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Early interventions to prevent psychosis: systematic review and meta-analysis

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EDITORIAL by Van Os and Murray

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STUDY QUESTION

Do any psychological, pharmacological, or nutritional interventions prevent or delay transition to psychotic disorders for people at high risk?

SUMMARY ANSWER

It may be possible to delay or to prevent psychosis; psychological and family interventions should be considered for people who present with symptoms of psychosis.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS

Schizophrenia is usually preceded by a prodromal period after which 22-44% of people at ultra high risk undergo transition to schizophrenia. This review shows that individual cognitive behavioural therapy (CBT) with or without family therapy could reduce transition rates, and that psychological interventions might have other benefits; however, there was no evidence suggesting that pharmacological interventions may benefit people who have not undergone transition.

Selection criteria for studies

We included randomised controlled trials of any intervention (pharmacological, psychological, nutritional, or combination) for participants with prodromal symptoms. We searched Embase, Medline, PreMedline, PsycINFO, and CENTRAL to November 2011 without restriction to publication status.

Primary outcome

The primary outcome was transition to psychosis. We also evaluated symptoms of psychosis (total, positive, and negative), depression, and mania; quality of life; weight; and discontinuation of treatment.

Main results and role of chance

Eleven trials including 1246 participants were included. After one year of treatment, there was moderate quality evidence that CBT reduced transition to psychosis (risk ratio 0.54 (95% confidence interval 0.34 to 0.86); risk difference −0.07 (−0.14 to −0.01)). We found very low quality evidence that omega-3 fatty acids reduced transition (0.18 (0.04 to 0.75)), very low quality evidence that integrated psychotherapy was better than supportive counselling (0.19 (0.04 to 0.81)), and low quality evidence that integrated psychotherapy was better than standard treatment (0.24 (0.07 to 0.81)).

Bias, confounding, and other reasons for caution

Most studies investigating CBT, integrated psychotherapy, and omega-3 fatty acids were at a low risk of bias, and trials of CBT provided an adequate sample size. We considered it unlikely that blinding of participants or providers would introduce any important bias. There was a high rate of attrition, but outcomes for CBT were not sensitive to different assumptions about dropouts. We found some heterogeneity between studies, including varying definitions of a "high risk mental state."

Study funding/potential competing interests

TK is codirector of the National Collaborating Centre for Mental Health, which receives £1.4 million per year from the National Institute for Health and Clinical Excellence to develop guidelines for the treatment of mental health problems. This work was conducted as part of a guideline about psychosis in children and young people, and the full review protocol is available from the authors. AM was an author of two studies included in this review.

Treatment effects on transition to psychosis at 6-12 months

Comparison	No of trials (participants)	Risk ratio (95% CI)	Quality of evidence (GRADE)
CBT *v* supportive counselling	5 (645)	0.54 (0.34 to 0.86)	Moderate*
CBT and risperidone *v* supportive counselling	2 (130)	0.63 (0.33 to 1.21)	Very low*†‡
Integrated psychotherapy *v* supportive counselling	1 (125)	0.19 (0.04 to 0.81)	Very low*†§
Integrated psychotherapy *v* standard care	1 (67)	0.24 (0.07 to 0.81)	Low*†
CBT and risperidone *v* CBT and placebo	1 (87)	1.02 (0.39 to 2.67)	Very low*†‡
Olanzapine *v* placebo	1 (60)	0.43 (0.17 to 1.08)	Very low*†‡
Omega-3 fatty acids *v* placebo	1 (81)	0.18 (0.04 to 0.75)	Low*‡

CBT=cognitive behavioural therapy.
*Reason for downgrading: imprecision.
†Reason for downgrading: risk of bias.
‡Reason for downgrading: risk of publication bias.
§Reason for downgrading: indirectness.

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Women's views on overdiagnosis in breast cancer screening: a qualitative study

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bmj.com/blogs
Tracey Koehlmoos: To screen or not to screen—mixed messages on mammography

STUDY QUESTION

How do women respond to information about the nature and extent of overdiagnosis in mammography screening?

