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Comparison of fluoroscopically guided and blind corticosteroid injections for greater trochanteric pain syndrome: multicentre randomised controlled trial

Steven P Cohen,[1,2] Scott A Strassels,[3] Leslie Foster,[4] John Marvel,[5] Kayode Williams,[5] Matthew Crooks,[5] Andrew Gross,[6] Connie Kurihara,[2] Cuong Nguyen,[7] Necia Williams[8]

EDITORIAL by Bahr and Khan

[1]Departments of Anesthesiology and Critical Care Medicine, Johns Hopkins School of Medicine, Baltimore, MD, USA
[2]Walter Reed Army Medical Center, Washington, DC, USA
[3]Division of Pharmacy Practice, University of Texas at Austin, Austin, TX, USA
[4]Department of Orthopedic Surgery, Walter Reed Army Medical Center
[5]Department of Anesthesiology, Johns Hopkins School of Medicine
[6]Department of Anesthesiology, Emory University School of Medicine, Atlanta, GA, USA
[7]Physical Medicine and Rehabilitation Service, Department of Surgery, Landstuhl Regional Medical Center, Landstuhl, Germany
[8]Integrated Anesthesia Services, Walter Reed Army Medical Center and National Naval Medical Center, Bethesda, MD
Correspondence to: S P Cohen, 550 North Broadway, Suite 301, Baltimore, MD 21029
scohen40@jhmi.edu

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ABSTRACT

Objective To determine whether fluoroscopic guidance improves outcomes of injections for greater trochanteric pain syndrome.

Design Multicentre double blind randomised controlled study.

Setting Three academic and military treatment facilities in the United States and Germany.

Participants 65 patients with a clinical diagnosis of greater trochanteric pain syndrome.

Interventions Injections of corticosteroid and local anaesthetic into the trochanteric bursa, using fluoroscopy (n=32) or landmarks (that is, "blind" injections; n=33) for guidance.

Main outcome measures Primary outcome measures: 0-10 numerical rating scale pain scores at rest and with activity at one month (positive categorical outcome predefined as ≥50% pain reduction either at rest or with activity, coupled with positive global perceived effect). Secondary outcome measures included Oswestry disability scores, SF-36 scores, reduction in drug use, and patients' satisfaction.

Results No differences in outcomes occurred favouring either the fluoroscopy or blind treatment groups. One month after injection the average pain scores were 2.7 at rest and 5.0 with activity in the fluoroscopy group compared with 2.2 and 4.0 in the blind injection group. Three months after the injection, 15 (47%) patients in the blind group and 13 (41%) in the fluoroscopy group continued to have a positive outcome.

Conclusion Although using fluoroscopic guidance dramatically increases treatment costs for greater trochanteric pain syndrome, it does not necessarily improve outcomes.

Trial registration Clinical trials NCT00480675.

INTRODUCTION

Greater trochanteric pain syndrome is a common condition with a lifetime prevalence exceeding 20%; it occurs more frequently in women, older people, and people with low back pain.[1-5] Corticosteroid injections can provide considerable relief in most patients who fail to respond to conservative treatment.[2 6-9] Only a few studies evaluating the efficacy of corticosteroid injections have been published, none of which was controlled or used fluoroscopy or other imaging techniques. The average success rate in these studies ranged between 50% and 70%, with follow-up ranging between two weeks and two years.[4 6 7 10 11] An observational study of "blind" trochanteric bursa injections found that intra-bursal spread of contrast occurred in only 45% of landmark guided trochanteric bursa injections.[12] The authors concluded that fluoroscopic guidance is necessary to ensure placement of the needle within the bursa. However, this study did not assess outcomes.

To determine whether fluoroscopy should be routinely used during trochanteric bursa corticosteroid injections, we did a multicentre, randomised controlled study comparing fluoroscopically guided and blind procedures.

METHODS

The trial took place between January 2007 and March 2008 at Johns Hopkins Medical Institutions, Walter Reed Army Medical Center, and Landstuhl Regional Medical Center, a US military treatment facility operating in Landstuhl, Germany. Inclusion criteria included pain of more than three months' duration, spontaneous pain in the lateral aspect of the hip, tenderness overlying the greater trochanter, and one of the following three minor diagnostic criteria: increased pain with extremes of rotation, abduction, or adduction; pain with forced hip abduction; and pseudoradicular pain extending down the lateral aspect of the thigh.

Randomisation and treatment

Participants were randomised to receive either fluoroscopically guided or landmark guided (that is, "blind") trochanteric bursa injections. In the blind injection group a "sham" cross table antero-posterior image of the femur was taken to facilitate blinding. Using only landmarks for guidance, the physician inserted a spinal needle into the suspected bursa, injected 0.5 ml of

contrast and took a true antero-posterior image to determine whether the contrast was within one of the subgluteus maximus or subgluteus medius trochanteric bursas. The physician injected a 4 ml solution containing 60 mg of depo-methylprednisolone and 2.5 ml of 0.5% bupivacaine regardless of whether the contrast entered the bursa. For patients in the fluoroscopy group, the same solution was injected when the image revealed intra-bursal spread.

Outcome measures and follow-up

All patients were seen one month after the procedure. Patients who had a positive global perceived effect and significant (≥50%) pain relief obviating the need for further treatment were re-evaluated three months post-treatment. Patients who did not have adequate pain relief one month after the procedure left the study to receive alternative medical care. The two main questions we sought to answer were whether fluoroscopically guided trochanteric bursa injections were superior to "blinded" injections and whether intra-bursal injections were better than extra-bursal injections.

The primary outcome measures were pain scores on a 0-10 numerical rating scale at rest and with activity one month post-injection. Secondary outcome measures were the SF-36, Oswestry disability index, reduction in drug use (predefined as a 20% reduction in opioid use or complete cessation of a non-opioid analgesic),[13] global perceived effect, and a composite "successful outcome." We designated the variable "successful outcome" before the start of the study as a reduction of at least 50% in numerical rating scale pain score either at rest or with activity and a positive global perceived effect obviating the need for further interventions.

RESULTS

Overall, neither baseline differences between study centres nor those between injection method groups were statistically significant. Most patients were women, in their mid-50s, not obese, and not using opioid analgesics. Patients randomised to receive a blind injection reported a mean duration of pain of 4.4 years, whereas those allocated to receive fluoroscopically guided injections had had pain for an average of 3.3 years. Average pain intensity at rest was moderate, but it increased to severe with activity. Baseline ability to function was severely limited in the blind injection group and moderately limited in the fluoroscopic group, although the between group differences were small.

