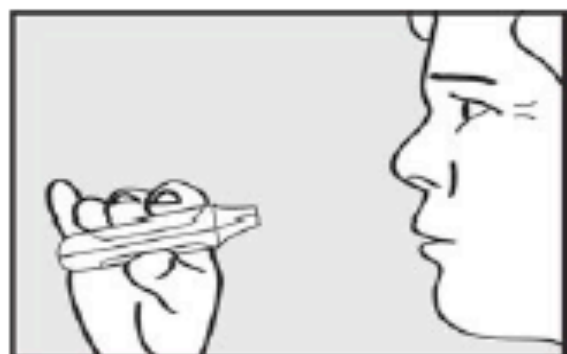
Hold the inhaler away from the mouth and breathe out fully to empty lungs.



4. Inhale

Inhale through the mouthpiece with a steady deep breath.

IMPORTANT: Check that the green light turns off after the patient inhales.



5. Hold breath

Remove the mouthpiece from the mouth and hold breath briefly.

NOTE: If the green light stays on after the patient inhales, instruct the patient to repeat steps 3-5.

Rapid acute treatment of agitation in individuals with schizophrenia: multicentre, randomised, placebo-controlled study of inhaled loxapine*

Michael D. Lesem, Tram K. Tran-Johnson, Robert A. Riesenber, David Feifel, Michael H. Allen, Robert Fishman, Daniel A. Spyker, John H. Kehne and James V. Cassella

Background

There is a need for a rapid-acting, non-injection, acute treatment for agitation.

Aims

To evaluate inhaled loxapine for acute treatment of agitation in schizophrenia.

Method

This phase III, randomised, double-blind, placebo-controlled, parallel-group study (ClinicalTrials.gov number NCT00628589) enrolled 344 individuals who received one, two or three doses of inhaled loxapine (5 or 10 mg) or a placebo. Lorazepam rescue was permitted after dose two. The primary efficacy end-point was change from baseline in Positive and Negative Syndrome Scale–Excited Component (PANSS–EC) 2 h after dose one. The key secondary end-point was Clinical Global Impression–Improvement scale (CGI–I) score 2 h after dose one.

Results

Inhaled loxapine (5 and 10 mg) significantly reduced agitation compared with placebo as assessed by primary and key secondary end-points. Reduced PANSS–EC score was evident 10 min after dose one with both 5 and 10 mg doses. Inhaled loxapine was well tolerated, and the most common adverse events were known effects of loxapine or minor oral effects common with inhaled medications.

Conclusions

Inhaled loxapine provided a rapid, well-tolerated acute treatment for agitation in people with schizophrenia.

Declaration of interest

The study was sponsored by Alexza Pharmaceuticals. M.D.L., T.K.T-J, R.A.R. and D.F. were investigators. M.H.A., R.F., D.A.S., J.H.K. and J.V.C. were consultants to or employees of Alexza Pharmaceuticals during study design, execution and/or analysis.

Good practice in prescribing and managing medicines and devices

- 1 In *Good Medical Practice (2006)*¹ we say:
 2. Good clinical care must include:
 - a adequately assessing the patient's conditions, taking account of the history (including the symptoms, and psychological and social factors), the patient's views, and where necessary examining the patient.
 3. In providing care you must:
 - a recognise and work within the limits of your competence
 - b prescribe drugs or treatment, including repeat prescriptions, only when you have adequate knowledge of the patient's health, and are satisfied that the drugs or treatment serve the patient's needs.
 - c provide effective treatments based on the best available evidence.
 - f keep clear, accurate and legible records, reporting the relevant clinical findings, the decisions made, the information given to patients, and any drugs prescribed or other investigation or treatment.
 - g make records at the same time as the events you are recording or as soon as possible afterwards.
 - j make good use of the resources available to you.
 13. You must keep up to date with, and adhere to, the laws and codes of practice relevant to your work.

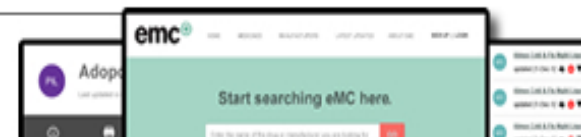


Summary of Product Characteristics (SPCs)

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Olanzapine 10mg film-coated tablets	olanzapine	Zentiva	13-Jul-12
Olanzapine 10mg orodispersible tablets	olanzapine	Zentiva	13-Jul-12
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Summary of Product Characteristics last updated on the eMC: 13/06/2013

SPC Zyprexa 2.5mg, 5mg, 7.5mg, 10mg, 15mg, and 20mg coated tablets. Zyprexa Velotab 5mg, 10mg, 15mg, and 20mg orodispersible tablets

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- 1. Name of the medicinal product
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Legal Categories

- > POM – Prescription Only Medicine



Summary

- Long term violence – **clozapine**
- Depots – advantage for adherence
- No drug is without risks
- Know the drugs you prescribe (GMC)

Any Questions?



Further Reading / References

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<http://www.bap.org.uk/docsbycategory.php?docCatID=2>
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