The Cochrane Library

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:

Quetiapine for schizophrenia - THE LEADERS GUIDE

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

from
Srisurapanont M, Maneeton B, Maneeton N. Quetiapine for schizophrenia. Cochrane Database of Systematic Reviews 2004, Issue 2. Art. No.: CD000967. DOI: 10.1002/14651858.CD000967.pub2.

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

PRINTING GUIDE

Pages 1-5 - one copy for you

Pages 6-7 - one copy for each participant - distributed at **start** of journal club

Page 8– one copy for each participant distributed at **end** of journal club

Page 9 - 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 service user arrives, 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 – service user

Introduce participants in the journal club to their scenario

39 year old single male suffering from schizophrenia has limited insight. He is from an educated middle class background and uses the internet extensively. He has been treated with various medications with no remarkable benefit. You have discussed with him the possibility of initiating Quetiapine and build the dose up to about 500mg/day. You have also sent him the summary of product characteristics and he is due to see you in clinic this afternoon to ask you further questions to assist him in making the decision whether he need to take Quetiapine or not?

Questions for participants:

Q 1. What do you think service user may ask?

A 1. [Suggestion] "Well, doc, what are my odds of getting better?"

Q 2. What do you think service user means by 'better'?

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

Q 3. Would it be okay for me to take a smaller dose?

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 service user in less than an hour you are nevertheless compelled to attend journal club.

You have not had time to read the paper and need some lunch.

By a stroke of luck the paper for discussion focuses on the value of Quetiapine.

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 the service user now arrive 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

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 *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?

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 the service user?

a. Can I apply the results to the service user?

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

b. Should I apply the results to the service user?

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

Is the intervention consistent with the service user's values and preferences?

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 1.5, providing data for 'Mental state: average change (BPRS low score = good) best fits service user's request of information about getting 'better'.

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

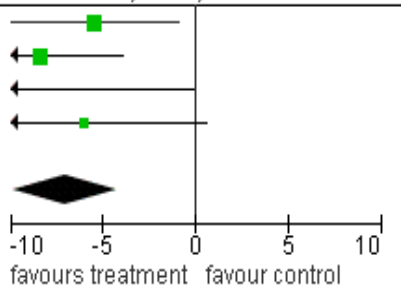
"Well, doc, what are my odds of getting better?''

Part 2.4 A quick and dirty way to work out NNT

COMPARISON 1. QUETIAPINE (any dose) versus PLACEBO (all short term data)
Outcome 1.5 Mental state. 2 Average change (BPRS low score = good)

Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Europe-USA 1994	-6.43	15.72	92	-1	15.44	92	38.8%	-5.43 [-9.93, -0.93]
North America 1996	-6.66	14.76	255	1.71	14.71	51	40.2%	-8.37 [-12.79, -3.95]
USA 1990	-20.9	8.5	8	-4.7	13.2	3	3.1%	-16.20 [-32.26, -0.14]
USA 1994	-8.1	17.4	53	-2.1	17.4	53	17.9%	-6.00 [-12.62, 0.62]
Total (95% CI)			**408**			**199**	**100.0%**	**-7.04 [-9.85, -4.24]**

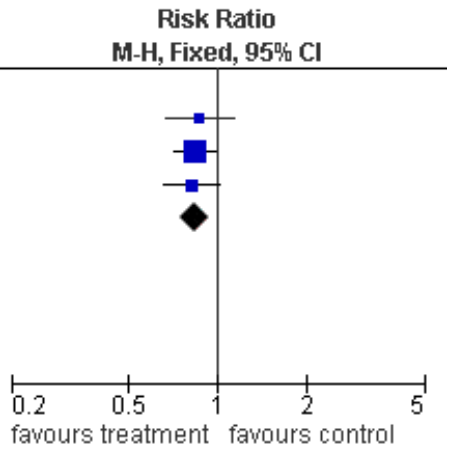
Heterogeneity: Chi² = 2.18, df = 3 (P = 0.54); I² = 0%
Test for overall effect: Z = 4.92 (P < 0.00001)



COMPARISON 2. >/=250mg/day QUETIAPINE versus <250mg/day QUETIAPINE - all short term data
Outcome 2.1 Leaving the study early

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
2.1.1 any cause						
Europe-USA 1994	48	96	54	94	18.9%	0.87 [0.67, 1.13]
Multi-country 1995	195	409	119	209	54.5%	0.84 [0.72, 0.98]
North America 1996	80	157	63	101	26.6%	0.82 [0.66, 1.01]
Subtotal (95% CI)		**662**		**404**	**100.0%**	**0.84 [0.75, 0.94]**
Total events	323		236			

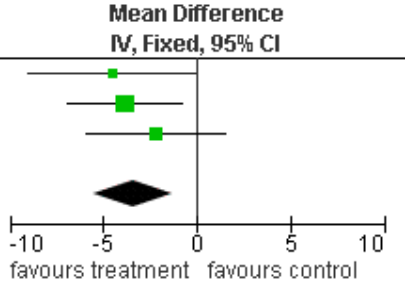
Heterogeneity: Chi² = 0.13, df = 2 (P = 0.94); I² = 0%
Test for overall effect: Z = 3.03 (P = 0.002)



