



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

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Clozapine 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

Essali A, Al-Haj Haasan N, Li C, Rathbone J. Clozapine versus typical neuroleptic medication for schizophrenia. Cochrane Database of Systematic Reviews 2009, Issue 1. Art. No.: CD000059. DOI: 10.1002/14651858.CD000059.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 1-4 - 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 collect 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 Bill 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 – Bill

Introduce participants in the journal club to their scenario

Bill is a 26 year old, once good looking, intelligent man. He has had schizophrenia for 4 years, kept off illicit drugs, but only had partial response to antipsychotic medication.

At night he still screams at the devil who he feels taunts him.

Bill has some insight. He was a student of mathematics before dropping out of university, and now devotes his time to betting on horse racing.

Bill has had every adverse effect imaginable from the many antipsychotic drugs he has been given.

Bill hates psychiatrists.

Bill's parents are to accompany him today to your clinic [in 30 mins].

You have been taught that clozapine is useful for treatment-resistant schizophrenia and think that it may help Bill.

You know that Bill [and his parents] will ask very to-the-point questions.

Questions for participants:

Q 1. What do you think Bill may ask?

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

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

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

Q 3. What do you think Bill's parents will ask?

A 3. Again, list answers.



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

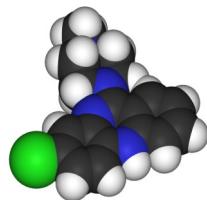
Part 1.2 Setting the scene – the Journal club

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

Knowing you are due to see Bill and his family 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 clozapine.



8-chloro-11-(4-methyl-1-piperazinyl)-5H-dibenzo(b,e)(1,4)diazepine

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 Bill?

You now have only 20 mins to get participants through 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 Bill and parents 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.

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 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 Bill?

a. Can I apply the results to Bill?

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

b. Should I apply the results to Bill?

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

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

Were all the clinically important outcomes considered?

Are the benefits worth the harms and costs?

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 if I take this stuff?"



Part 2.3 Doing the appraisal

Bill and parents now arrive in 10 mins or so.

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 re-

port 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.**

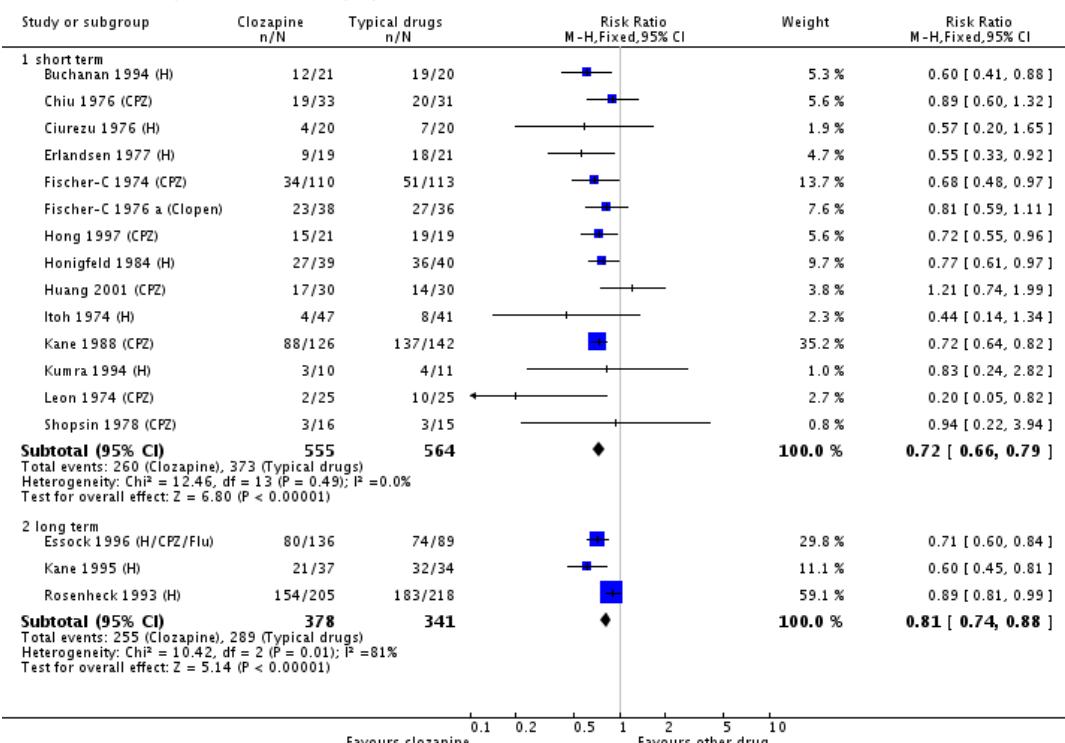
We suggest that the Graph providing data for 'Global impression: 1. Not clinically improved – for people with treatment resistant illnesses' best fits Bill's request of information about getting 'better'.

