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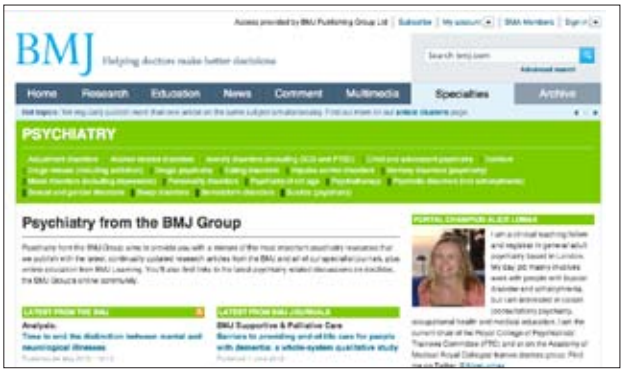


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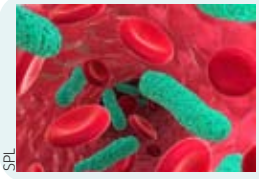
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### Relation between volume and outcome for patients with severe sepsis in United Kingdom

This retrospective cohort study showed no relation between volume and outcome in admissions with severe sepsis treated in adult general critical care units in the UK. The accompanying editorial says that high standards of care in low volume critical care units may have reduced differences between centres.

# Clinical and cost effectiveness of booklet based vestibular rehabilitation for chronic dizziness in primary care: single blind, parallel group, pragmatic, randomised controlled trial

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## STUDY QUESTION

Is booklet based vestibular rehabilitation in primary care (with or without telephone support from a therapist) an effective and cost effective alternative to routine care for chronic dizziness?

## SUMMARY ANSWER

No significant differences were seen between treatments at 12 weeks, but by one year follow-up, booklet based rehabilitation with and without telephone support was highly cost effective.

## WHAT IS KNOWN AND WHAT THIS TRIAL ADDS

Few eligible patients with dizziness are taught vestibular rehabilitation exercises, even though these exercises are effective and can be done at home. Simply providing patients with chronic dizziness in primary care with a booklet teaching vestibular rehabilitation exercises can have lasting benefits at low cost.

### Design

Pragmatic, single blind, randomised controlled trial, with blocked randomisation to three groups (routine care, booklet based vestibular rehabilitation only, and booklet rehabilitation with telephone support) done by an independent randomisation service, stratified by severity of dizziness at baseline.

### Participants and setting

Adult patients with chronic dizziness (not attributed, by their general practitioner, to non-vestibular causes) that could be aggravated by head movement, recruited from 35 general practices in England between October 2008 and July 2009.

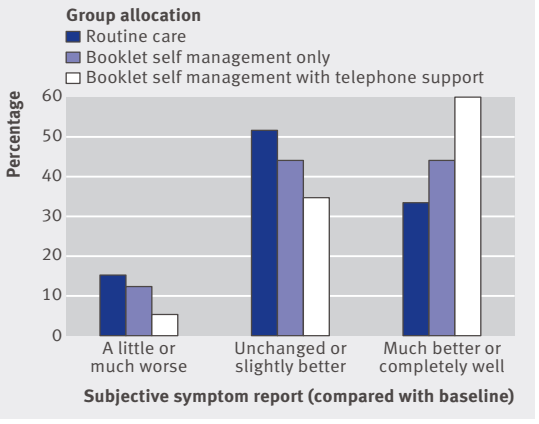
### Primary outcomes

We assessed clinical effectiveness by using the vertigo symptom scale-short form (VSS-SF) at 12 weeks, and cost effectiveness by calculating total healthcare costs related to dizziness per quality adjusted life year (QALY) at one year follow-up.

### Main results and the role of chance

At 12 weeks, VSS-SF scores of the telephone support group and the routine care group did not differ significantly (adjusted mean difference −1.79, 95% confidence interval −3.69 to 0.11; P=0.064). However, both booklet intervention groups had significantly improved scores relative to the routine care group at one year follow-up (with telephone support −2.52, −4.52 to −0.51; P=0.014; booklet only −2.43, −4.27 to −0.60; P=0.010). Using the booklet approach with telephone support, five (three to 12) patients would need to be treated for one patient to report subjective improvement at one year. Analysis of cost effectiveness acceptability curves showed that both interventions were highly cost effective. At low QALY values, the booklet only group was most likely to be cost effective, but the booklet approach with telephone support was most likely to be cost effective at QALY values greater than £1200 (€1488; $1932). The figure shows reported subjective improvement at one year follow-up.

