Clinical effectiveness of collaborative care for depression in UK primary care (CADET): cluster randomised controlled trial

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- Research: Long term effect of depression care management on mortality in older adults (*BMJ* 2013;346:f2570)
- Clinical review: Depression in older adults (*BMJ* 2011;343:d5219)

STUDY QUESTION

Is collaborative care clinically more effective than usual care in the management of patients with moderate to severe depression, using primary care resources in the United Kingdom?

SUMMARY ANSWER

UK based collaborative care has persistent positive effects on depression symptoms up to 12 months after initiation of the intervention, and is preferred by patients over usual care.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS

Collaborative care is an effective model of depression management in the United States, but has uncertain effects in health systems internationally. Collaborative care in the UK improves depression immediately after treatment compared with usual care, with positive effects at 12 month follow-up.

Design

Cluster randomised controlled trial of collaborative care versus usual care, with remote randomisation and allocation concealment of primary care practices, minimised by Index of Multiple Deprivation (IMD) rank, number of general practitioners, and practice size.

Participants and setting

Adults aged 18 years and older who met ICD-10 (international classification of diseases, 10th revision) criteria for a depressive episode were eligible. Participants were allocated to collaborative care (n=276) or usual care (n=305), conducted in UK primary care. Collaborative care—including depression education, drug management, behavioural activation, relapse prevention, and primary care liaison—was delivered by care managers over 14 weeks. Usual care was family doctors' standard clinical practice.

Primary outcome

Depression severity in individual participants, measured by the patient health questionnaire 9 (PHQ-9) at four month follow-up.

Main results and the role of chance

Mean depression score at four months was 1.33 PHQ-9 points lower in the collaborative care group than the usual care group, after adjustment for baseline depression (table). More participants receiving collaborative care than usual care met criteria for recovery (number needed to treat 8.4) and response (7.8). At 12 month follow-up, the mean PHQ-9 score was 1.36 points lower (95% confidence interval 0.07 to 2.64, P=0.04) in collaborative care than in usual care (standardised effect size 0.26 (0.01 to 0.52)). At 12 months, more participants in collaborative care than in usual care also met criteria for recovery (number needed to treat 6.5) and response (7.3).

Harms

None.

Bias, confounding, and other reasons for caution

Although our results accord with findings reported in recent international trials, their clinical implications are more difficult to interpret. The average difference in treatment response (0.26) was less than what we had expected (0.4), but these more modest differences were sustained over the longer term with 15% more participants recovered in collaborative care compared to usual care at 12 month follow up. The cluster design avoided contamination of the usual care arm by testing for changes in behaviour in the collaborative care arm. Potential selection bias in cluster trials was minimised by recruiting participants through electronic case note searches rather than doctor referral. Self reported outcome measures were used to minimise detection bias, given the impossibility of blinding healthcare providers and participants and consequent risk of unblinding outcome assessors. And because our intervention was brief, a longer intervention might have improved outcomes further.

Generalisability to other populations

The Clinical and Cost Effectiveness of Collaborative Care for Depression in UK Primary Care Trial (CADET) has established the portability of collaborative care outside its US origins.

Study funding/potential competing interests

This study was funded by the UK Medical Research Council (MRC; reference G0701013), managed by the National Institute for Health Research (NIHR) on behalf of the MRC-NIHR partnership. DAR receives funding support from NIHR Collaborations for Leadership in Applied Health Research and Care. We declare no other interests.

Trial registration number ISRCTN32829227.

Primary outcome and rates of recovery and response

	Collaborative care		Usual care		Adjusted difference/odds ratio* (95% CI)	P	Effect size/ No needed to treat*
	No of participants	Outcome	No of participants	Outcome			
Primary outcome: mean (standard deviation) PHQ-9 score							
Baseline	276	17.4 (5.2)	305	18.1 (5.0)	—	—	—
4 months	230	11.1 (7.3)	275	12.7 (6.8)	−1.33 (−2.31 to −0.35)	0.009	0.26
Recovery: No (%) of participants with PHQ-9 score ≤9 at follow-up							
4 months	230	108 (47.0)	275	96 (34.9)	1.67 (1.22 to 2.29)	0.001	8.4
12 months	235	131 (55.7)	263	106 (40.3)	1.88 (1.28 to 2.75)	0.001	6.5
Response: No (%) of participants with ≥50% reduction in PHQ-9 score at follow-up *v* PHQ-9 score at baseline							
4 months	230	99 (43.0)	275	83 (30.2)	1.77 (1.22 to 2.58)	0.003	7.8
12 months	235	115 (48.9)	263	93 (35.4)	1.73 (1.22 to 2.44)	0.002	7.3

*Adjusted difference and effect size applies to primary outcome; odds ratio and number need to treat applies to recovery and response rates.

