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Chlorpromazine versus placebo for schizophrenia - THE LEADERS GUIDE

Produced by the Editorial base of the Cochrane Schizophrenia Group
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from
Adams CE, Awad G, Rathbone J, Thornley B. Chlorpromazine versus placebo for schizophrenia. Cochrane Database of Systematic Reviews 2007, Issue 2. Art. No.: CD000284. DOI: 10.1002/14651858.CD000284.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

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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 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 Malcom 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 – Malcom

Introduce participants in the journal club to their scenario

You are due to see Malcom, who is a 43 year old gentleman suffering from schizophrenia for the last 5 years. He has tried various medications in the past, but does not seem to take them long term. In the last six months, he has not been taking any medications apart from a small dose of Chlorpromazine to help him sleep. He keeps busy with his interest in the races and discusses the Grand National with a great deal of interest. You reckon that if you spoke his language of odds and betting, you may have a better chance of getting him to take his medications. You feel that at this time increasing his dose of Chlorpromazine may be the best way forward.

Questions for participants:

Q 1. What do you think Malcom may ask?

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

Q 2. What are the risks of me becoming unwell in a year's time?

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

Q 3. What are the risks of me having nasty side effects compare to not taking any medication at all?

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

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

By a stroke of luck the paper for discussion focuses on the value of Chlorpromazine!

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 Malcom now arrives in about 20 mins.

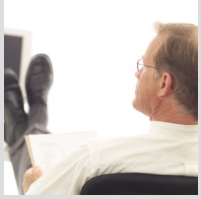
You should be able to fit most of the suggestions supplied by participants into the three categories of question outlined above.

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 Malcom?

a. Can I apply the results to Malcom?

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

b. Should I apply the results to Malcom?

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

Is the intervention consistent with Malcom'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 1.2 providing data for 'Relapse' best fits Malcom'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

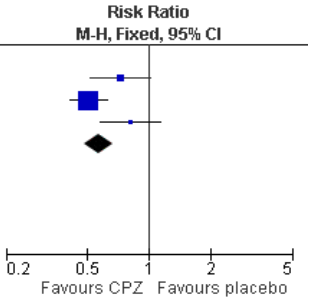
"Well, Doc, what are my odds of getting better ?"

Part 2.4 A quick and dirty way to work out NNT

Comparison: CHLORPROMAZINE versus PLACEBO
Outcome: 1.2 Relapse

Study or Subgroup	Chlorpromazine Events	Chlorpromazine Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.2.3 long term (6 months - 2 years)						
Engelhardt 1960	28	62	35	56	20.2%	0.72 [0.51, 1.02]
Hogarty 1973	70	192	131	182	74.0%	0.51 [0.41, 0.62]
Nishikawa 1982	8	10	10	10	5.8%	0.81 [0.57, 1.14]
Subtotal (95% CI)		**264**		**248**	**100.0%**	**0.57 [0.48, 0.67]**
Total events	106		176			

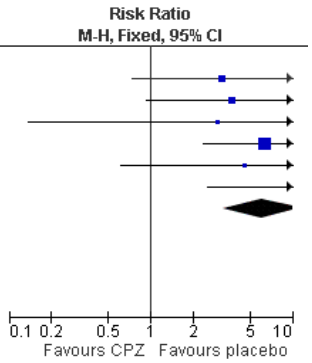
Heterogeneity: Chi² = 7.13, df = 2 (P = 0.03); I² = 72%
Test for overall effect: Z = 6.67 (P < 0.00001)



Comparison: CHLORPROMAZINE versus PLACEBO
Outcome: 1.17 Adverse effects: 3. Blood, skin, liver, eyes

Study or Subgroup	Chlorpromazine Events	Chlorpromazine Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.17.4 photosensitivity						
Clark 1971	7	23	2	21	18.5%	3.20 [0.75, 13.70]
Clark 1972	8	19	2	18	18.1%	3.79 [0.93, 15.51]
Clark 1977	1	9	0	9	4.4%	3.00 [0.14, 65.16]
Prien 1968	50	416	4	212	46.8%	6.37 [2.33, 17.40]
Serafetinides 1972	5	14	1	13	9.2%	4.64 [0.62, 34.65]
Somerville 1960	10	15	0	30	3.0%	40.69 [2.54, 650.71]
Subtotal (95% CI)		**496**		**303**	**100.0%**	**6.04 [3.22, 11.32]**
Total events	81		9			

Heterogeneity: Chi² = 3.25, df = 5 (P = 0.66); I² = 0%
Test for overall effect: Z = 5.61 (P < 0.00001)



106 people out of 264 given Chlorpromazine had relapse within two years(**40%**), but 176 people out of 248 allocated to placebo had relapse within the same period (**71%**). So, because a few people would have avoided relapse without Chlorpromazine, the proportion *attributable* to taking Chlorpromazine, according to these results, is the difference between the groups (or 71% minus 40% = 31%). Just round up or down to make it easy. Lets say, in this case, 30%. So 30% of people in these trials, in the long term, have avoided relapse – or put another way, 1 in 3, or put another way NNT = 3.

Part 3. Malcom 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 Malcom.

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 Malcom 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 a small Cochrane review - but there is the impression that, for people not too dissimilar to you, about 1in 3 manage to avoid relapse on Chlorpromazine within 2 years."

What are the risks of me having nasty side effects compare to not taking any medication at all?

Again there is no right answer but think about how to put into words what the research outcome really means. Perhaps - "there has been several trials suggesting that large dose of Chlorpromazine can cause photosensitivity. Compare to not taking any medication, people taking Chlorpromazine are 6 times more likely to develop photosensitivity.'

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 it 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 not make a difference.

NNT = 4, CI 3 to 5

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

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

Box 1. Additional questions

☑ **Do people get better on this medication? And if so, by how much?**

You could be numerical here—after all Malcom is good with numbers—but do you understand them yourselves? Can you put Relative Risk into words? Graph 1.3.1 suggests that about 1 in 5 people given Chlorpromazine do experience a global improvement by just 8 weeks.

☑ **Will I put weight on?**

There is, indeed, evidence suggesting Chlorpromazine causes weight gain. About 1 in 4 people given Chlorpromazine experience a weight gain.

☑ **Does it cause excessive sedation that will keep me away from my races?**

Unfortunately, taking Chlorpromazine is more likely to make you feel sleepy, compared to not taking any medication at all.

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.

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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

Chlorpromazine versus placebo 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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Malcom *will* arrive soon

What do you think Malcom 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.

***Malcom 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.

***Malcom arrives in 10 mins**

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

Clue: focus on what you think Malcom may ask - main effects and adverse effects - graph 1.2 may be a good one to use

1. Can you put relative risk into words?

2. Can you work out the proportion of relapse avoided *attributable* to use of Chlorpromazine?

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

4. Can you put that into words?

Malcom arrives

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

Chlorpromazine versus placebo for schizophrenia - PARTICIPANTS' CRIB SHEET

The three parts of appraising a review

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Chlorpromazine versus placebo 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

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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