

# itamin E for neurolepticinduced tardive dyskinesiaTHE LEADERS GUIDE

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

#### from

Soares-Weiser K, Maayan N, McGrath J. Vitamin E for neuroleptic-induced tardive dyskinesia. Cochrane Database of Systematic Reviews 2011, Issue 2. Art. No.: CD000209. DOI: 10.1002/14651858.CD000209.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:

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Participants crib sheet

Feedback sheet

### 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:

- ☐ 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 John 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 – John

### Introduce participants in the journal club to their scenario

John is 30 years old. He has had schizophrenia for 10 years and been treated with various antipsychotic medications. He began to develop disfiguring tardive dyskinesia quite swiftly after being changed to the newer generation drugs. His psychotic symptoms are reasonably well controlled. He is articulate and intelligent and handsome. He is greatly disfigured by the tardive dyskinesia that shows no sign of easing off over time. He has done his homework and knows there are a variety of other drugs that can be used for this condition. He does not want to change anti-psychotic treatment or modify the current dose he is on. He is coming to see you this afternoon to discuss options.



#### Questions for participants:

- Q 1. What do you think John may ask?
- A 1. [Suggestion]: "Any fantastic new treatments for tardive dyskinesia?"
- Q 2. "Any fantastic old treatments for tardive dyskinesia?"
- A 2. *List* the suggestions from participants as these are what John will come back to in the role play
- Q 3. "I have heard some places that Vitamin E could be of use, what do you think?"
- A 3. Again, list answers.



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

LIST 1:

1.

2.

3.

4.

5.

List 2:

1.

2.

3.

,

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 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 John 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 Vitamin E for tardive dyskinesia.

#### 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 service user?

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 John 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.



### 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 bottomline?

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 John?

### a. Can I apply the results to John?

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

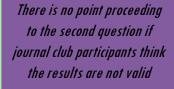
### b. Should I apply the results to John?

How great would the benefit of therapy be for John?

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

Were all the clinically important outcomes considered?

Are the benefits worth the harms and costs?





"Well Doc, what's the chances of vitamins reducing these movements?"



### 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 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 Graph
1.1 - 'Tardive dyskinesia:
1. Not improved to a
clinically important extent'
is a good one to use to
answer John's question.

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



### Part 2.4 A quick and dirty way to work out NNT

Comparison 1: VITAMIN E versus PLACEBO Outcome: 1.1 Tardive dyskinesia: 1. Not improved to a clinically important extent Vitamin F Placeho Risk Ratio Risk Ratio Study or Subgroup Events Total Events Total Weight M-H, Fixed, 95% CI M-H, Fixed, 95% CI 1.1.1 short-term Elkashef 1990 5 5 5 5 1.00 [0.71, 1.41] 4.4% Schmidt 1991 11 13 10 10 9.4% 0.86 [0.65, 1.13] Subtotal (95% CI) 18 15 13.8% 0.90 [0.73, 1.12] Total events 15 16 Heterogeneity:  $Chi^2 = 0.46$ , df = 1 (P = 0.50);  $I^2 = 0\%$ Test for overall effect: Z = 0.91 (P = 0.37) 1.1.2 medium-term Adler 1993 17 0.96 [0.75, 1.23] 15 11 12 10.3% Lam 1994 6.8% 8 8 1.00 [0.80, 1.25] Subtotal (95% CI) 25 20 17.1% 0.98 [0.82, 1.16] Total events 23 19 Heterogeneity:  $Chi^2 = 0.06$ , df = 1 (P = 0.81);  $I^2 = 0\%$ Test for overall effect: Z = 0.26 (P = 0.79) 1.1.3 long-term Adler 1999 68 73 82 85 60.7% 0.97 [0.90, 1.04] Sajjad 1998 9 9 8.3% 1.00 [0.83, 1.20] 11 11 Subtotal (95% CI) 94 84 69.0% 0.97 [0.91, 1.04] Total events 91 Heterogeneity:  $Chi^2 = 0.12$ , df = 1 (P = 0.73);  $I^2 = 0\%$ Test for overall effect: Z = 0.87 (P = 0.38) Total (95% CI) 129 100.0% 0.96 [0.90, 1.02] Total events 118 125

Above graph shows, across any period of time 118 out of 127 people had no improvement on Vitamin E (93%), this was compared to 125 people out of 129 given placebo (97%). According to these results, the difference that seems attributable to the giving of Vitamin E is a matter of about 4% (97% minus 93% = 4%). Just round up or down to make it easy. Lets say, in this case, 5%. So 5% of people in these trials seem to get some sort of improvement from Vitamin E – or put another way, 1 in 20, or put another way NNT = 20.