In the fluoroscopy group, 12 of 32 injections entered the bursa on the first attempt compared with 12 of 33 in the landmark guided treatment group, for an overall accuracy rate of 37%. In the overall cohort, 39 (61%) of the 64 patients experienced a positive categorical outcome at one month and therefore remained in the study. At three months, 28 (44%) participants continued to report substantial relief coupled with a positive global perceived effect; we found no significant differences between treatment groups.

For the SF-36 scales, the only statistically significant difference between injection methods was in the mental health scale at the one month follow-up; patients who received a blind injection reported slightly better scores (see bmj.com). When examined by success at three months, the clinical and demographic characteristics of the study participants were similar.

The table shows outcomes by method of injection. For the primary outcome measure, the mean hip pain score at rest declined from 5.1 to 2.7 (P=0.0001) in the fluoroscopically guided injection group and from 4.6 to 2.2 (P=0.0001) in the blind injection group. With respect to activity related pain intensity, scores in the fluoroscopy group fell from 7.8 to 5.0 (P<0.0001) at one month, which was comparable to the improvement found in the blind injection group (decrease from 7.2 to 4.0; P<0.0001). Other differences between the injection method groups also failed to reach statistical significance, apart from a greater decrease in disability among patients who received blind injections. When examined by location of injection, no significant differences existed between the intra-bursal and extra-bursal groups.

Outcomes stratified by injection method. Values are numbers (percentages) unless stated otherwise

Outcome	Blind	Fluoroscopically guided	P value
Overall success:	(n=32)	(n=32)	
None	10 (31)	15 (47)	0.38
At 1 month only	7 (22)	4 (13)	
At 3 months	15 (47)	13 (41)	
Mean (SD, range) pain intensity* at 1 month:	(n=32)	(n=32)	
Rest	2.2 (2.4, 0-10)	2.7 (2.5, 0-9)	0.41
Activity	4.0 (2.6, 0-10)	5.0 (2.9, 0-10)	0.16
Mean (SD, range) pain intensity* at 3 months:	(n=22)	(n=16)	
Rest	2.6 (2.5, 0-7.5)	1.9 (1.7, 0-6)	0.34
Activity	4.8 (2.6, 0-10.0)	4.7 (2.8, 0-10)	0.90
Mean (SD, range) Oswestry disability index at 1 month†	32.1 (15.2, 0-60)	32.3 (17.4, 0-66)	0.96
Mean (SD, range) Oswestry disability index at 3 months†	31.7 (15.1, 6-64)	33.6 (13.6, 14-60)	0.69
Positive global perceived effect at 3 months‡:	(n=32)	(n=32)	
No	15 (47)	16 (50)	0.80
Yes	17 (53)	16 (50)	
Reduction in drug use at 3 months:	(n=19)	(n=15)	
No	11 (58)	10 (67)	0.60
Yes	8 (42)	5 (33)	

*Numerical rating pain scale.
†Lower Oswestry disability index indicates better functioning.
‡Failed treatment at one month carried over as negative global perceived effect at three months.

WHAT IS ALREADY KNOWN ON THIS TOPIC

Trochanteric bursa injections have been shown to reduce pain and disability for patients with clinical bursitis

Although no standard exists for giving bursa injections, a recent study found that only a minority of non-fluoroscopically guided injections end up in the bursa

WHAT THIS STUDY ADDS

Referring patients for fluoroscopically guided injections, which increases treatment costs by more than 600%, does not necessarily improve outcomes

DISCUSSION

The principal finding of this study suggests that the use of fluoroscopy does not improve outcomes in patients with greater trochanteric pain syndrome who receive corticosteroid injections. This is consistent with our secondary finding showing comparable success rates for intra-bursal and extra-bursal injections. The results from this pilot study should not be surprising considering that most patients clinically diagnosed as having greater trochanteric pain syndrome have no radiological evidence of bursal inflammation.[14 15]

Our results suggest that referral to a pain specialist with fluoroscopic capability is not warranted in most patients with greater trochanteric pain syndrome. The delay in treatment entailed by referral to a subspecialty may even be detrimental, as previous interventional studies have found an inverse relation between duration of pain and likelihood of success.[16-18] Patients who fail "blind" trochanteric bursa injections and those with radiological evidence of bursal inflammation, however, may benefit from referral to a pain treatment centre, as this study (37% accuracy rate) and a previous one found that injections guided by landmarks alone are unlikely to diffuse into the bursa.[12] On the basis of current third party reimbursement codes for the 10 most recent procedures done at Johns Hopkins, the cost for a subspecialty consultation and subsequent procedure using fluoroscopy (including facility fees) is $1216 (£843; €897), compared with $188 if the procedure is done during an office visit.

An examination of the relative strengths and weaknesses of this study is needed to put the results in context. Firstly, this is the only controlled study that has evaluated trochanteric bursa injections. Secondly, our outcomes are less positive than several others reported for trochanteric bursa injections.[6 7] However, all previous studies evaluating trochanteric bursa injections were unblinded and uncontrolled.

Another concern about this study stems from the fact that only 39 of the 65 participants had outcome data recorded at three months. Not carrying over one month treatment failures limits the long term conclusions on efficacy and differences between treatment groups that can be reached from these results.

Conclusions

Fluoroscopically guided trochanteric bursa injections were not associated with superior outcomes to injections guided by landmarks alone in patients who presented with clinical greater trochanteric pain syndrome. Referral to a pain treatment centre should be reserved for patients with greater trochanteric pain syndrome who fail landmark guided injections and conservative treatment.

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Competing interests: None declared.
Ethics approval: Internal review boards at Johns Hopkins and Walter Reed Army Medical Center gave approval for the study. Landstuhl Regional Medical Center fell under the jurisdiction of Walter Reed Army Medical Center. All patients gave informed consent.