SUMMARY ANSWER

he highest overdiagnosis rate (50%) prompted some women to think more carefully about their screening choices, whereas lower and intermediate estimates (1-10%, 30%) had limited impact on attitudes, with many women staying committed to screening.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS

Mammography screening carries a risk of overdiagnosis of breast cancer, but estimates of the level of overdiagnosis vary widely and public awareness is low. Study participants found overdiagnosis surprising, and, although most remained positive about screening, many women found the possibility of substantial overdiagnosis concerning and wanted to take this risk into account when deciding about breast cancer screening and treatment.

Rationale, design, data collection method

Improving communication about overdiagnosis requires better understanding of women's perspectives, including how views may vary depending on the amount of overdiagnosis. In a focus group study, we elicited women's responses to information about overdiagnosis in breast screening and explored how this knowledge might influence attitudes and intentions regarding screening. Each session included a presentation explaining both overdiagnosis (incorporating a range of estimates of its rate: 1–10%, 30%, 50%) and the breast cancer mortality reduction from screening.

Participants and setting

The study took place in Sydney, Australia, and involved a community sample of 50 women aged 40–79 years.

Women's responses to a rate of 50% overdiagnosis for mammography screening

May decline breast screening entirely	Example: "I probably think, 'Oh yeah, 50% is a high number, and I won't do it'" (Participant 01, age 40, 1 screen)
Seek other forms of breast cancer screening	Example: "I may think about trying another sort of way of testing or checking, because I think, 50%, it's really unreliable" (Participant 18, age 49, 0 screens)
Reconsider in light of personal risk factors	Example: "You'd have to look at your general health, your history… If I knew I had a good healthy lifestyle all along, I'd be inclined to say, 'No, I wouldn't do it'" (Participant 22, age 50, 0 screens)
Delay screening or rescreening	Example: "I may delay it a little bit more but probably not too much" (Participant 13, age 47, 0 screens)
Views unchanged – would still screen	Example: "Doesn't change anything for me. It wouldn't matter how high it was … I'd rather be safe than sorry. I think any death is one death too many" (Participant 34, age 67, 5 or more screens)

Recruitment/sampling strategy

We approached potential participants via telephone by randomly sampling households in Sydney suburbs varying in socioeconomic status. We ensured inclusion of women with different levels of education and prior screening, and excluded women who had ever been diagnosed with breast cancer.

Data analysis method

Focus group participants engaged in discussions guided by two moderators. Discussions were audio recorded, transcribed verbatim, and analysed thematically.

Main findings

Prior awareness of breast cancer overdiagnosis was minimal, and women generally reacted with surprise. However, most were able to understand the issue after our explanation. At the highest overdiagnosis estimate presented (50%), some women perceived a need for more careful personal decision making about screening (see figure). By contrast, the lower and intermediate estimates (1–10%, 30%) had limited impact on attitudes and intentions, with most women remaining committed to screening. For some women, the information raised concerns not about whether to screen but whether to treat a screen detected cancer or consider alternative approaches (such as watchful waiting). Many women found overdiagnosis important and would prefer information about it to be more widely available, but many also wanted to be encouraged to have screening.

Implications

Screening preferences were sensitive to the level of overdiagnosis, underscoring the importance of continuing efforts to clarify this. Many women would value the opportunity to make more informed choices about screening. However, information about overdiagnosis may influence both screening and treatment decisions in unintended and potentially problematic ways, highlighting the need for careful communication.

Bias, limitations, generalisability

We recruited a broad community sample of women. The focus groups did not attempt to replicate the setting of "real life" decision making about screening or to cover all potentially relevant information, but provided a way to communicate in detail about the complex and unfamiliar topic of overdiagnosis. Our presentation enabled the majority of participants to comprehend the concept of overdiagnosis, though some women displayed limited understanding.

Study funding/potential competing interests

This work was supported by grants from the Informed Medical Decisions Foundation (US) and National Health and Medical Research Council (Australia).