Use of antidepressants near delivery and risk of postpartum hemorrhage: cohort study of low income women in the United States

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Research: Parental depression, maternal antidepressant use during pregnancy, and risk of autism spectrum disorders (*BMJ* 2013;346:f2059)

STUDY QUESTION

Is use of serotonin and non-serotonin reuptake inhibitors near delivery associated with an increased risk of postpartum hemorrhage?

SUMMARY ANSWER

Exposure to antidepressants near delivery is associated with an increased risk of postpartum hemorrhage.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS

Use of serotonin reuptake inhibitor antidepressants is associated with an increased risk for gastrointestinal bleeding. Our study suggests that use of antidepressants near the time of delivery is also associated with an increased risk of postpartum hemorrhage.

Participants and setting

Pregnant women enrolled in Medicaid in 2000-07, aged 12-55, with a diagnosis of mood or anxiety disorder.

Design, size, and duration

This cohort study included 106 000 pregnant women with Medicaid claims data. Women were categorized into four mutually exclusive exposure groups according to pharmacy dispensing data: current (delivery date), recent (1-30 days before delivery date), past (1-5 months before delivery date), and no (reference group) exposure to antidepressants. We compared the risk of postpartum hemorrhage by timing of exposure and by serotonin or non-serotonin reuptake inhibitors, antidepressant classes, and antidepressant types. Relative risks and 95% confidence intervals were adjusted for delivery year, risk factors for hemorrhage, severity indicators for mood/anxiety disorder, other indications for antidepressants, and other drugs. We also used high dimensional propensity score (hdPS) methods to empirically identify and adjust for additional factors.

Main results and the role of chance

There were 12 710 (12%) women with current exposure to a serotonin reuptake inhibitor and 1495 (1.4%) with current exposure to a non-serotonin reuptake inhibitor. Among women with mood/anxiety disorders, the risk of hemorrhage ranged from 2.8% in women with no exposure to antidepressants to 2.5-4.0% in the women with exposure during pregnancy, depending on class of drug and timing of exposure. Women who were taking serotonin or non-serotonin reuptake inhibitors at the time of delivery had an increased risk of postpartum hemorrhage, and results were similar after adjustment for high dimensional propensity score. For women with current exposure, the adjusted excess risk was 1.26% (number needed to harm of 80) for serotonin reuptake inhibitors and 1.03% (number needed to harm of 97) for non-serotonin reuptake inhibitors.

Current treatment with a selective serotonin reuptake inhibitor, a serotonin norepinephrine (noradrenaline) reuptake inhibitor, or a tricyclic was associated with increased risk (1.42, 1.27 to 1.57), 1.90 (1.37 to 2.63), and (1.77, 0.90 to 3.47), respectively). All types of selective serotonin reuptake inhibitors available for analysis and venlafaxine, a serotonin norepinephrine reuptake inhibitor, were significantly associated with risk.

Bias, confounding, and other reasons for caution

Results could reflect residual confounding by unmeasured behavioral factors associated with depression and use of antidepressants, including inadequate diet and tobacco, alcohol, and illegal drugs. Misclassification of exposure was possible because we could not confirm that women were taking antidepressants on the days we assumed. This could attenuate the true association. Outcome misclassification is another source of bias that could result in an underestimation of a true association.

Generalizability to other populations

Unless there are important effect modifiers that we did not identify, we anticipate that the results will generalize to other populations with a similar baseline risk for postpartum hemorrhage.

Fully adjusted* relative and excess risks for postpartum hemorrhage in pregnant women exposed to antidepressants in pregnancy

Exposure group	Total	No (%) of women with hemorrhage	Relative risk (95% CI)*	Excess risk (95% CI)*
Serotonin reuptake inhibitor monotherapy:				
Current	12 710	503 (4.0)	1.47 (1.33 to 1.62)	1.26% (0.90% to 1.62%)
Recent	6096	196 (3.2)	1.19 (1.03 to 1.38)	—
Past	10 416	264 (2.5)	0.93 (0.82 to 1.06)	—
Non-serotonin reuptake inhibitor monotherapy:				
Current	1495	56 (3.8)	1.39 (1.07 to 1.81)	1.03% (0.07% to 1.99%)
Recent	829	26 (3.1)	1.17 (0.80 to 1.70)	—
Past	2132	73 (3.4)	1.26 (1.00 to 1.59)	—
Unexposed	69 044	1896 (2.8)	Reference	—

*Delivery year, age, race, multiple pregnancy, diabetes, coagulopathy, number of outpatient mood/anxiety disorder diagnoses, number of inpatient mood/anxiety disorder diagnoses, psychotic disorder, other mental health disorder, pain indication, sleep disorder, anticonvulsant dispensing, benzodiazepine dispensing, aspirin dispensing, heparin dispensing, low molecular weight heparin dispensing, warfarin dispensing, and number of outpatient visits and days in hospital during baseline.