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Social deprivation and prognostic benefits of cardiac surgery: observational study of 44 902 patients from five hospitals over 10 years

D Pagano,[1] N Freemantle,[2] B Bridgewater,[3] N Howell,[1] D Ray,[1] M Jackson,[4] B M Fabri,[5] J Au,[6] D Keenan,[7] B Kirkup,[8] B E Keogh,[9,8] on behalf of the Quality and Outcomes Research Unit (QuORU) UHB Birmingham and the North West Quality Improvement Programme in Cardiac Interventions (UKNWQIP)

EDITORIAL by Denvir and Zamvar

[1]Cardiothoracic Surgical Unit, University Hospital Birmingham Foundation Trust, Queen Elizabeth Hospital, Birmingham B15 2TH
[2]School of Health and Population Sciences, University of Birmingham, Edgbaston, Birmingham B15 2TT
[3]Department of Cardiothoracic Surgery, South Manchester University Hospital, Manchester M23 9LT
[4]Department of Clinical Quality, Liverpool Heart and Chest Hospital NHS Trust, Liverpool L14 3PE
[5]Department of Cardiothoracic Surgery, Liverpool Heart and Chest Hospital NHS Trust, Liverpool
[6]Department of Cardiothoracic Surgery, Blackpool Victoria Hospital, Blackpool FY3 8NR
[7]Department of Cardiothoracic Surgery, Manchester Royal Infirmary, Manchester M13 9WL
[8]Department of Health, London SW1A 2NS
[9]University College Hospital, London W1G 8PH
Correspondence to: D Pagano
domenico.pagano@uhb.nhs.uk

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ABSTRACT

Objective To assess the effects of social deprivation on survival after cardiac surgery and to examine the influence of potentially modifiable risk factors.

Design Analysis of prospectively collected data. Prognostic models used to examine the additional effect of social deprivation on the end points.

Setting Birmingham and north west England.

Participants 44 902 adults undergoing cardiac surgery, 1997-2007.

Main outcome measures Social deprivation with census based 2001 Carstairs scores. All cause mortality in hospital and at mid-term follow-up.

Results In hospital mortality for all cardiac procedures was 3.25% and mid-term follow-up (median 1887 days; range 1180-2725 days) mortality was 12.4%. Multivariable analysis identified social deprivation as an independent predictor of mid-term mortality (hazard ratio 1.024, 95% confidence interval 1.015 to 1.033; P<0.001). Smoking (P<0.001), body mass index (BMI, P<0.001), and diabetes (P<0.001) were associated with social deprivation. Smoking at time of surgery (1.294, 1.191 to 1.407, P<0.001) and diabetes (1.305, 1.217 to 1.399, P<0.001) were independent predictors of mid-term mortality. The relation between BMI and mid-term mortality was non-linear and risks were higher in the extremes of BMI (P<0.001). Adjustment for smoking, BMI, and diabetes reduced but did not eliminate the effects of social deprivation on mid-term mortality (1.017, 1.007 to 1.026, P<0.001).

Conclusions Smoking, extremes of BMI, and diabetes, which are potentially modifiable risk factors associated with social deprivation, are responsible for a significant reduction in survival after surgery, but even after adjustment for these variables social deprivation remains a significant independent predictor of increased risk of mortality.

INTRODUCTION

The link between poverty, socioeconomic inequalities, and increased mortality is well established,[1 2] but the extent to which such inequalities can be modified is unknown. Cardiovascular disease is closely related to socioeconomic deprivation,[3-6] and cardiac surgery offers several procedures that are known to carry considerable prognostic benefit. We examined whether this prognostic benefit applies across the socioeconomic spectrum.

METHODS

Patient population

We reviewed data from the cardiac surgical databases of QuORU (the quality and outcomes research unit) and NWQIP (the north west quality improvement programme in cardiac interventions), which hold prospectively collected clinical information on all adults undergoing cardiac surgery in Birmingham and the north west of England. The data were acquired prospectively. We excluded patients undergoing surgery for relatively uncommon and higher risk procedures. Social deprivation was calculated for all patients from their home postcode with the 2001 Carstairs scores, which range from −5.71 (least deprived) to 21.39 (most deprived).[7] We classified patients into three groups according to their self reported smoking status: "current smokers" for patients smoking up to or including a week before surgery, "ex-smokers" for those who discontinued smoking habits any time before surgery, and "never smoked." Body mass index (BMI) was calculated as weight (kg)/height (m)^2.

Aims of the study

We examined the influence of social deprivation on survival after cardiac surgery, identified clinical factors associated with social deprivation, and assessed whether adjustment for these factors influences the effect of social deprivation on outcomes.

Study end points

In hospital mortality was recorded locally. We used the central cardiac audit database, to check this status and provide survival data after discharge (census date 1 December 2007 for QuORU and 1 July 2007 for NWQIP). In hospital mortality was defined as death at any time after surgery during the hospital admission.

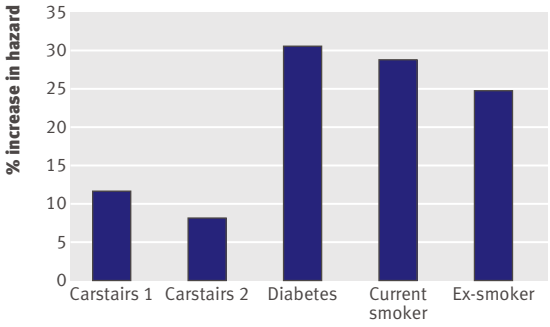
Statistical analysis

The analysis was conducted in two stages. First, we examined whether deprivation, as described by the Carstairs score, was predictive of mortality in hospital and in longer term follow-up. Secondly, after identifying current and past smoking behaviour, body mass index, and diabetes as clinical factors associated with social deprivation, we examined the degree to which

these mediated any excess mortality associated with deprivation.

The risk profile in cardiac surgery is commonly assessed with the European system for cardiac operative risk evaluation (EuroSCORE),[8] which contains variables such as age, sex, and ventricular function known to influence outcomes. We developed prognostic models to examine whether there was an additional effect of social deprivation on all cause in hospital mortality and mid-term survival. In these models we added type of surgical procedure and surgeon (as a random effect/grouped frailty) to the (log) EuroSCORE value as patient level covariates. We identified further factors associated with deprivation and included these in further models to explore the extent to which these measures described the risks associated with deprivation. See bmj.com.

Data on EuroSCORE, Carstairs score, diabetes, type of surgery, sex, and consultant or centre were available for all patients. Data were unavailable on smoking in 53 patients, hypertension in 43, age in 45, and BMI in 480. Data on in hospital death were missing for one patient and on time to death for mid-term analysis for 1625.



