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Risperidone versus Olanzapine for schizophrenia - THE LEADERS GUIDE

Produced by the Editorial base of the Cochrane Schizophrenia Group
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from
Jayaram MB, Hosalli P, Stroup TS. Risperidone versus olanzapine for schizophrenia. Cochrane Database of Systematic Reviews 2006, Issue 2. Art. No.: CD005237. DOI: 10.1002/14651858.CD005237.pub2.

Special points of interest:

- This should take no longer than 1 hour to prepare
- First time you undertake a journal club in this way it may be a bit nerve-wracking

but….

- It should be fun to conduct and attend
- It should begin and end on the practical day-to-day clinical situation

Inside this guide:

Background explanation

Thank you for giving this guide a go. The idea behind this is to make things easier for you when you lead the journal club.

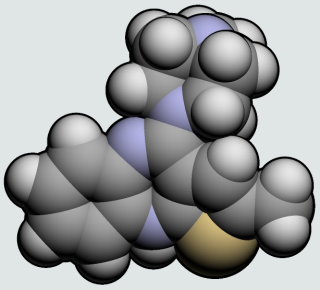
Journal clubs are often difficult to conduct and far removed from clinical life. Even if the leaders do prepare well, those turning up may be more in need of lunch, coffee or a social time than practical academic stimulation and the implicit pressure to read a difficult paper.

This suggested design is an attempt to allow for those needs, whilst getting the very best out of the session.

This journal club design should really help those attending see that this research may have some clinical value.

What you will need to do is:

- ☑ Have a good read of this
- ☑ Then read the review to which this is attached.
- ☑ Distribute the review to those attending well before the club
- ☑ Make more copies for those turning up on spec
- ☑ Do not really expect many to have read the review



Space-filling model of Olanzapine

PRINTING GUIDE

Pages 1-4 - one copy for you

Pages 5-6 - one copy for each participant - distributed at **start** of journal club

Page 7– one copy for each participant distributed at **end** of journal club

Page 8 - one copy for you to collate feedback

Full review for everyone

Try to find a colour printer that does double sided printing

The three parts

Part 1. Set the clinical scene (5 mins)

Be clear, but really make the participants feel the pressure of the situation...just like you would in clinical life

Part 2. Critical appraisal of the review (20 mins)

Get participants to list what is needed from the review before Patient and parents arrive, get them to talk, split into groups—with a feeling of urgency.

Part 3. Use of evidence in clinical life (20 mins)

Having distilled the evidence use role play to see how the participants would use what they have learned in everyday life.

Part 1.1 Setting the scene – The Panel

You are one clinical member of the local Guideline Panel for prescribing.

Funds are very limited. Risperidone has come off patient and is now inexpensive. Olanzapine is still costly.

You have been asked to review relevant evidence for the next panel meeting and are expected to present best evidence to the panel.

You know that the panel consists of managers, fellow clinicians, consumers of care and their advocates as well as two representatives from the relevant drug companies.

One of your colleague clinicians loves using Olanzapine. The other loves Risperidone. You know there is an argument brewing.

It has been really busy and you did not really get time to prepare properly…

Questions for participants:

Q 1. What do you think panel members may ask?

A 1. [Suggestion] "Is one drug clearly better than the other?"

Q 2. What do you think is meant by 'better'?

A 2. ***List*** the suggestions from participants as these are what you will come back to in the role play

Q 3. What do you think the managers/consumers will ask?

A 3. Again, list answers.

Part 1.2 Setting the scene – the Journal club

Complicate the scenario by adding the need to attend this journal club

Knowing you are due to see the panel in less than an hour and have not done your preparation.

You are nevertheless compelled to attend journal club.

You have not even had time to read the paper for the journal club….and need some lunch.

By a stroke of [rather remarkable] luck the paper for discussion focuses on the value of risperidone vs olanzapine.

Questions for participants:

Q 1. If you had not had this paper fall into your lap where might you have gone for reliable information?

A 1. There are now lots of answers to this - The Cochrane Library, Clinical Evidence, NICE Technology Appraisals.

Anything that has a **reproducible method** by which results are obtained.

Part 2.1 Critical appraisal of the review

For every review there are only three important questions to ask:

1. Are the results valid?

2. What *are* the results?

3. Are the results applicable to Patient?

You now have only 20 mins to get participants though this large review. To do this quickly is not easy, especially as many will not have read the paper in preparation.

Suggestion: Ask participants what salient facts they want to know - especially considering their tight time-scale.

