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Dr. Cochrane

Anxiety above the clouds

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The first in this series of Dr Cochrane clinical vignettes is based upon an overview of Cochrane Reviews that was published in the previous issue of *Evidence-Based Child Health*: Manassis K, Russell K, Newton AS: **The Cochrane Library and the treatment on childhood and adolescent anxiety disorders: an overview of reviews.** *Evid-Based Child Health* 2010, **5**: 541–554.
Dr Cochrane is a unique self-learning experience – the integration of Cochrane evidence with a quirky fictional story and multiple-choice questions provides readers with the opportunity to explore and understand the applicability of a Cochrane Review or Overview in a new way.
In this series of fictional clinical vignettes, Dr Cochrane travels across time from the past century to the present day, to solve clinical problems using evidence from Cochrane Reviews. Read the associated article and/or listen to the Evidence-Based Child Health podcast available online at www.cochrane.org/podcasts/ and then test your knowledge with six multiple choice questions. You can find the answers to the questions on page 1547.
In the next issue of *Evidence-based Child Health*, Dr Cochrane explores the evidence for chronic cough, based upon the Cochrane Overview available in this issue (Russell K, Chang AB, Foisy M, Thomson D, Williams K: The Cochrane Library and the Treatment of Chronic Cough in Children: An Overview of Reviews. *Evid-Based Child Health* 2010, **5**: 1196–1205).

"Good Evening Ladies and Gentlemen! Welcome aboard this flight from London Gatwick to Rome. My name is John Graham and I'm your in-flight service manager... Please place your hand baggage in the overhead lockers...". **Dr Cochrane** was looking for his seat – a bulkhead aisle seat at the front of the aircraft – a good place to stretch his legs in peace after a long day of patient visits. He was exhausted, but looking forward to a good glass of wine in a nice restaurant in Trastevere, where he was planning to meet his colleague Franco Basaglia, a psychiatrist.

While taking his seat, **Dr Cochrane** noticed two ladies making their way through the other passengers, loaded with hand baggage and glossy magazines. They descended towards the two seats next to his, obliging him to make some uncomfortable contortions so that they could get settled. Finally, the older of the two women introduced herself, though not asked to do so. Leslie described herself as a 'young' widow from Bristol, who was planning to travel around the Mediterranean with her daughter, so she could show her the beauty of ancient cities, while also spending some time at the coast. "After the loss of my husband, I'm taking two months off to travel with my daughter. We both need rest and distraction. Something I always wanted... now with my husband's death...to travel", her sentence trailed off. In the seat beside her, Leslie's daughter Helene was a pretty adolescent with a distracted air.

"Cabin crew, please take your seats for takeoff, thank you" the captain announced. Helene was becoming increasingly restless. She focussed her attention on one of her magazines, ripping out small pieces at first, but it was not long before she was tearing whole pages. Now she was repeatedly pressing the cabin crew call button voicing: "Is the plane taking off? What happens if doesn't take off properly?" Her mother's attempts to calm her were fruitless. From the front of the aircraft a seated flight attendant was looking in their direction to see what the source of the problem was. Helene's questions were making other passengers uncomfortable. Suddenly, Helene unfastened her seat belt and stood up. The plane was about to take off. It was time to take action.

Question 1 (One correct answer)
Which of the following statements on lifetime prevalence rates of panic disorder in

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children or adolescents in industrialized countries is true?

1. Panic disorder is rare in children and adolescents (1%); onset is typically in late adolescence.
2. Panic disorder is the most common anxiety disorder diagnosed in more than 10% of children and adolescents.
3. Panic disorder occurs in fewer than 1% of children, with a slightly higher prevalence in adolescents (2–3%); onset is typically in late adolescence.
4. Panic disorder occurs in fewer than 4% of children, with a slightly higher prevalence in adolescents (8%).
5. Panic disorder is rare both in children and adolescents (1%); social phobias are more frequently diagnosed (7%).

Dr Cochrane looked Helene straight in the eyes. "Yes, the air is so thin, I can hardly breathe", he said. With one arm he touched his shirt collar to loosen his tie and with the other he gently took her arm and guided her back into her seat as he seemingly suffered his own "breathing difficulties". Helene was dumbfounded, and was immediately distracted from her own anxiety attack to help the man sitting beside her. His arms and voice were holding her attention completely. Without stopping to think that a choking man would not usually be so compliant, Helene sat down to help him with his tie. This took a few minutes, and when Helene had finished the aircraft was already in steady, level flight.