Percentage increase in hazard of death during mid-term follow-up. Carstairs 1: increased risk for 5 point increment in Carstairs score when diabetes, smoking, and BMI are not included in model. Carstairs 2: increased risk for 5 point increment in Carstairs score when diabetes, smoking, and BMI are included in model

Predictors of mid-term mortality

	Hazard ratio (95% CI)	P value
Multivariable frailty model*		
Log EuroSCORE†	3.649 (3.447 to 3.863)	<0.001
CABG	1	
CABG + other	0.944 (0.783 to 1.137)	0.540
CABG + valve(s)	1.243 (1.149 to 1.345)	<0.001
CABG + valve(s) + other	1.163 (0.842 to 1.605)	0.36
Other	0.979 (0.820 to 1.170)	0.82
Valve(s) only	0.902 (0.838 to 0.972)	<0.007
Valve(s) + other	0.903 (0.713 to 1.143)	0.39
Carstairs score‡	1.024 (1.015 to 1.033)	<0.001
Multivariable frailty model plus predictors of social deprivation*		
Log EuroSCORE†	3.525 (3.327 to 3.736)	<0.001
Diabetes	1.305 (1.217 to 1.399)	<0.001
CABG	1	
CABG + other	0.952 (0.790 to 1.147)	0.6
CABG + valve(s)	1.246 (1.150 to 1.350)	<0.001
CABG + valve(s) + other	1.228 (0.889 to 1.696)	0.21
Other	0.973 (0.807 to 1.174)	0.78
Valve(s) only	0.919 (0.851 to 0.993)	0.032
Valve(s) + other	0.930 (0.734 to 1.177)	0.540
Carstairs score‡	1.017 (1.007 to 1.026)	<0.001
Current smoker	1.294 (1.191 to 1.407)	<0.001
Ex-smoker	1.245 (1.165 to 1.330)	<0.001
BMI	0.941 (0.928 to 0.954)	<0.001
BMI 1§	1.000 (1.000 to 1.000)	0.56
BMI 2§	1.003 (1.001 to 1.004)	<0.001
BMI 3§	0.994 (0.991 to 0.998)	<0.001

CABG=coronary artery bypass grafting (reference procedure); BMI=body mass index.
*Includes consultant surgeon as frailty term (P<0.0001).
†Hazard ratio represents change in 1 natural log transformed EuroSCORE point.
‡Hazard ratio represents change in 1 untransformed Carstairs score point.
§Higher order terms from fitting restricted cubic spline with 5 knots to describe effects of BMI as non-linear function. Knots for restricted cubic spline for BMI were placed at 21.1, 24.9, 27.2, 29.8, and 35.38.

RESULTS

The study population comprised 44 902 patients (32 889 male), undergoing cardiac surgery between 1 January 1997 and 31 December 2007, who received procedures at five different hospitals from 51 surgeons. The median age was 65 (interquartile range 58-71). Diabetes (type 1 or 2) was present in 7363 (16.4%) patients and hypertension in 24 010 (53.5%). At the time of surgery 9803 (21.9%) patients were current smokers, 21 697 (48.4%) were ex-smokers, and 13 349 (29.8%) had never smoked. Medians were 27 (25-30) for BMI, 4 (2-6) for EuroSCORE, and −0.54 (−2.19-2.27) for Carstairs score. See bmj.com for table showing type of cardiac surgery.

In hospital mortality

The all cause in hospital mortality was 3.3% (1461/44 902). In the initial multivariable analysis EuroSCORE, type of surgery and social deprivation were all independent predictors of in hospital mortality. See bmj.com.

Survival analysis

The median follow-up was 5.2 years (1887 days, interquartile range 1180-2725 days), and 5563 patients died during follow-up (12.4%). In the initial multivariable analysis EuroSCORE, type of surgery, and social deprivation were all independent predictors for reduced long term survival. There was a 2.4% increased risk of mortality for each point increment in Carstairs score (table).

Factors associated with social deprivation

Additional multivariable analysis identified that deprivation was associated with smoking, extremes of BMI, and diabetes, in addition to EuroSCORE, and type of procedure. See bmj.com. The final multivariable

WHAT IS ALREADY KNOWN ON THIS TOPIC

The link between poverty, socioeconomic inequalities, and increased mortality is well established

Cardiovascular disease is a common cause of premature death in the West

Cardiac surgery offers a range of operations to improve prognosis

WHAT THIS STUDY ADDS

Social deprivation reduces the prognostic benefits of cardiac surgery

Addressing issues of smoking, obesity, and diabetes could reduce the negative impact of social deprivation on outcome after cardiac surgery

model for in hospital mortality included BMI, diabetes, smoking, and social deprivation.

The inclusion of BMI, diabetes, and smoking in the multivariable model for mid-term survival led to a reduction in the risk of mortality because of social deprivation from 2.4% to 1.7% for each point increment in Carstairs score, resulting in an overall reduction in mortality of 29%. In this model, diabetes carried a 31% increased risk and smoking a 29% increased risk of death (table, figure). There were non-linear effects of varying BMI on the risk of mid-term mortality, where lower and higher BMI both carry increased risk.

DISCUSSION

Social deprivation has a substantial independent adverse effect on survival in patients undergoing cardiac surgery. Smoking, extremes of BMI, and diabetes were strongly associated with social deprivation, but even after we adjusted for these factors, deprivation remained a predictor of reduced survival in hospital and at mid-term. Our study included a large number of patients from five centres, and is probably representative of patients and practice in the United Kingdom and other similar health systems.

Predictors of in hospital mortality

EuroSCORE is the most widely used risk stratification scoring system in Europe to evaluate the patients' operative risk of death after cardiac surgery.[8] It does not, however, contain diabetes or obesity as risk factors. In the initial multivariable model for in hospital mortality, social deprivation had a small but significant negative influence on mortality. Smoking, diabetes, and BMI were strongly associated with social deprivation and when they were introduced in the analysis as potential predictive variables the effect of social deprivation was largely retained.

Predictors of mid-term mortality

The EuroSCORE has also been shown to be a strong predictor of long term survival after cardiac surgery,[9] and our report confirms this finding. We found that social deprivation was an additional strong predictor of mortality, even when we introduced smoking, diabetes, and BMI in the analysis. The most deprived patients also present to surgery with a higher risk profile.

Limitations of the study

The mortality data refer to all cause mortality and do not allow an analysis of the relations between causes of death and risk factors associated with social deprivation. We used Carstairs scores to evaluate social deprivation and, while they have limitations, they have been shown to perform well particularly in explaining variations in health inequalities.[7] The data on smoking represent a temporal snapshot at the time of surgery. We have no data to validate the compliance of non-smokers at the time of surgery, neither have we information on smoking habits after surgery for all patients. Our study was also based on several datasets and, finally, we have no data on ethnicity.

In summary, people from deprived socioeconomic groups not only have a shorter life expectancy but also spend a greater proportion of their lives affected by disability or illness.[1] A proved healthcare intervention like cardiac surgery might not be equally distributed across socioeconomic boundaries. We have identified some important modifiable clinical factors that if addressed might substantially reduce the adverse effects of social deprivation on mid-term survival after cardiac surgery.