Study funding/potential competing interests

The authors received funding from the Agency for Healthcare Research and Quality (AHRQ), the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD), National Institutes of Health. The pharmacoepidemiology program at the Harvard School of Public Health and the authors have received funding and financial remuneration from Pfizer, Asisa, GSK, Novartis, the National Institute on Alcohol Abuse and Alcoholism (NIAAA), the National Institute of Mental Health (NIMH), the National Institute on Drug Abuse (NIDA), Otsuka, Janssen, Pine Rest Foundation, University of Chicago, Michigan State University, AssureRx, and Priority Health. Full details are on bmj.com.

Unhealthy behaviours and disability in older adults: Three-City Dijon cohort study

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- Research: Lifestyle, social factors, and survival after age 75 (*BMJ* 2012;345:e5568)
- Research: Combined impact of lifestyle factors on mortality (*BMJ* 2008;337:a1440)

STUDY QUESTION

What is the relation between unhealthy behaviours, with each behaviour examined separately and in combination, and the hazard of disability?

SUMMARY ANSWER

An unhealthy lifestyle (physical inactivity, unhealthy diet, smoking) was associated with a greater hazard of disability in a cohort of French older people followed for 12 years.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS

Some evidence shows that unhealthy behaviours are associated with an increased hazard of disability in older people, but their independent contribution remains unclear. Low/intermediate physical activity, a diet poor in fruit and vegetables, and smoking (current smokers and recent quitters) were independently associated with an increased hazard of disability; people with all three unhealthy behaviours had more than a twofold increased hazard of disability compared with people without unhealthy behaviours.

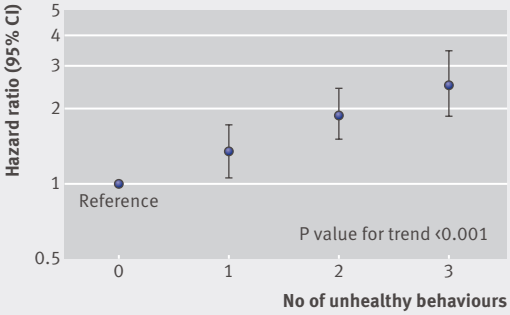
Participants and setting

We studied French community dwellers aged 65 or above included in 1999-2001 in the Dijon centre (France) of the Three-City (3C) study.

Design, size, and duration

We followed 3982 participants, free of disability at baseline, for a maximum of 12 years. Health behaviours were assessed at baseline. The main outcome was a hierarchical indicator of disability (none, light, moderate, severe) combining information from three disability scales (mobility, instrumental activities of daily living, basic activities of daily living) assessed five times in 2001-12.

Hazard ratios of disability according to number of unhealthy behaviours*



*Low/intermediate physical activity, consumption of fruits and vegetables less than once a day, current smoking or short term ex-smoking

Main results and the role of chance

Of the 3982 participants, 1236 (861 (69.7%) women) developed moderate/severe disability. Interval censored survival analyses (adjusted for age, sex, marital status, and education) showed low/intermediate physical activity (hazard ratio 1.72, 95% confidence interval 1.48 to 2.00), consuming fruit and vegetables less than once a day (1.24, 1.10 to 1.41), and smoking (current smokers and recent quitters) (1.26, 1.05 to 1.50) to be independently associated with an increased hazard of disability. We found no robust association with alcohol consumption. The hazard of disability increased progressively with the number of unhealthy behaviours. For the score of unhealthy behaviours, 30.5% of the association with disability was explained by time dependent mediators (body mass index, cognitive function, depressive symptoms, trauma, chronic conditions, cardiovascular disease and its risk factors); the main contributors were chronic conditions and, to a lesser extent, depressive symptoms, trauma, and body mass index.

Bias, confounding, and other reasons for caution

Associations between unhealthy behaviours and disability remained present after exclusion of events that occurred during the first four years of follow-up, ruling out reverse causation as a major explanation. We used a statistical method to account for the interval censored nature of the outcome and competing risks of death. Potential reasons for caution include the self reported nature of the outcome (disability) and exposures (unhealthy behaviours) and the risk of misclassification of exposure due to the relatively simple questions used to define unhealthy behaviours.

Generalisability to other populations

The 3C cohort was volunteer based and is not representative of the general population over age 65. Although this may lead to underestimation of the incidence of disability, provided that follow-up is adequate the association between baseline exposures and the incidence of an outcome is unlikely to be biased.