Effectiveness of screening and brief alcohol intervention in primary care (SIPS trial): pragmatic cluster randomised controlled trial

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STUDY QUESTION

What is the most effective brief intervention strategy to help primary care patients reduce hazardous and harmful drinking?

SUMMARY ANSWER

There was no evidence that five minutes of brief advice or 20 minutes of brief lifestyle counselling provided significant additional benefit in reducing hazardous or harmful drinking compared with feedback after screening plus a patient information leaflet focused on alcohol factors.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS

Systematic reviews have reported that screening and brief intervention can significantly reduce alcohol consumption in hazardous and harmful drinkers identified opportunistically in primary care. This study strongly suggests that screening followed by simple feedback and written information may be the most appropriate strategy in primary care.

Design

Pragmatic cluster randomised controlled trial with practices randomised to three interventions, each building on the previous one: an alcohol information leaflet control group, five minutes of structured brief advice, and 20 minutes of brief lifestyle counselling. The patient leaflet and brief advice was delivered directly after screening and brief lifestyle counselling in a subsequent consultation.

Participants and setting

Patients (n=3562) aged 18 or more routinely presenting to primary care practices in the north east and south east of England and in London. Of 2991 (84%) patients eligible to enter the trial, 900 (30.0%) screened positive for hazardous or harmful drinking and 756 (84%) consented to participate.

Primary outcomes

Patients' self reported hazardous or harmful drinking status as measured by the alcohol use disorders identification test (AUDIT) at six months; a negative AUDIT result indicated non-hazardous or non-harmful drinking. Secondary outcomes included a negative AUDIT result at 12 months.

Main results and the role of chance

83% of patients (n=644) were followed up at six months and 79% (n=617) at 12 months. At both time points an intention to treat analysis found no significant differences in AUDIT negative status between the three interventions. Compared with the alcohol information leaflet group, the odds ratio of having a negative AUDIT result was 0.85 (95% confidence interval 0.52 to 1.39) for brief advice and 0.78 (0.48 to 1.25) for brief lifestyle counselling. A per protocol analysis confirmed these findings.

Harms No adverse outcomes were reported.

Bias, confounding, and other reasons for caution

Cluster randomisation avoided the potential problems of contamination between the trial arms. However, a lack of direct monitoring of the consultations meant it was difficult to ascertain the extent to which the interventions were delivered as intended. Also only 57% of participants in the brief lifestyle counselling group actually received the intervention, which could have lessened its impact. Reduced drinking in the three interventions could have been due to a regression to the mean effect. However, levels of drinking were not particularly extreme and changes over time in our control condition were similar to those reported after brief intervention in other studies. It seems more plausible that screening, feedback, and the delivery of alcohol information contained components of behaviour change that were equivalent to the additional input of five minutes of structured brief advice.

Generalisability to other populations

This was a large pragmatic multicentre evaluation of screening and brief intervention in typical primary care conditions. High rates of patient eligibility, consent, and follow-up adds weight to the wider applicability of the findings. There was also no differential loss to follow-up between the three study interventions.

Proportions of patients with negative alcohol use disorders identification test (AUDIT) result at baseline and six and 12 month follow-up. Values are numbers (percentages) unless stated otherwise

				Odds ratio (95% CI), P value		
Time point	Patient information leaflet	Brief advice	Brief lifestyle counselling	Brief advice/patient information leaflet*	Brief lifestyle counselling/patient information leaflet*	ICC (SE)
Baseline	50/247 (20)	51/249 (21)	37/249 (15)	—	—	0.02 (0.02)
6 months	72/202 (36)	61/208 (29)	59/205 (29)	0.85 (0.52 to 1.39), 0.51	0.78 (0.48 to 1.25), 0.30	0.03 (0.02)
12 months	74/190 (39)	72/205 (35)	72/203 (36)	0.91 (0.53 to 1.56), 0.73	0.99 (0.60 to 1.62), 0.96	0.04 (0.02)

ICC=intracluster correlation coefficient.
*Odds ratio from logistic regression models adjusting for screening approach, screening tool, age, sex, and baseline AUDIT score.