Even after correction for smoking history, BMI, and diabetes, however, the influence of social deprivation on survival remained predictive, indicating that some additional factors related to deprivation might influence outcome. In the face of easy access to effective health care, the challenge lies in developing a coherent health conscious approach to education and to the environment. This is essential to maximise the benefits of expensive and complex healthcare interventions such as cardiac surgery.

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Baseline self reported functional health and vulnerability to post-traumatic stress disorder after combat deployment: prospective US military cohort study

Cynthia A LeardMann,[1] Tyler C Smith,[1] Besa Smith,[1] Timothy S Wells,[2] Margaret A K Ryan,[3] for the Millennium Cohort Study Team

[1]Department of Defense Center for Deployment Health Research, Naval Health Research Center, 140 Sylvester Road, San Diego, CA 92106, USA

[2]Biosciences and Protection Division, Air Force Research Laboratory, Wright-Patterson Air Force Base, 2800 Q Street, OH 45433, USA

[3]Naval Hospital Camp Pendleton, Box 555191, CA 92055, USA

Correspondence to: C LeardMann Cynthia.LeardMann@med.navy.mil

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ABSTRACT

Objective To determine if baseline functional health status, as measured by SF-36 (veterans), predicts new onset symptoms or diagnosis of post-traumatic stress disorder among deployed US military personnel with combat exposure.

Design Prospective cohort analysis.

Setting Millennium Cohort.

Participants Combat deployed members who completed baseline (2001-3) and follow-up (2004-6) questionnaires. Self reported and electronic data used to examine the relation between functional health and post-traumatic stress disorder.

Main outcome measures New onset post-traumatic stress disorder as measured by either meeting the DSM-IV criteria with the 17 item post-traumatic stress disorder checklist-civilian version or self report of a physician diagnosis at follow-up with the absence of both at baseline.

Results Of the 5410 eligible participants, 395 (7.3%) had new onset symptoms or diagnosis of post-traumatic stress disorder at the time of follow-up. Individuals whose baseline mental or physical component summary scores were below the 15th centile had two to three times the risk of symptoms or a diagnosis of post-traumatic stress disorder by follow-up compared with those in the 15th to 85th centile. Of those with new onset symptoms or diagnosis of post-traumatic stress disorder, over half (58%) of cases occurred among participants with scores below the 15th centile at baseline.

Conclusions Low mental or physical health status before combat exposure significantly increases the risk of symptoms or diagnosis of post-traumatic stress disorder after deployment. More vulnerable members of a population could be identified and benefit from interventions targeted to prevent new onset post-traumatic stress disorder.

INTRODUCTION

Most previous studies of post-traumatic stress disorder (PTSD) have used cross sectional or retrospective data, making it difficult to ascertain the effects of decreased mental or physical health on new onset or persistent symptoms of PTSD. There have been a few prospective studies; one found that young adults with high levels of anxiety or depression in first grade (at age 6-7) were 1.5 times more likely to develop PTSD after a traumatic event,[1] and another using data from the Millennium Cohort Study, reported a twofold increased risk of new onset symptoms of PTSD at follow-up among those who reported previous assault.[2] Another study using this cohort suggested that exposure to combat, as opposed to deployment itself, leads to a significantly increased risk of new onset PTSD.[3] On the basis of those findings we examined whether baseline mental or physical health, as measured by the medical outcomes study SF-36 health survey for veterans (SF-36V), predicts new onset symptoms or diagnosis of PTSD among those service members who are at the highest risk of developing new onset PTSD—that is, those who have deployed in support of the current conflicts and reported combat exposure.

METHODS

Study population

The Millennium Cohort Study, a 21 year longitudinal study, was launched in 2001 to evaluate data on behavioural and occupational characteristics related to military service that might be associated with adverse health.[4 5] See bmj.com for details.

As service members exposed to combat are at the highest risk of PTSD after deployment,[3] we included only participants who reported combat-like exposures. We defined this as personal exposure to at least one of the following experiences in the three years before completion of the follow-up questionnaire: witnessing a person's death due to war, disaster, or tragic event, witnessing instances of physical abuse (torture, beating, rape), dead and/or decomposing bodies, maimed soldiers or civilians, or prisoners of war or refugees.

Participants for this current study must have completed the baseline (2001-3) and the first follow-up (2004-6) questionnaires, been free from symptoms and diagnosis of PTSD at baseline, had their first complete deployment in support of the wars in Iraq and Afghanistan between the baseline and first follow-up questionnaires, and had complete demographic, behavioural, military specific, and SF-36V data.

Health and behaviour

The baseline and follow-up questionnaires included questions on physical health, mental health, deployment, occupational exposures, and other health outcomes. The SF-36V was used to examine self reported mental and physical health status at baseline.[6 7] Like the original SF-36, the SF-36V has mental and physical component summary scores.[8]

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The mean (SD) normative US score for each summary score is 50 (10).[8] Higher scores reflect more favourable health status. To examine if mental or physical health status before deployment confers resilience or vulnerability for developing PTSD after deployment among combat deployers we classified participants into three groups based on component summary scores. We decided, a priori, that the groups would be based on about 1 SD, with the highest and lowest groups representing 30% of the study population, and the middle group representing the 70% remaining.

The Millennium Cohort questionnaire includes the PTSD checklist-civilian version (PCL-C), a 17 item self report measure of PTSD symptoms.[9 10] We used two separate screening criteria to classify those with PTSD symptoms. The sensitive definition of PTSD symptoms uses criteria from the *Diagnostic and Statistical Manual of Mental Disorders*, fourth edition (DSM-IV), alone, while the specific definition requires a total score of 50 or more on a scale from 17 to 85 points (based directly on the Likert scale, where a response of "not at all" receives 1 point and "extremely" receives 5 points for each of the 17 items) in addition to meeting the DSM-IV criteria.[10-14] This instrument is highly specific (99%) but less sensitive (60%),[14] while use of the DSM-IV criteria alone increases sensitivity (100%) but has a lower specificity (92%).[14] We excluded from all analyses participants who had symptoms of PTSD at baseline, based on the specific criteria, while those who met the sensitive criteria were excluded only from the analyses based on the sensitive criteria.

At baseline, we also excluded any participants with self reported PTSD. We classified participants as having new onset symptoms or diagnosis of PTSD if they met the PCL-C criteria or self reported PTSD on the follow-up questionnaire. We also obtained self reported information on alcohol intake and smoking. See bmj.com.