#### Part 3. John arrives

Heterogeneity:  $Chi^2 = 0.97$ , df = 5 (P = 0.97);  $I^2 = 0\%$ 

Test for overall effect: Z = 1.20 (P = 0.23)

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 John.

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 John may ask- use them.

#### "Any fantastic new treatment for tardive dyskinesia?"

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 how do you (and probably not for the first time to John) break the news that this very long standing adverse effect is likely to be with him for a considerable period of time?

"I have heard some places that Vitamin E could be of use, what do you think?"

Again there is no right answer but think about how to put into words what the research outcome really means. Perhaps - "the best evidence we have is from a Cochrane review, which suggests that for people not too dissimilar to you, taking Vitamin E has a slim chance of helping the tardive dyskinesia, but we are not sure. The data also do not rule out the possibility that it could even make things worse. It might be as good as about 1 in 10 people receiving some benefit, if given this treatment, or as bad as about 1 in 50 getting worse from it."

Favours vitamin F Favours control

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. As can be seen from the graph, it is also possible that Vitamin E has no effect whatsoever. The small diamond crosses the line of no effect and is compatible with a real (albeit small) effect of Vitamin E for the positive - but also for the negative.

In this case factoring in baseline risk of the control group does not make much of a difference, but considering the confidence intervals does highlight how this can be both beneficial (number needed to treat, to benefit NNTB) or harm (number needed to harm NNTH). Calculated number needed to treat 26, NNTB 11 to NNTH 52.

NNT = 26, CI (11 to 52)

http://www.nntonline.net/ebm/ visualrx/examples/statins/



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

#### **Box 1. Additional Questions**

### ✓ Well Doc, what about adverse effects?

Graph 1.6 presents outcomes on adverse events. There is no difference found between Vitamin E and placebo. Using the method we used in Part 2.4, could you put this into words quickly as regards number needed to treat?

# 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

## itamine E for neurolepticinduced tardive dyskinesia - HANDOUT FOR PARTICIPANTS

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

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### John will arrive soon

What do you think John may ask?

#### List:

- 1.
- 2.
- 3.
- 4.

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

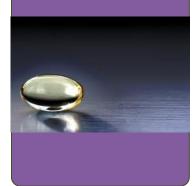
What key points do you need to know to see if this review can help?\*

- 1.
- 2.
- 3.
- 4.
- 5.

\*John arrives in 30 mins

After discussion do you want to change the key p to know to see if this review can help?*	points you need
1.	
2.	
3.	
*John arrives in 10 mins	
Can you extract numbers that will be useful to you clue: focus on what you think John may ask - main effects and adverse effects - gragood one to use	
1. Can you put relative risk into words?	
2. Can you see any improvements attributable to use of Vitamin E?	
3. Can you work out the number needed to treat?	The arithmetic is not Complicated!
4. Can you put that into words?	
John arrives Is there a good use of words you would want to use?	

## The Cochrane Library



#### Special points of interest:

- Best evidence suggests that clinically focused problembased learning "has positive effects on physician competency" even long into the future.
- 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

### itamin E for neurolepticinduced tardive dyskinesia

### - PARTICIPANTS' CRIB SHEET

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### A quick and dirty way to work out NNT (Graph 1.1)

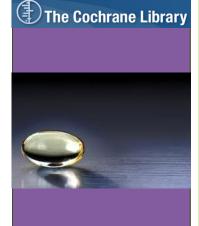
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this case, 5%.

So 5% of people in these trials seem to get some sort of improvement from Vitamin E – or put another way, 1 in 20, or put another way NNT = 20.



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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

# itamin E for neurolepticinduced tardive dyskinesiaFEEDBACK

Date and place of journal club

1. How many attended?	
About	
2. What was the background of th	ne people attending? (please tick)
Health care professionals	
Consumers	
Policymakers	
Undergraduate	
Postgraduate	
Others	
3. Marks out of ten compared wit	h usual journal club  (10=much better, 5=same, 0 = much worse)
Free text feedback	