Incidence of pulmonary and venous thromboembolism in pregnancies after in vitro fertilisation: cross sectional study

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STUDY QUESTION

What is the risk of pulmonary embolism and venous thromboembolism in pregnant women after in vitro fertilisation compared with age and calendar period matched control women?

SUMMARY ANSWER

In vitro fertilisation was associated with an increased risk of pulmonary embolism and venous thromboembolism during the first trimester.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS

Embolism is an important cause of maternal mortality in developed countries. We found that the risk of pulmonary and venous thromboembolism increased during the first trimester after in vitro fertilisation.

Participants and setting

23 498 Swedish women who had given birth after in vitro fertilisation between 1990 and 2008 and 116 960 individually matched women with natural pregnancies.

Design

Cross sectional study of women who had given birth after in vitro fertilisation individually matched with women identified from the Swedish medical birth register with natural pregnancies. Information on inpatient and outpatient diagnoses of pulmonary embolism and venous thromboembolism in the participants was obtained by linkage to the Swedish national patient register.

Primary outcomes

Risk of pulmonary embolism and venous thromboembolism during pregnancy.

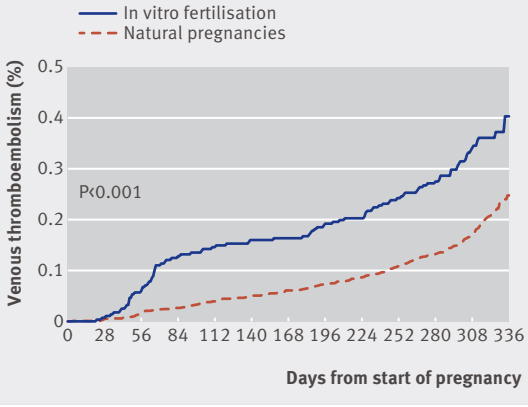
Main results and the role of chance

Venous thromboembolism occurred in 4.2/1000 (n=99) women after in vitro fertilisation compared with 2.5/1000 (n=291) matched women. The risk after in vitro fertilisation increased during the whole pregnancy (P<0.001; hazard ratio 1.77, 95% confidence interval 1.41 to 2.23) and differed between the trimesters (P=0.002). In particular the risk was increased during the first trimester (1.5/1000 *v* 0.3/1000, hazard ratio 4.05, 2.54 to 6.46). The risk of pulmonary embolism also increased during the first trimester (3.0/10 000 *v* 0.4/10 000, 6.97, 2.21 to 21.96).

Bias, confounding, and other reasons for caution

We tested the effect modification of body mass index on in vitro fertilisation in a time dependent model. There was no significant interaction. The incidence of venous thromboembolism in the control women, however, increased as expected by body mass index (P<0.001) but no such effect was found in the women after in vitro fertilisation (P=0.46). Multivariate analysis taking parity, single or multiple births, smoking, education, maternal age, country of birth, calendar period, and marital status into account was carried out on the material stratified on body mass index and restricted to women with a body mass index <30. The multivariate adjustment did not alter the significance of the main finding.

Proportional hazard regression of venousthromboembolism in pregnant women after in vitro fertilisation (n=23 498) and women with natural pregnancies (n=11 960) matched on age and calendar period of delivery



Generalisability to other populations

The study was population based comprising women who had given birth after in vitro fertilisation during two decades in Sweden. We found no indication of a decrease in the risk of thromboembolism despite a practice change over time with more patient friendly protocols, less vigorous stimulation with lower doses of gonadotropins, and a concomitant decreased rate of multiple births, favouring the generalisibility of the results. We could not, however, rule out an effect of ethnicity.

Study funding/potential competing interests

This study was funded through a regional agreement on medical training and clinical research between Stockholm County Council and Karolinska Institutet, the Swedish Research Council, and Karolinska Institutet. The sponsors had no role in study design, data collection, data analysis, data interpretation, or writing of the report. We have no competing interests.