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



Part 2.4 A quick a dirty way to work out NNT

Review: Clozapine versus typical neuroleptic medication for schizophrenia
 Comparison: 1 CLOZAPINE versus TYPICAL ANTIPSYCHOTICS - OVERALL
 Outcome: 2 Global impression: 1. Not clinically improved



260 people out of 555 given clozapine were **not** clinically improved in the short term (**47%**) but 373 people out of 564 allocated to the typical drug did not improve in the sort term (**66%**).
 So, because a few people

would have got better without clozapine, the proportion attributable to taking clozapine, according to these results, is the difference between the groups (or 66% minus 47% = 19%). Just round up or down to

make it easy. Lets say, in this case, 20%. So 20% of people in these trials, in the short term, have the 'global impression of an improvement' – or put another way, 1 in 5, or put another way NNT = 5.

Part 3. Bill and his parents arrive

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 Bill.

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 Bill 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:

"The best evidence we have is from the drug companies and is imperfect - but there is the impression that, for people not too dissimilar to you, about 1 in 4 really show an improvement by only a few weeks."

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 about 1 in 4 people 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.

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 = 6, CI 5-8

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

Box 1. Additional questions

What are my odds of getting better, Doc?

You could be numerical here - after all Bill is good with numbers - but do you understand them yourselves? Can you put Relative Risk into words?

How much of your salary would you put on me getting better in the next few weeks?

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 Bill and his parents. 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 (hypersalivation, drowsiness) but few on agranulocytosis (trials of short duration - end before key risk period). 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.

Remember Bill's parents are there. They will want to know **what side effects will you give to their son?**





Special points of interest:

- The idea of this is to lead you from the clinical situation, through 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

Clozapine 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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Bill and parents will arrive soon

What do you think Bill and parents 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.

***Bill and parents arrive 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.

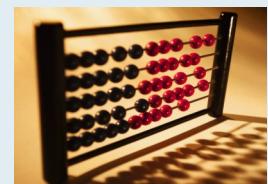
3.

*Bill parents arrives in 10 mins

Can you extract numbers that will be useful to you and Bill?

Clue: focus on what you think Bill and parents may ask - main effects and adverse effects - Analysis graph number '1.2' may be a good one to use

1. Can you put relative risk into words?



The arithmetic is not complicated

2. Can you work out the proportion of improvements attributable to use of clozapine?

3. Can you work out the number needed to treat?

4. Can you put that into words?

Bill and his parents arrive

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



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))



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

Clozapine for schizophrenia

- PARTICIPANTS' CRIB SHEET

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Please return to:
Jun Xia
Cochrane Schizophrenia Group
Division of Psychiatry
University of Nottingham
The Sir Colin Campbell Building
Jubilee Campus
Innovation Park, Triumph Road
Nottingham
NG7 2RT
UK

E-mail:
jun.xia@nottingham.ac.uk
Tel: +44 (0)115 823 1287
Fax: +44 (0)115 823 1392

Thank you

This is one of 40 Cochrane Schizophrenia Group Guides for Journal Clubs

A full list is found on

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

Clozapine 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