Statistical analysis

We completed a descriptive investigation of demographic, behavioural, and military specific characteristics compared with baseline self reported health status. Univariate analyses compared characteristics and categories of mental and physical component summary scores between combat deployed participants with and without new onset symptoms or diagnosis of PTSD. Multivariable logistic regressions investigated associations between the component summary scores before deployment and new onset symptoms or diagnosis of PTSD using both specific and sensitive criteria.

RESULTS

There were 55 021 participants who completed the baseline (July 2001 to June 2003) and the first follow-up (June 2004 to February 2006) questionnaires, of whom 22 208 (40%) were deployed in support of the conflicts in Iraq and Afghanistan. The mean time between baseline and submission of the first follow-up questionnaire was 2.7 years (SD 0.5; median 2.8). To study a more homogeneous group of deployers who were exposed to one or more traumatic events during deployment, we removed from the analyses those participants whose first deployment did not occur between baseline and follow-up or who did not report combat exposures (n=16 172). After removing those with PTSD at baseline and other exclusions we had 5410 for analysis. See bmj.com for details, and baseline population characteristics by centile of mental and physical component summary scores.

Using the specific criteria of the DSM-IV, we identified new onset PTSD in 7.3% (395) of the study group with a sum of 50 points or a physician diagnosis. With the sensitive criteria of the DSM-IV alone or a physician diagnosis, 8.6% (457) were identified with new onset PTSD. After adjustment for all other variables in the model, individuals whose baseline mental component summary score was below the 15th centile were

Percentages and adjusted odds ratios (95% confidence intervals) of new onset PTSD among combat deployed* participants of Millennium Cohort Study according to centile of mental and physical component summary score at baseline, 2001-6

	Specific criteria† (n=395)		Sensitive criteria‡ (n=457)	
Centile of component summary score	No (%§)	OR¶ (95% CI)	No (%§)	OR¶ (95% CI)
Mental (mean score):				
‹15th (‹46.2)	156 (19.2)	3.51 (2.74 to 4.50)	158 (21.5)	3.18 (2.50 to 4.05)
15-85th (46.2-60.4)	199 (5.3)	1.00	252 (6.7)	1.00
›85th (›60.4)	40 (4.9)	0.87 (0.60 to 1.24)	47 (5.8)	0.80 (0.57 to 1.12)
Physical (mean score):				
‹15th (‹48.2)	116 (14.3)	2.22 (1.71 to 2.89)	124 (15.9)	2.11 (1.64 to 2.70)
15-85th (48.2-59.7)	221 (5.8)	1.00	267 (7.1)	1.00
›85th (›59.7)	58 (7.1)	0.87 (0.63 to 1.21)	66 (8.3)	0.89 (0.65 to 1.21)

*Combat deployed defined as having at least one deployment in support of wars in Iraq and Afghanistan between submission dates of baseline and first follow-up questionnaires and report of at least one combat-like exposure on follow-up questionnaire.
†PTSD symptoms based on PCL-C with DSM-IV criteria and 50/85 points possible or diagnosis of PTSD within three years before completion of follow-up questionnaire.
‡PTSD symptoms based on PCL-C and DSM-IV criteria or diagnosis of PTSD within three years before completion of follow-up questionnaire.
§Percentage of participants with PTSD within baseline category.
¶Adjusted for other component summary score as well as sex, birth year, education, marital status, race/ethnicity, smoking status, alcohol/CAGE, military rank, service component, branch of service, occupation, combat exposure severity.

WHAT IS ALREADY KNOWN ON THIS TOPIC

Post-traumatic stress disorder (PTSD) is associated with reduced mental and physical health status as well as many comorbidities

As previous studies have mostly used retrospective or cross sectional data it is unclear if those with decreased mental or physical health are more vulnerable to developing PTSD

WHAT THIS STUDY ADDS

Diminished mental or physical health status before combat deployment is strongly associated with an increased risk of PTSD after deployment

over three times as likely to have new onset symptoms or diagnosis of PTSD (table). Individuals whose baseline physical component summary score was below the 15th centile were over twice as likely to have new onset symptoms or diagnosis of PTSD.

Other baseline characteristics and percentage new onset PTSD are shown on bmj.com. In particular, participants who reported three or more combat exposures were also more than twice as likely to have new onset symptoms or diagnosis of PTSD by follow-up (2.60, 1.89 to 3.58, specific; 2.32, 1.74 to 3.08, sensitive). Additionally, women (2.33, 1.80 to 3.03), current smokers (1.56, 1.21 to 2.01), non-officers (1.77, 1.11 to 2.85), Reserve/National Guard (1.85, 1.47 to 2.33), and army (2.04, 1.39 to 3.02) members had increased odds for new onset symptoms or diagnosis of PTSD (measures are based on sensitive criteria). Participants of other races or ethnicities (excluding black non-Hispanic) were 1.57 times more likely to have new onset symptoms or diagnosis of PTSD by follow-up compared with white non-Hispanics (1.18 to 2.08, sensitive criteria).

DISCUSSION

An identifiable population of combat deployers from a population based military cohort who were below the 15th centile for self reported baseline mental health accounted for 35% of the incidence of PTSD after combat deployment. Furthermore, 58% of those with new onset PTSD fell below the 15th centile for mental or physical health at baseline. Previous research has shown that combat deployments significantly increase the likelihood of symptoms of PTSD, but little is known about baseline factors, screening factors before deployment, or modifiable factors associated with new onset PTSD.

Limitations

The study population consisted of a sample of responders to the Millennium Cohort questionnaire and might not be representative of all combat deployers in the US military population. However, investigation of potential biases in the cohort, have found it to be representative. Combat exposures were identified with self reported data, which inherently has some biases. Furthermore, the questions used to identify combat exposures were not specific to deployment, so participants might have experienced these exposures at times other than during their deployment. The PTSD checklist-civilian was used to assess symptoms of PTSD, and is a surrogate for a clinician diagnosis and might misclassify PTSD status for some participants. However, it might also more accurately capture those with symptoms of PTSD compared with ambulatory or hospital admission data, as many with symptoms might not seek treatment for fear of attached stigma.

Implications

Service members have better overall physical and mental health than the general US population. However there is a broad range in mental and physical health status of service members, as shown in this study.

The normative mean scores for "healthy" US individuals without chronic conditions are 55.8 and 52.5 for mental and physical component summary scores, respectively.[8] In comparison, mean scores before deployment for those who reported no symptoms or diagnosis of PTSD at baseline or follow-up (54.4. and 54.3, respectively) are similar to "healthy" individuals, while the mean scores before deployment of those who met the specific criteria for PTSD symptoms or diagnosis at follow-up (51.5 and 48.1, respectively), while still close to the 50 point mean for the US general population, are lower and might represent meaningful differences.