**Subjective improvement at one year follow-up**




### Harms

No adverse events or serious adverse reactions reported.

### Bias, confounding, and other reasons for caution

Uptake was less than 10% of those patients invited, many of whom were no longer dizzy, suggesting that only those with persistent and distressing dizziness might benefit. Participants were not blinded, and psychological aspects of the intervention (such as effective reassurance) probably contributed to subjective improvement. However, previous efficacy trials have shown that improvement in subjective outcomes after vestibular rehabilitation is accompanied by improved objective measures of balance function.

### Generalisability to other populations

Inclusion criteria were broad; therefore, the findings should be generalisable to cases of dizziness in primary care with a wide range of possible causes.

### Study funding/potential competing interests

This trial was funded by the National Institute for Health Research under its Research for Patient Benefit Programme (grant PB-PG-0107-12069). The study was sponsored by the University of Southampton. The sponsor and the funder of the study had no role in the study design, data collection and analysis, interpretation or reporting of this work, or the decision to submit the work for publication. All authors are independent of the funding source.

# Facilitated physical activity as a treatment for depressed adults: randomised controlled trial

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EDITORIAL by Daley and Jolly

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## STUDY QUESTION

Does facilitated physical activity provide an effective treatment for adults with depression presenting in primary care?

## SUMMARY ANSWER

Although trial participants receiving the physical activity intervention in addition to usual care reported increased physical activity compared with those receiving usual care alone, there was no evidence to suggest that the intervention brought about any improvement in depressive symptoms or reduction in antidepressant use.

## WHAT IS KNOWN AND WHAT THIS PAPER ADDS

Numerous studies have reported the positive effects of physical activity, but most of the current evidence originates from small non-clinical samples using interventions that are not practicable in a healthcare setting. Our results indicate that offering patients a facilitated physical activity intervention is not an effective strategy for reducing symptoms of depression, although it increased self reported physical activity and sustained this effect over 12 months.

### Design

Participants were individually randomised into a pragmatic, multicentre, two arm parallel randomised controlled trial and assigned to receive either facilitated physical activity in addition to usual care or usual care alone. Treatment allocation, concealed from the study researchers using an automated telephone system, was administered remotely and employed a computer generated code. None of the participants, general practices, clinicians, or researchers performing the outcome assessments could be blinded to treatment allocation. The intervention was based on theory and aimed to provide individually tailored support and encouragement to engage in sustainable physical activity. This consisted of up to three face to face sessions and 10 telephone calls with a trained physical activity facilitator over an eight month period.

### Participants and setting

361 patients aged 18-69 years who had recently consulted with symptoms of depression were recruited from general practices in south west England. All those randomised had a diagnosis of depression as assessed by the clinical interview schedule-revised and a Beck depression inventory score of 14 or more.

### Primary outcome

The primary outcome of the trial was self reported symptoms of depression, assessed with the Beck depression inventory at four month follow-up.

### Main results and the role of chance

There was no evidence that participants offered the physical activity intervention reported any improvement in symptoms of depression by the four month follow-up point compared with those in the usual care group; adjusted between group difference in mean Beck depression inventory score −0.54 (95% confidence interval −3.06 to 1.99; P=0.68). Similarly, there was no evidence for the effect of the intervention on depression by the eight or 12 month follow-up points. Nor was there evidence that the intervention reduced antidepressant use compared with usual care (adjusted odds ratio 0.63, 95% confidence interval 0.19 to 2.06; P=0.44) over the duration of the trial. However, participants allocated to the intervention group reported more physical activity during the 12 month follow-up period than those allocated to the usual care group (adjusted odds ratio 2.27, 95% confidence interval 1.32 to 3.89; P=0.003).

### Harms

No adverse events related to the physical activity intervention were reported.