Study funding/potential competing interests

The 3C study is conducted under a partnership agreement between INSERM, Victor Segalen-Bordeaux II University, and Sanofi-Synthélabo and is supported by FRM, CNAMTS, DGS, HAS, INPES, MGEN, Conseils Régionaux de Bourgogne, Fondation de France, Ministère de la Recherche, Institut de la Longévité, Conseil Général de la Côte d'or, and Fondation Plan Alzheimer. FA is the recipient of a doctoral grant from the Ministère de l'Enseignement Supérieur et de la Recherche and the EHESP (Ecole des Hautes Etudes en Santé Publique).

Performance of English stop smoking services in first 10 years: analysis of service monitoring data

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- Research: Nortriptyline plus nicotine replacement versus placebo plus nicotine replacement for smoking cessation (*BMJ* 2008;336:1223)
- Research: Effectiveness and safety of nicotine replacement therapy assisted reduction to stop smoking (*BMJ* 2009;338:b1024)

STUDY QUESTION

How well have the English stop smoking services performed in the 10 years since 2001, in terms of numbers treated, success rates, and estimated numbers of ex-smokers created?

SUMMARY ANSWER

The services have had a substantial and increasing impact in helping smokers to stop, treating 8% of smokers in 2010/11, with estimates suggesting that more than 20 000 smokers were helped to stop long term, saving some 25 000 life years, and successfully reaching disadvantaged groups.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS

The English stop smoking services have been successful in recruiting large numbers of smokers. The services have trebled their estimated impact in terms of numbers of smokers led to stop by increasing the numbers treated with only a small decline in the success rates, but substantial variability exists between local services.

Participants and setting

Data came from national monitoring of smokers offered free behavioural support and medication (on prescription) through stop smoking services in England between April 2001 and March 2011.

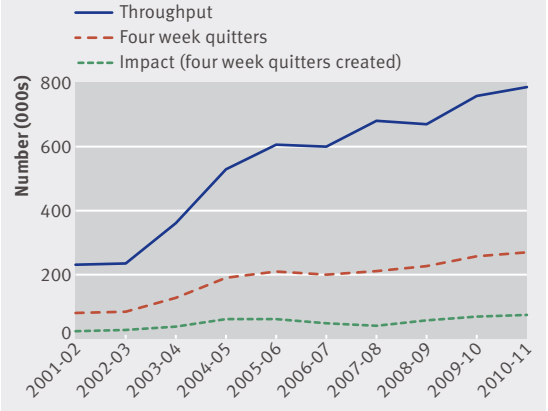
Design

This was an analysis of national service monitoring data.

Primary outcomes

We obtained annual figures for the number of quit dates set (throughput) and the percentage of these leading to biochemically verified abstinence after four weeks (four week quit rate). We used these to calculate "impact" in terms of the number of four week quitters beyond those who would be estimated to have stopped with only a prescription for smoking cessation medication, by multiplying the four week success rate in smokers trying to stop unaided by the rate ratio of 1.6 attributable to medications from Cochrane reviews. We assessed variability across local services in throughput, four week quit rates, and impact for 2010/11. We used known relapse curves to estimate numbers of long term ex-smokers generated.

Annual number of quit dates set in English stop smoking services 2001/02 to 2010/11



Main results and the role of chance

Throughput rose from 227 335 in 2001/02 to 787 527 (8% of all smokers) in 2010/11. The percentage of those attending who were four week quitters declined slightly from 35% to 34%. Impact rose from 22 933 four week quitters created in 2001/02 to 72 411 in 2010/11 (corresponding to an estimated 21 723 quitters at 12 months). The services were successful in reaching disadvantaged smokers; 54% (n=425 684) were in receipt of free prescriptions in 2010/11. We found substantial variation across local services in throughput, success rates, and impact

Bias, confounding, and other reasons for caution

Estimates of throughput and success rates are dependent on stop smoking services accurately reporting their data. Some variability between local services could be due to differences in the characteristics of their local populations.

Generalisability to other populations

Over the period of study, England had a comprehensive, integrated National Health Service funded by taxation and a strong tobacco control climate. Monitoring performance closely following fundamental changes taking place to the funding and delivery of healthcare will be important.

Study funding/potential competing interests

The study was funded by the National Centre for Smoking Cessation and Training (NCSCT). RW and AMcE are funded by Cancer Research UK and are directors of the NCSCT. RW, MW, AMcE have shares of a patent for a novel nicotine delivery device. RW undertakes research and consultancy for companies that develop and manufacture smoking cessation medications. EC previously worked at the English Department of Health as the delivery lead for tobacco control policy; has received travel funding, honorariums, and consultancy payments from manufacturers of smoking cessation products; and receives royalties from a book on smoking cessation and a book on health promotion. AMcE has received travel funding, honorariums, and consultancy payments from manufacturers of smoking cessation products; receives payment for providing training to smoking cessation specialists; and receives royalties from books on smoking cessation.