While sex, race/ethnicity, smoking status, military rank, service component, branch of service, combat exposures, and low physical component summary score were significantly associated with PTSD after deployment (based on the sensitive and specific criteria), the largest risk factor for developing new onset PTSD in this study was low mental health scores at baseline before deployment. Among previous studies of deployed military members, severity of combat has been found to be one of the strongest predictors of PTSD.[11 15] Diminished mental health status before a stressful experience might be an underlying factor that not only affects the reaction during the traumatic event but possibly also the coping strategies after the event.

We have identified an at risk population whose functional health seems to predict vulnerability to PTSD after combat deployment. Such a population could be targeted for PTSD prevention programmes, early intervention after exposure to stress, or even protection from stressful exposures, when possible.

In addition to the authors, the Millennium Cohort Study Team includes Lacy Farnell, Gia Gumbs, Isabel Jacobson, Molly Kelton, Travis Leleu, Jamie McGrew, Beverly Sheppard, Katherine Snell, Steven Spiegel, Kari Welch, Martin White, James Whitmer, and Charlene Wong, from the Department of Defense Center for Deployment Health Research, Naval Health Research Center, San Diego, CA; Paul J Amoroso, from the Madigan Army Medical Center, Tacoma, WA; Edward J Boyko, from the Seattle Epidemiologic Research and Information Center, Veterans Affairs Puget Sound Health Care System, Seattle, WA; Gary D Gackstetter, from the Department of Preventive Medicine and Biometrics, Uniformed Services University of the Health Sciences, Bethesda, and the Analytic Services

(ANSER), Arlington, VA; Gregory C Gray, from the College of Public Health, University of Iowa, Iowa City, IA; Tomoko I Hooper, from the Department of Preventive Medicine and Biometrics, Uniformed Services University of the Health Sciences, Bethesda; and James R Riddle, from the US Air Force Research Laboratory, Wright-Patterson Air Force Base, OH. We are indebted to the Millennium Cohort Study participants, without whom these analyses would not be possible. We thank Scott L Seggerman and Greg D Boyd from the Management Information Division, US Defense Manpower Data Center, Seaside, CA; Michelle Stoia from the Naval Health Research Center; and all the professionals from the US Army Medical Research and Materiel Command, especially those from the Military Operational Medicine Research Program, Fort Detrick, MD. We appreciate the support of the Henry M Jackson Foundation for the Advancement of Military Medicine, Rockville, MD.

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Competing interests: None declared.

Ethical approval: The Millennium Cohort Study was approved by the Institutional Review Board of the Naval Health Research Center (Protocol NHRC.2000.0007). All participants gave informed consent.

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We welcome submission of any trial of a drug or device that asks an original research question that will sufficiently aid doctors' decisions. This is most likely to be a trial that directly compares a new drug or device (or new regimen or indication) with the best current treatment(s) using clinically valid doses or administration of both study and comparator interventions. Placebo controlled trials often have much more limited relevance to practice than head to head trials and may not sufficiently help *BMJ* readers' decisions, but we welcome emailed presubmission inquiries about these too.

We will give priority to a drug or device trial if it

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- Is reported fully in line with the CONSORT statement or the relevant CONSORT extension statement and has sufficient internal and external validity
- Is submitted with the original study protocol, for use in confidence during peer review
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If you are submitting a report of such a clinical trial please follow all the good publication practice (GPP) guidelines and the European Medical Writers Association (EMWA) guidelines on properly reporting the role of professional medical writers. Please provide the trial registration details, declare the details of all sources of funding for the study, provide statements of competing interests and contributorship, fully describe the role of the study sponsors, provide a statement on the independence of researchers from funders, and state whether all authors had full access to and can take responsibility for the data and analyses. All of these items are explained at http://resources.bmj.com/bmj/authors/types-of-article/research.

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pico

The effect of high dose inhaled corticosteroids on wheeze in infants after respiratory syncytial virus infection: randomised double blind placebo controlled trial

Marieke J J Ermers,[1] Maroeska M Rovers,[2] Job B van Woensel,[3] Jan L L Kimpen,[1] Louis J Bont,[1] on behalf of the RSV Corticosteroid Study Group

EDITORIAL by Handforth and colleagues

[1]Department of Paediatric Infectious Diseases, Wilhelmina Children's Hospital, University Medical Centre Utrecht, 3508 AB Utrecht, Netherlands
[2]Julius Centre for Health Sciences and Primary Care, University Medical Centre Utrecht
[3]Department of Paediatric Intensive Care, Emma Children's Hospital, Academic Medical Centre, Amsterdam, Netherlands
Correspondence to: L J Bont
l.bont@umcutrecht.nl

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STUDY QUESTION What is the effect of early initiated anti-inflammatory therapy with prolonged, high dose, inhaled glucocorticoids on the occurrence and severity of recurrent wheeze in infants after lower respiratory tract infection with respiratory syncytial virus?

SUMMARY ANSWER Early initiated, high dose extra fine hydrofluoroalkane beclometasone during the first 3 months after admission for respiratory syncytial virus infection has no major effect on the development of recurrent wheeze. The general use of such treatment for respiratory syncytial virus infection should not be advocated.

Design

Infants were randomly assigned to treatment with either 200 µg extra fine hydrofluoroalkane beclometasone or placebo, administered with a pressurised metered dose inhaler and a spacer during the first three months after hospital admission. Randomisation was by means of a computer generated list of six numbers in each block and fixed blocks within each hospital. Blinding was accomplished by using active and placebo drugs of identical shape and taste. Randomisation codes were secured for physicians, nurses, parents, and investigators until data entry was complete.

Participants and setting

This study was conducted in 19 Dutch paediatric departments, and 243 infants (126 boys, 117 girls) hospitalised because of respiratory syncytial virus related lower respiratory tract infection participated. Infants were younger than 13 months and previously healthy. Infants with a history of cardiac or pulmonary disease were excluded.

Primary outcome(s)

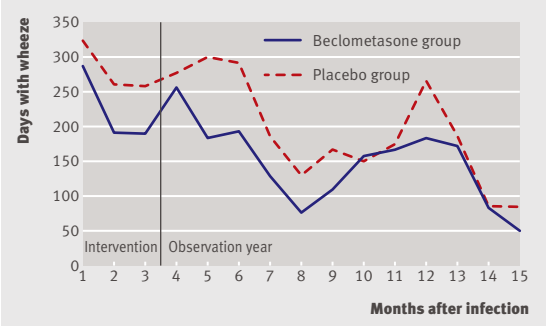
The primary outcome was the number of days of wheeze in the year after the intervention.