Remind them that Guideline Panel starts in about 20 mins.

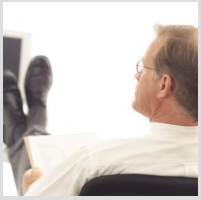
You should be able to fit most of the suggestions supplied by participants into the three categories of question outlined above.

Read 2.2 as this give more detail of the issues that will, in some shape or form, be supplied by the participants.

If they are not lively—give them a hand.

Do not panic. Bright journal club attendees will come up with all the answers—your job is to help focus their efforts and categorise their answers.

Do not be worried by silence.



Take time to read and think about the review - this is the only time-consuming bit

LIST 1:

1.

2.

3.

4.

5.

List 2:

1.

2.

3.

4.

5.

Participants will think of most of the issues - you just need to catch them and write them on a board or flip chart

Part 2.2 The three parts of appraising a review

1. Are the results valid?

There is no point looking at the result if they are clearly not valid.

a. Did the review address a clearly focused issue?

Did the review describe the population studied, intervention given, outcomes considered?

b. Did the authors select the right sort of studies for the review?

The right studies would address the review's question, have an adequate study design

c. Do you think the important, relevant studies were included?

Look for which bibliographic databases were used, personal contact with experts, search for unpublished as well as published studies, search for non-English language studies

d. Did the review's authors do enough to assess the quality of the included studies?

Did they use description of randomization, a rating scale?

2. What <u>are</u> the results?

a. Were the results similar from study to study?

Are the results of all included studies clearly displayed?

Are the results from different studies similar?

If not, are the reasons for variations between studies discussed?

b. What is the overall result of the review?

Is there a clinical bottom-line?

What is it?

What is the numerical result?

c. How precise are the results?

Is there a confidence interval?

3. Can I use the results to help Patient?

a. Can I apply the results to local panel needs?

Is the local situation so different from those in the trial that the results don't apply?

b. Should I apply the results to the local situation?

How great would the benefit of therapy be for this particular situation?

Is the intervention consistent with the values and preferences of your locality?

Were all the clinically important outcomes considered?

Are the benefits worth the harms and costs?

Part 2.3 Doing the appraisal

Having managed the interactive session with the participants - acquiring the three questions that need to be addressed by those appraising a review and some idea of how to answer each of those questions - now divide the room into three.

Apportion one of the questions per group and ask each group to get a feel for the whole review (1 min) but to focus on answering their particular question for the rest of the participants (5 mins or so).

Encourage talking to each other.

Move round the room to help the groups if they seem to need it.

Have your copy of the review marked up with where they may look for answers -although in a good review it should be obvious.

Stop the flow after about 10 minutes and ask each group to report in turn.

Do Group 1 really think that the review uses valid methods? Why?

After the first group's report you may want to ask everyone to vote whether to proceed or not.
If they agree to proceed —see if you can **get Group 2 to give you the clinical bottom line.**

We suggest that the Graph providing data for 'Global effect: 1. various outcomes' best fits Panel's request of information about if one drug is 'better' than the other.

And from **Group 3 get some feel of how applicable the findings are.**

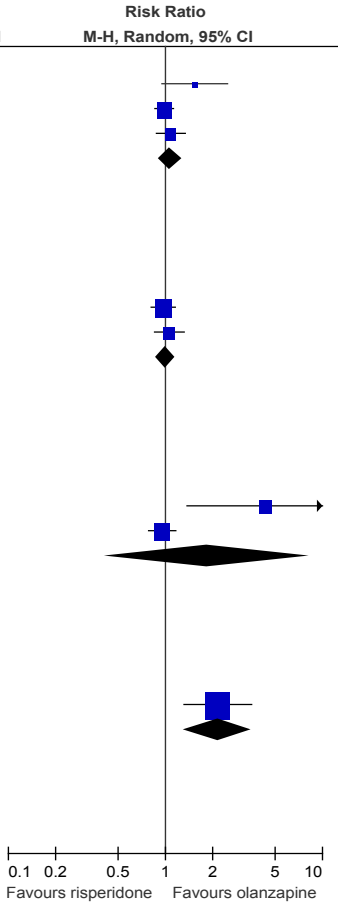
There is no point proceeding to the second question if journal club participants think the results are not valid

"Is one drug clearly better than the other?"