### Bias, confounding, and other reasons for caution

Baseline comparability of the treatment groups was good and high retention rates throughout the follow-up period minimised the impact of any missing data on our findings.

### Generalisability to other populations

Our approach towards increasing physical activity put emphasis on promoting choice and autonomy, drawing on a range of behaviour change techniques rather than simple advice giving. This approach could prove useful for treating people with medical conditions such as obesity, diabetes, and cardiovascular disease.

### Study funding/potential competing interests

The trial was funded as part of the National Institute for Health Research Health Technology Assessment programme, with contributions from the Department of Health and local primary care trusts in relation to excess treatment and service support costs.

**Mean (standard deviation) Beck depression inventory score and differences in means at four month follow-up of adults with depression allocated to usual care plus facilitated physical activity or to usual care only**

| | | Difference in means* (95% CI), P value | |
|---|---|---|---|
| Study arm | Mean (SD) depression score | Intention to treat estimate | Multiple imputation chained equation estimate |
| Intervention (n=142) | 16.12 (11.34) | −0.54 (−3.06 to 1.99), 0.68 | −0.76 (−3.37 to 1.84), 0.56 |
| Usual care (n=146) | 16.87 (12.63) | | |

*Adjusted for baseline Beck depression inventory score, antidepressant use, severity of depression, level of physical activity, and recruiting centre.

# Effectiveness of a diabetes education and self management programme (DESMOND) for people with newly diagnosed type 2 diabetes mellitus: three year follow-up of a cluster randomised controlled trial in primary care

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## STUDY QUESTION

Is the reduction in glycated haemoglobin ($HbA_{1c}$) seen at 12 months from a single education and self management programme for people with newly diagnosed type 2 diabetes sustained at three years?

## SUMMARY ANSWER

$HbA_{1c}$ levels at three years had decreased in both those attending the education and self management programme and those receiving standard care. After adjusting for baseline and cluster the difference between the groups was not significant.

## WHAT IS KNOWN AND WHAT THIS PAPER ADDS

The National Institute for Health and Clinical Excellence promotes structured education for those with diabetes. Differences in biomedical and lifestyle outcomes at 12 months from a structured group education programme for people with newly diagnosed type 2 diabetes were not sustained at three years, although illness beliefs remained significantly improved in the intervention group. The results support the model of an ongoing education programme, although the optimum interval and contact time needs further evaluation.

### Design

Three year follow-up of a multicentre cluster randomised controlled trial in primary care, with randomisation at practice level comparing a structured group education programme for six hours delivered in the community by two trained healthcare professional educators compared with usual care.

### Participants and setting

731 of the 824 participants included in the original trial were eligible for follow-up from 207 general practices in 13 primary care sites in the United Kingdom. Biomedical data were collected on 604 (82.6%) and questionnaire data on 513 (70.1%) participants.

### Primary outcomes

$HbA_{1c}$ levels at three years.

### Main results and the role of chance

$HbA_{1c}$ levels at three years had decreased in both groups. After adjusting for baseline and cluster the difference was not significant (difference −0.02, 95% confidence interval −0.22 to 0.17). The groups did not differ for the other biomedical and lifestyle outcomes and drug use. The significant benefits in the intervention group across four out of five health beliefs seen at 12 months were sustained at three years (P<0.01). Depression scores and quality of life did not differ at three years.

**Changes in biomedical outcomes at three years**

| Variable | No (%) of participants | Model summary, coefficient (95% CI) | P value |
|---|---|---|---|
| $HbA_{1c}$ (%) | 585 (96.9) | −0.02 (−0.22 to 0.17) | 0.81 |
| Body weight (kg) | 592 (98.0) | −0.20 (−1.33 to 0.93) | 0.73 |
| Total cholesterol (mmol/L) | 589 (97.5) | −0.03 (−0.19 to 0.12) | 0.68 |
| Systolic blood pressure (mm Hg) | 595 (98.5) | −1.07 (−3.42 to 1.28) | 0.37 |
| Diastolic blood pressure (mm Hg) | 595 (98.5) | −0.68 (−2.20 to 0.83) | 0.38 |
| Waist circumference (cm) | 264 (43.7) | −0.38 (−4.43 to 3.66) | 0.85 |
| Body mass index | 586 (97.0) | −0.03 (−0.45 to 0.39) | 0.88 |

### Harms

No serious adverse events reported.