COMPARISON 2. >/=250mg/day QUETIAPINE versus <250mg/day QUETIAPINE - all short term data
Outcome 2.6 Mental state: 2. Average change (BPRS, low score = good)

Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Europe-USA 1994	-8.7	15.73	92	-4.2	15.71	94	21.7%	-4.50 [-9.02, 0.02]
Multi-country 1995	-9.27	18.3	409	-5.41	18.79	209	46.1%	-3.86 [-6.96, -0.76]
North America 1996	-7.52	14.76	155	-5.33	14.77	100	32.2%	-2.19 [-5.90, 1.52]
Total (95% CI)			**656**			**403**	**100.0%**	**-3.46 [-5.57, -1.35]**

Heterogeneity: Chi² = 0.72, df = 2 (P = 0.70); I² = 0%
Test for overall effect: Z = 3.22 (P = 0.001)



Graph 2.1.1 above tells us the likelihood of the service user stop taking Quetiapine on a high dose. So, 323 people out of 662 given high dose (≥250mg/day) Quetiapine left the study early in the short term (**49%**), but 236 people out of 404 allocated to the low dose (< 250mg/day) Quetiapine left the study early in the sort term (**58%**).
So, because more people would have stopped taking Quetiapine on a lower dose, the proportion of improvement *attributable* to taking high dose, according to these results, is the difference between the groups (or 58% minus 49% = 9%). Just round up or down to make it easy. Lets say, in this case, 10%.
So 10% of people in these trials, in the short term, would continue to take Quetiapine – or put another way, 1 in 10, or put another way NNT = 10.

End on a positive note. Feedback how in a matter of minutes they have got though the bare bones of a big review, appraised and applied it - and, you hope, enjoyed doing it.

Part 2.4 A quick and dirty way to work out NNT– continued

Limitations of using this means of calculating NNT is that is does not take into account the baseline risk of the control group and does not give confidence intervals.

In this case factoring in baseline risk of the control group does make a difference.

NNT = 11(CI 7 to 29)

http://www.nntonline.net/ebm/visualrx/what.asp

Part 3. Service user arrives

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 two chairs in consultation style.

Do not call for a volunteer - just nominate someone to be the clinician and you be the service user.

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 patients may ask - use them.

Well, Doc, what are my odds of getting better?

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:

"Evidence from a Cochrane review shows that people do experience an improvement with Quetiapine within a few weeks. The effect of a higher dose is more obvious than that of a low dose and those who are on a higher dose is more likely to stay on the medication - about 1 in 10 people avoid the risk of stop taking medication "

What do YOU mean by "improvement"? 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 you would want or hope for - but there is the residing suggestion that people taking Quetiapine do get a clinical improvement in the short term that is reasonably easily recognisable. That does not necessarily mean a cure but the measures used in these studies could on the other hand have averaged up so much that they missed out on the really important detailed changes like the devil becoming quiet."

As has been said - there is no right answer and all depends on personal style and situation. Your job is to encourage the best answer out of the clinician.

If it is going well there are other questions that you may ask - see side **Box 1**.

Box 1. Additional questions

☑ **Is it better than Risperidone?**

There is no indication that one treatment is better than the other. Available evidence suggest that the effect of Risperidone and Quetiapine is equivocal in the medium term (13– 26 weeks).

☑ **How much of your salary would you put on me staying on Quetiapine in six months time?**

It may not be good practice to rise to this challenge literally - but it may be that some evidence-based deal could be arrived at with the service user. After all, data are only of 12 weeks duration. You could say that if he has not really noticed good effects by 12 weeks you would understand if he wanted to stop. To give it a consistent go up to 12 weeks does seem indicated.

☑ **What about the nasty side effects, Doc?**

Well, there are some data on movement disorder and general adverse effects reported . How do you use these limited data? Do you have to use other sources - after all small short trials are not great sources of rare important adverse effects.

CATmaker

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

The Cochrane Library

End on a positive note. Feedback how in a matter of minutes they have got though the bare bones of a big review, appraised and applied it—and, you hope, enjoyed doing it.

The Cochrane Library

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

Quetiapine 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

from

Srisurapanont M, Maneeton B, Maneeton N. Quetiapine for schizophrenia. *Cochrane Database of Systematic Reviews* 2004, Issue 2. Art. No.: CD000967. DOI: 10.1002/14651858.CD000967.pub2.

The service user ***will*** arrive soon

What do you think the service user 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.

***service user 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.

***service user arrives in 10 mins**

Can you extract numbers that will be useful to you and service user?

Clue: focus on what you think service user may ask - main effects and adverse effects - graph number '1.5 and 2.1' may be good ones to use

1. Can you put relative risk into words?

2. Does high dose of Quetiapine increase the risk of stopping medication?

3. Can you work out the number needed to treat for leaving the study early on high dose Quetiapine?

4. Can you put that into words?

Service user arrives

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

Please: Let the journal club leader know what you thought of this format. We wish to gather feedback to improve things.

The Cochrane Library

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

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Quetiapine for schizophrenia - PARTICIPANTS' CRIB SHEET

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Thank you

This is one of 40 Cochrane Schizo-phrenia Group Guides for Journal Clubs

A full list is found on

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

Quetiapine 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