Part 2.4 Interpret Numerical Outcomes

COMPARISON 1: RISPERIDONE VERSUS OLANZAPINE
Outcome 1.1: Global effect: 1. Various outcomes

Study or Subgroup	Risperidone Events	Risperidone Total	Olanzapine Events	Olanzapine Total	Weight	Risk Ratio M-H, Random, 95% CI
1.1.1 short term - no clinically important response (CGI)						
Chan 2003	20	30	13	30	11.0%	1.54 [0.95, 2.49]
Conley 2001	128	188	131	189	53.0%	0.98 [0.86, 1.13]
Jeste 2003	60	87	56	88	36.0%	1.08 [0.88, 1.34]
Subtotal (95% CI)		**305**		**307**	**100.0%**	**1.07 [0.90, 1.27]**
Total events	208		200			
Heterogeneity: Tau² = 0.01; Chi² = 3.40, df = 2 (P = 0.18); I² = 41%						
Test for overall effect: Z = 0.76 (P = 0.45)						
1.1.2 short term - unchanged / worse (CGI)						
Conley 2001	105	188	109	189	60.3%	0.97 [0.81, 1.16]
Jeste 2003	56	83	56	88	39.7%	1.06 [0.85, 1.32]
Subtotal (95% CI)		**271**		**277**	**100.0%**	**1.00 [0.88, 1.15]**
Total events	161		165			
Heterogeneity: Tau² = 0.00; Chi² = 0.41, df = 1 (P = 0.52); I² = 0%						
Test for overall effect: Z = 0.06 (P = 0.96)						
1.1.3 short term - needing addtional benzodiazepines						
Chan 2003	13	30	3	30	43.1%	4.33 [1.37, 13.67]
Conley 2001	93	188	98	189	56.9%	0.95 [0.78, 1.16]
Subtotal (95% CI)		**218**		**219**	**100.0%**	**1.83 [0.41, 8.24]**
Total events	106		101			
Heterogeneity: Tau² = 1.02; Chi² = 6.78, df = 1 (P = 0.009); I² = 85%						
Test for overall effect: Z = 0.79 (P = 0.43)						
1.1.4 long term (by 1 year) - relapse/hospitalisation						
Namjoshi 2002	39	136	19	143	100.0%	2.16 [1.31, 3.54]
Subtotal (95% CI)		**136**		**143**	**100.0%**	**2.16 [1.31, 3.54]**
Total events	39		19			
Heterogeneity: Not applicable						
Test for overall effect: Z = 3.04 (P = 0.002)						



This is the most important part of the journal club—the *practical application* of what knowledge you have gained. This is one way of doing it.

Set out chairs in committee style. Do not call for a volunteer - just nominate someone to be the clinician and you be a manager, another person to be a consumer representative.

Make sure that the clinician feels they can have time to ask their [relieved for not being singled out] colleagues for help [remember - this has got to be a combination of practical and fun].

Back on page 2 there are suggestions for what the panel may ask - use them.

Well, is Olanzapine any better than Risperidone?

See if they can put across in a supportive way the best evidence as they understand it. There is no perfect way to do this - but perhaps something like this:

"The best evidence we have is from the drug companies and is imperfect - but there is the impression that, on average, in terms of global and mental state there is no clear difference."

What do you mean by "better"? would be a good next question.

Again there is no right answer but think about how to put into words what the research outcome really means.

Perhaps - "the improvement that the best evidence suggests may not be all that great - "better" is described in a matter of points on scales that are not usually used clinically - but that does not mean that they do not represent real improvements. These are averages and one person may respond when another does not. Response can be idiosyncratic. Cost data are few, out-dated, difficult to apply and, perhaps, biased. Olanzapine is now, undoubtedly more expensive. Taking all into consideration I recommend to the panel...WHAT AND WHY?"

As has been said - there is no right answer and all depends on personal style and situation. Your job is to encourage the best debate - just like would happen in the real world. If it is going well there are other questions that you may ask - see side **Box 1**.

This turns out to be a [quite common] situation where there is little to choose between two treatments where it comes to best evidence.

No data are great.

These drugs are more different for adverse effects than they are for positive outcomes.

It is important to be able to argue your case from an informed standpoint even if evidence is not conclusive.

Box 1. Additional questions

☑ **What about adverse effects?**

These are different and important. Data are, however, not great (as might be expected from rival drug companies). Olanzapine causes weight gain. Risperidone causes movement disorder and sexual dysfunction. You could be numerical here. Can you put numbers regarding 'abnormal ejaculation' and 'weight gain' into words?