### Bias, confounding, and other reasons for caution

Not all eligible participants were followed up at three years. The group on whom follow-up data were obtained were older (P=0.01) and had a lower body weight (P=0.004), body mass index (P=0.004), waist circumference (P<0.001), and depression score (P<0.001). When taking into account the treatment group, no interactions between responders and group were found for these outcomes.

### Generalisability to other populations

The results have widespread generalisability as the sample size was large and participants were recruited from 13 sites across the country and are representative of a newly diagnosed white European population in the United Kingdom. In addition, the intervention was designed for consistent reproducibility of training and had a relatively low up-front training investment, enabling implementation across other sites. All educators participating in the intervention were fully trained and quality assured, ensuring generalisability of the findings in other DESMOND studies and out of the research setting.

### Study funding/potential competing interests

This study was funded by Diabetes UK. The study funder had no input into the study design or analysis, nor the interpretation of data. We have no competing interests.

### Trial registration number

Current Controlled Trials ISRCTN17844016.

# The effect of the Talking Diabetes consulting skills intervention on glycaemic control and quality of life in children with type 1 diabetes: cluster randomised controlled trial (DEPICTED study)

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**STUDY QUESTION** Does team wide training of healthcare professionals in consulting skills improve glycaemia in young people with diabetes?

**SUMMARY ANSWER** The Talking Diabetes training programme did not affect $HbA_{1c}$ levels, despite modest improvements in shared agenda setting and use of a guiding consultation style by trained staff.

**WHAT IS KNOWN AND WHAT THIS PAPER ADDS**
Psychoeducational interventions delivered by specialist therapists can improve outcomes in childhood diabetes. We found that brief, paediatric diabetes team-wide training in consultation skills did not improve diabetes related outcomes, despite modestly improved consultation skills.


## Design
A web based and workshop training programme informed by a systematic review, surveys, and observation of UK clinical practice, focus group work with young people with type 1 diabetes and their carers, and experimental consultations was developed for professionals in paediatric diabetes services to improve consultation skills. We tested the effectiveness of the intervention on $HbA_{1c}$ levels in a pragmatic cluster randomised controlled trial; centres were randomised balanced by list size, in three blocks for practicality. We recruited the young people and carers before group allocation.

## Participants and setting
693 young people aged 4-15 years and their carers from 26 UK paediatric diabetes services.

## Primary outcome
Child's centrally measured $HbA_{1c}$ level one year after training of the healthcare professionals.

## Main results and the role of chance
Blood samples were obtained from 660 (95.2%) young people at follow-up. Trained teams had no effect on $HbA_{1c}$ levels: the intervention effect adjusted for baseline $HbA_{1c}$ level using log transformed data was 0.01, which can be interpreted as a 1% increase. 390 children (≥7 years) with diabetes (62%) and 441 carers (64%) completed follow-up questionnaires at 12 months. Some aspects of diabetes specific quality of life improved in control participants (reduced problems with treatment barriers and with treatment adherence. The ability to cope with diabetes (enablement) in the short term increased in the young people in intervention clinics. Carers in the intervention arm reported greater excitement about clinic visits and improved continuity of care. A process evaluation sample of consultation recordings found that trained staff (n=29) were more capable than controls (n=29) in guiding (difference in means 1.14, P<0.001) and agenda setting (difference in proportions 0.45, 95% confidence interval 0.22 to 0.62). Although skills waned over time, the reduction was not significant. Consultation lengths were not significantly different between intervention and control groups. No adverse consequences for patients were identified.

## Bias, confounding, and other reasons for caution
More intervention centres achieved recruitment targets than control centres, although all achieved the minimum required for adequate statistical power. Participants with missing follow-up $HbA_{1c}$ levels had slightly higher baseline values, had a lower mean baseline body mass index, and were more likely to be girls. Replacing missing $HbA_{1c}$ data with local clinic results did not change the outcome. The primary analysis was adjusted for baseline $HbA_{1c}$ values and, although sex was significantly associated with follow-up $HbA_{1c}$ level, adjusting for age or sex did not alter the results.