Main results and the role of chance

Of the 243 randomised infants, 119 were assigned to receive beclometasone. There was no significant difference in the number of wheezing days between the two groups in the year after intervention (1761/33 568 total days in the beclometasone group *v* 2301/36 556 total days in the placebo group, P=0.31). There was no difference between the two groups in the proportion of infants with wheeze.

In the main pre-defined subgroup of infants who did not need mechanical ventilation (n=221), beclometasone treatment reduced the number of wheezing days by 32% (relative reduction, 1315/30 405 total days in the beclometasone group *v* 2120/33 149 total days in the placebo group, P=0.046). This reduction was most pronounced during the first six months of the year after intervention.

WHEEZE IN ALL INFANTS



There was no difference in the proportion of infants with wheeze between the two groups.

Harms

We found no evidence of side effects with the intervention.

Bias, confounding, and other reasons for caution

The study might be confounded because infants with severe disease who needed mechanical ventilation were analysed along with infants with more mild disease. However, a separate analysis of the subgroup of non-ventilated children showed only a modest and temporary reduction in days with wheeze. Most parents carried out all essential steps correctly for administering the drugs, and it is unlikely that the results were affected by inadequate administration of drugs. The logs of wheezing kept by the parents were not externally validated, but the almost identical occurrence of wheeze in an earlier study of respiratory syncytial virus infection with the same log supports their validity.

Generalisability to other populations

Our results agree with those of several earlier studies which found that corticosteroids are not effective in the acute treatment of respiratory syncytial virus infections. To our knowledge this is the first randomised controlled trial that was sufficiently powered to evaluate the effect of early high dose inhaled glucocorticoids.

Study funding/potential competing interests

This study was fully supported by the Dutch Asthma Foundation (grant number 3.2.03.22). No financial support was obtained from pharmaceutical companies. Study drugs and inhalers were provided unconditionally by the manufacturers.

Trial registration number

Current Controlled Trials ISRCTN12352714.

pico

Improving quality of mother-infant relationship and infant attachment in socioeconomically deprived community in South Africa: randomised controlled trial

Peter J Cooper,[1] Mark Tomlinson,[2,3] Leslie Swartz,[3] Mireille Landman,[4] Chris Molteno,[5] Alan Stein,[6] Klim McPherson,[7] Lynne Murray[1]

[1]School of Psychology, University of Reading, Reading RG6 6AL
[2]Health Systems Research Unit, Medical Research Council, and University of Cape Town, 7505 Tygerberg, South Africa
[3]Department of Psychology, Stellenbosch University, Matieland 7602, South Africa
[4]Parent Centre and Stellenbosch University, Matieland
[5]Department of Psychiatry and Mental Health, Groote Schuur Hospital, Cape Town, South Africa
[6]Department of Psychiatry, University of Oxford, Oxford OX3 7JX
[7]Department of Obstetrics and Gynaecology, John Radcliffe Hospital, Oxford University, Oxford OX3 9DU

Correspondence to: P J Cooper
p.j.cooper@rdg.ac.uk

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STUDY QUESTION Can a home based mother-infant intervention improve the mother-infant relationship and reduce the rate of insecure attachment later in infancy in a socioeconomically deprived community in South Africa?

SUMMARY ANSWER At six and 12 months post partum, mothers in the intervention group were significantly more sensitive in their interactions with their infants and significantly less intrusive than control mothers. At 18 months, the intervention group had a higher rate of secure infant attachments.

Design

Pregnant women were randomly assigned to a control group (n=229) who received routine postnatal care or to an intervention group who received support to encourage sensitive, responsive interactions with their infant. The intervention was delivered by four local women, trained by the research team, who visited participants in their homes for hour long sessions, twice antenatally, weekly for the first eight weeks post partum, fortnightly for a further two months, and then monthly for two months.

We used videotaped play interaction to assess the quality of mother-child interactions before treatment and at 6, 12, and 18 months post partum.

Participants and setting

Of a consecutive series of 452 pregnant women in Khayelitsha, a poor settlement on the outskirts of Cape Town, South Africa, three refused to participate, and 342 were still available for the 18 month assessment.

Primary outcome(s)

The primary outcomes at six and 12 months were those aspects of the mother-infant relationship associated with both socioeconomic adversity and maternal depression (that is, maternal sensitivity and intrusiveness); at 18 months the primary outcome was infant attachment.

Main results and the role of chance

At six and 12 months, mothers in the intervention group were rated as interacting with their children in a significantly more sensitive and less intrusive manner than the control mothers (see table). Significantly more infants of mothers in the intervention group than control infants were rated as securely attached at 18 months (116/156 (74%) *v* 102/162 (63%), P=0.029).

The prevalence of depressive disorder was lower in the intervention group mothers than in the control group at both assessments, but not significantly. The mean depressive symptoms scores for the intervention group mothers were also lower, but significant only at six months.

Harms

The intervention was not associated with any risks to either the mother or the infant.

Bias, confounding, and other reasons for caution

The benefits seen in the intervention group could have been due to these women receiving more attention, but recent reviews of early interventions concluded that attention not directed at mother-infant engagement has no impact on the quality of the mother-child relationship.

Generalisability to other populations

An early mother-infant intervention designed for the developed world produced similar benefits in the deprived conditions of Khayelitsha. The intervention was delivered by local women with no formal training. The intervention is potentially sustainable and could be "scaled up" in developing countries with limited resources.

Study funding/potential competing interests

This study was supported by a grant (B574100) from the Wellcome Trust and a Fellowship award to MT from the Vlotman Trust.

Trial registration number

Current Controlled Trials ISRCTN25664149.

QUALITY OF MATERNAL ENGAGEMENT WITH INFANT AT SIX AND 12 MONTHS

	Mean (SD)		Difference		
	Intervention group	Control group	Mean (SE)	95% CI	P value
Six months					
Sensitivity	15.35 (3.36)	14.58 (3.18)	0.77 (0.36)	0.048 to 1.492	0.037
Intrusiveness	6.51 (2.73)	5.82 (2.64)	0.68 (0.36)	0.093 to 1.278	0.024
12 months					
Sensitivity	5.74 (1.88)	5.31 (1.51)	0.42 (0.18)	0.058 to 0.797	0.043
Intrusiveness	6.41 (7.27)	8.17 (8.34)	-1.76 (0.86)	-3.466 to -0.058	0.023