Question 2 (More than one answer may be correct)

Cochrane systematic reviews often use statistical methods to summarize and combine the results of independent studies. Some of the following statements describe the authors' intended approach to summary effect measures for outcomes.

1. For binary outcomes, the authors' preferred measure is the odds ratio because these are more consistent across studies than relative risks, although relative risks are important when interpreting findings.
2. When the same scale was used to measure the outcome, a weighted mean difference (WMD) was calculated. If the outcome was measured using a variety of scales, a standardised mean difference (SMD) was calculated.
3. For binary outcomes, the authors' preferred measure is absolute differences because these are more consistent across studies than relative risks, although relative risks are important when interpreting findings.
4. Often the continuous scores obtained using symptoms scales were dichotomized to represent responders versus non-responders, or diagnosis remitted versus diagnosis not remitted.
5. None of the above.

A flight attendant was telling Helene off for standing up during takeoff, pointing out that she nearly caused takeoff to be aborted, not to mention putting the other passengers at risk. Although she had been distracted by helping Dr Cochrane, Helene was emotionally frustrated by what had happened. The steward's tone was paternalistic and insensitive. He then asked **Dr Cochrane** "Are you her father?" Without waiting for an answer, he looked at the magazine pages on the floor "I'd like to remind you all to keep the cabin tidy. It's not your airplane, you know?" **Dr Cochrane** stared at the junior attendant and said, "I'm not her father. She came on board as a passenger but she is leaving as my patient and you are requested kindly to leave us, right now".

Dr Cochrane: "Helene, do you want to talk a little about your worries?"

Helene: "Oh well, to tell you the truth, I don't like to speak about it. It is a pain even to think about it but I have noticed you feel something similar. Sometimes when I go to the mall or to the store with my friends thoughts will pop into my head and I can't get rid of it. It's hard to concentrate or do anything else when this happens. Sometimes my breathing feels weird too... like I'm going to stop breathing... my worries can sometimes get the better of me, I guess."

Dr Cochrane: "Do you think there is something wrong with you?"

Helene: "I feel very anxious when it happens, as though my mind is doing something odd. I usually manage to get out of this kind of state on my own and, for the most part, it hasn't reared its ugly head very often until recently. Now I get the feeling several times a day that I'm not really "here"; sometimes I feel as though I'm going to pass out or die. It might be because I'm tired. It strikes without warning and makes me wonder if I'm going crazy."

The cabin became a doctor's office. Other passengers were either distracted by the in-flight entertainment or doing their own thing.

Leslie, Helene's mother, said that the panic attacks started when Helene changed to a new school a couple of years earlier. Leslie defined them as "Helene's identity crisis". Everything got worse when Helene lost her father.

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Question 3 (More than one answer may be correct)

Among children and adolescents with an anxiety disorder, is cognitive behavioural therapy (CBT) compared to wait list or active control effective in treating fears?

1. There was a significant increase in remissions in anxiety diagnosis for all CBT formats (individual and group-based) (RR=0.58; 95% CI:0.50 to 0.67).
2. The largest meta-analysis pooled 12 trials and 765 patients.
3. There was a significant difference in the loss to follow-up: CBT caused twice as many patients to abandon therapy (10%) as wait list or active control (5% for both groups).
4. For every three children or adolescents (95% CI:2.5 to 4.5) who received CBT, one child or adolescent would recover.
5. CBT was similarly effective in increasing recovery when administered in an individual, in a group, or in a family environment.

"What can we do to help Helene build self-esteem and overcome insecurity?" asked Leslie "When I was young I thought my parents did not approve of me . . .I didn't measure up to their standards for things like integrity, intelligence, and wisdom. It was similar to what Helene is experiencing now. . . but the difference is I love her, and she knows that." Helene's mother's voice trailed off.

Helene was listening to her mother who then continued: "Looking back now, I think I was suffering from depression. I lost my lust for life. Sure, I was alive and able to do everyday tasks, but I couldn't see any point in it all."

"Mom, how did you get over it?"

"I traveled with my Grandparents. . .Italy, Greece, France. It was an unforgettable summer. In Naples I met your father. . . I was older than you!"

Dr Cochrane smiled, and then asked Leslie: "It would have been in the 1990's. Did your doctor prescribe any drugs to help with your feeling so blue?"

"He did. My GP put me on paroxetine. I once stopped taking it for four days and by the fourth I was housebound – I just could not leave the house – so I made sure to always take it regularly from then on. Then I had to take something to stop my hands sweating. . . a beta-blocker. It was so embarrassing leave sweaty handprints on anything I touched. Is there something that can help Helene with her worries?"