About 7% given Risperidone have abnormal ejaculation versus a little over 1% on Olanzapine. The risk of abnormal ejaculation with Risperidone is four times greater than that if prescribed Olanzapine.

Short term gain of 7% additional body weight is greater for those given Olanzapine (about 28%) compared with those on Risperidone (about 13%). The risk of putting on a lot of weight in the short term if given Risperidone is about half that if given Olanzapine.

Questions that may be useful - Why do you think that these adverse effects were not recorded in every study? Probably a function of reluctance of industry to record adverse effects in consistent manner.

If they had been - how would it have helped? Data would have had much greater precision - the percentages noted above do not have confidence intervals around them. We could calculate these - but they would be wide - the data are needlessly imprecise.

This can be part of a store of Critically Appraised Topics

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Special points of interest:

- The idea of this is to lead you from the clinical situation, trough the research and back to the real-world clinical situation again
- You may or may not have read the paper - but even if you have not that does not mean that you cannot get something out of this

- Make sure you participate, and speak up - you will have to in the real clinic
- There is no perfect way of doing this - each person has an individual way of interacting and conveying information

Risperidone versus Olanzapine for schizophrenia

- HANDOUT FOR PARTICIPANTS

Produced by the Editorial base of the Cochrane Schizophrenia Group
http://szg.cochrane.org/en/index.html, email: jun.xia@nottingham.ac.uk

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The Panel will arrive soon

What do you think the Panel may ask?

List:

1.

2.

3.

4.

5.

If you had not had this paper fall into your lap where might you have gone for reliable information?

What key points do you need to know to see if this review can help?*

1.

2.

3.

4.

5.

***The Panel arrives in 30 mins**

After discussion do you want to change the key points you need to know to see if this review can help?*

1.

2.

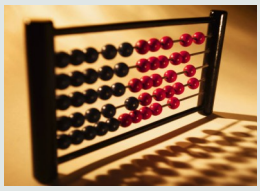
3.

***The Panel arrives in 10 mins**

Can you extract numbers that will be useful to you and the Panel?

Clue: focus on what you think the Panel may ask - main effects and adverse effects - graph number '1.1.1' may be a good one to use

1. Can you put relative risk into words?



The arithmetic is not complicated

2. Is there any improvements *attributable* to use of Risperidone?

3. Can you work out the number needed to treat for hospitalization/relapse?

4. Can you put that into words?

The Panel arrive

Is there a good use of words you would want to use?

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Special points of interest:

- Best evidence suggests that clinically focused problem-based learning "has positive effects on physician competency" even long into the future. [1]

1. Koh GC, Khoo HE, Wong ML, Koh D. The effects of problem-based learning during medical school on physician competency: a systematic review. CMAJ 2008; 178(1):34-41. (free online)

CATmaker

This can be part of a store of Critically Appraised Topics - see CATmaker online

Risperidone versus Olanzapine for schizophrenia - PARTICIPANTS' CRIB SHEET

The three parts of appraising a review

1. Are the results valid?

There is no point looking at the result if they are clearly not valid.

a. Did the review address a clearly focused issue?

Did the review describe the population studied, intervention given, outcomes considered?

b. Did the authors select the right sort of studies for the review?

The right studies would address the review's question, have an adequate study design

c. Do you think the important, relevant studies were included?

Look for which bibliographic databases were used, personal contact with experts, search for unpublished as well as published studies, search for non-English language studies

d. Did the review's authors do enough to assess the quality of the included studies?

Did they use description of randomization, a rating scale?

2. What *are* the results?

a. Were the results similar from study to study?

Are the results of all included studies clearly displayed?

Are the results from different studies similar?

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c. How precise are the results?

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3. Can I use the results to help the patient?

a. Can I apply the results to Patient?

Is patient so different from those in the trial that the results don't apply?

b. Should I apply the results to Patient?

How great would the benefit of therapy be for this particular person?

Is the intervention consistent with Patient's values and preferences?

Were all the clinically important outcomes considered?

Are the benefits worth the harms and costs?

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Risperidone versus Olanzapine for Schizophrenia - FEEDBACK

Date and place of journal club

1. How many attended?

About

2. What was the background of the people attending? (please tick)

Health care professionals

Consumers

Policymakers

Undergraduate

Postgraduate

Others

3. Marks out of ten compared with usual journal club

(10=much better, 5=same, 0 = much worse)

Free text feedback

Please return to:

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Thank you

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A full list is found on

http://szg.cochrane.org/journal-club