Question 4 (One correct answer)

Among children and adolescents with an anxiety disorder, what is the effectiveness of pharmacological treatment compared to placebo?

1. When assessed using the clinical global impression (CGI-I) scale, anxiety symptoms improved significantly with selective serotonin reuptake inhibitors (SSRI; RR 0.12, 95% CI:0.05 to 0.24).
2. Compared to placebo, treatment with a SSRI significantly reduced the severity of anxiety but did not have any impact on quality of life.
3. Children and adolescents treated with a SSRI enjoyed a significant reduction in anxiety symptoms; the same population did not significantly improve with serotonin and norepinephrine reuptake inhibitor (SNRI).
4. When assessed using CGI-I scale, anxiety symptoms significantly improved with SSRI (RR 0.42, 95% CI:0.35 to 0.50); quality of life was also significantly better (SMD 0.57, 95% CI:0.35 to 0.79).
5. Children and adolescents treated with SSRI often experience total physical healing and the resolution of psychological difficulties.

Dr Cochrane: "Helene, I can prescribe you medication, but a pill will not solve all your problems. There are other things that people try with the help of a doctor. One way is cognitive behavioural therapy. Once back home, you could look for a doctor to talk about this therapy with you. It may help you pull all your thoughts together and address your worries in an effective way.

This trip may be an opportunity to think about some of the big questions you are facing. That's a great start and one you should be proud of."

Question 5 (One correct answer)

What is the effect of the CBT or BT in combination with drug-based treatments in treating childhood and adolescent anxiety disorders?

1. Compared to SSRI medication alone, CBT/BT plus SSRI medication was more effective, significantly reducing OCD symptom severity across multiple clinical measurement scales.
2. The Authors did not identify any randomized trials exploring the effectiveness of CBT/BT plus SSRI medication in comparison with placebo or SSRI medication alone.
3. Though only few studies were available, CBT combined with medication did not reduce the severity of anxiety.

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Question 5 (*Continued*)

4. The Authors cannot interpret the results because the evidence is inconclusive.
5. In this representative sample of RCTs, the authors can undoubtedly conclude that the combined treatment of CBT/BT plus SSRI medication, was significantly more effective in reducing OCD symptom severity than any single component.

After an intense discussion with Helene and Leslie, explaining the potential benefit but also the drawbacks of medication and psychological treatments for anxiety, **Dr Cochrane** said, “I’ll also give you the number and address of an Italian psychiatrist, Dr Franco Basaglia. Helene, you can continue to talk with Dr. Basaglia about these interventions for anxiety. In any case, you should call and visit him in Rome if your mood deteriorates, or if you have any problems. I’ll inform Dr Basaglia, introducing you, and ask if he would be so kind as to see you during the coming weeks.”

Question 6 (More than one answer may be correct)

In relation to anxiety disorders in children and adolescents, which of the following statements are true?

1. Anxiety is often associated with other psychiatric disorders, primarily depression.
2. Experts generally advocate offering psychological treatment first to mildly affected children, reserving pharmacological strategies for non-responsive or severely impaired children and adolescents.
3. SSRIs have been associated with an increase in suicidal thinking in young people. This risk

Question 6 (*Continued*)

should be carefully assessed, but the benefits of these antidepressants usually outweigh the risks.
4. Clinicians should warn their patients not to expect anxiety to go away completely with treatment. Despite favorable results in clinical trials, many patients may report only a small reduction in symptoms rather than complete remission.
5. Frequent monitoring of the child for beneficial and adverse effects of SSRIs is prudent, especially in the first few weeks of treatment.

“We hope you have enjoyed the flight. We are now preparing to land”. **Dr Cochrane** thought that the flight could have been quieter, but Helene and Leslie had certainly kept him occupied, with the result that they were landing sooner than he expected.

When they had disembarked Helene suddenly asked: “**Dr Cochrane**, what if I need medication sooner rather than later?” **Dr Cochrane** replied, “It’s not surprising that you’re worried about this, Helene. But, from what you’ve told me, you’ve been able to manage a lot of your worries, and I think you’ll have a lot of good things to talk about with Dr. Basaglia.” Leslie smiled at her daughter, then turned to **Dr Cochrane** “Thank you – you’ve been so kind, and I do not even remember your name... oh I’m very forgetful ...”. **Dr Cochrane** confidently adjusted his open collar: “My name is Cochrane, **Dr Cochrane**.”

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