## Generalisability to other populations
Training improved consultation skills, but the programme cannot be recommended in its current form. It is likely that to achieve the benefits seen in other trials of specific behavioural interventions delivered by specialists the training will need to be intensified and subsequently reinforced and combined with longer consultation times.


**Study funding and competing interests** The study was commissioned and funded by the National Institute for Health Research Health Technology Assessment Programme (grant No HTA 03/46/09). We have no competing interests.

**Intervention effect adjusted for baseline scores for young people and carers one year after training diabetes care teams in consulting skills**

| Variables | ICC (%) | Intervention favoured | Intervention effect (95% CI) | P value |
|---|---|---|---|---|
| $HbA_{1c}$* | 0.06 | | 0.01 (−0.02 to 0.04) | 0.50 |
| Quality of life: | | | | |
| Barriers | 0.9 | Standard care | −4.6 (−8.5 to −0.6) | 0.03 |
| Symptoms | 3.3 | | −0.9 (−4.2 to 2.4) | 0.60 |
| Adherence | 0 | Standard care | −3.1 (−6.3 to −0.01) | 0.05 |
| Worry | 0 | | −3.4 (−7.4 to 0.7) | 0.10 |
| Communication | 0.1 | | −5.4 (−11.1 to 0.3) | 0.06 |
| Patients' confidence | 0 | | −0.2 (−0.4 to 0) | 0.06 |
| Patient enablement (interim) | 6.4 | Training programme | 10.4 (0.5 to 20.4) | 0.04 |
| Parents' continuity of care | 0 | Training programme | 0.2 (0.1 to 0.3) | 0.01 |
| Parent experiencing excitement† | 3.3 | Training programme | 1.90 (1.05 to 3.43) | 0.03 |

ICC=intraclass correlation coefficient. *Intervention effect is given for log transformed data.
†Proportion reporting "a little," "quite a bit," or "very much" in response to emotion item.

# Validation of two age dependent D-dimer cut-off values for exclusion of deep vein thrombosis in suspected elderly patients in primary care: retrospective, cross sectional, diagnostic analysis

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**STUDY QUESTION** Can age adapted D-dimer cut-off values be used to safely and efficiently exclude deep vein thrombosis (DVT) suspected in elderly patients in primary care?

**SUMMARY ANSWER** Combined with a low clinical probability of DVT, use of age adapted cut-off values of D-dimer resulted in a considerable increase in the proportion of primary care patients in whom DVT could be safely excluded, compared with the conventional cut-off value.

**WHAT IS KNOWN AND WHAT THIS PAPER ADDS**

Two age adapted D-dimer cut-off values proposed for the exclusion of venous thromboembolism in secondary care were translated to elderly patients in primary care with suspected DVT. Use of these values, combined with clinical probability assessments, led to an increase in the proportion of older patients in whom DVT could be safely excluded.

### Participants and setting

We included 1374 consecutive patients with suspected DVT who presented to 110 general practitioners affiliated with three hospitals in the Netherlands.

### Design, size, and duration

Retrospective analysis of data from two prospective studies performed from 2002 to 2006. Each patient was assessed for clinical probability of DVT (based on the Wells score) and measured for plasma D-dimer. DVT was established if the deep veins in a patient's leg were not completely compressible at one of two compression ultrasonography examinations. DVT was excluded after two negative examinations (revealing completely compressible veins). The performers and interpreters of these examinations were blinded to patients' diagnostic information. For patients with an unlikely clinical probability score, we calculated the proportions of those with D-dimer values below two age adapted cut-off levels (age dependent value, age×10 µg/L in patients aged >50 years; fixed value, 750 µg/L in patients aged >60 years), as well as the proportion of false negative results. We compared these proportions with those of the conventional cut-off value (500 µg/L).

### Main results and the role of chance

Of 647 patients with an unlikely clinical probability of DVT (Wells score ≤1), we could exclude DVT in 309 (47.8%) using the age dependent cut-off value, compared with 272 (42.0%) using the conventional cut-off value (increase 5.7%, 95% confidence interval 4.1% to 7.8%). These proportions resulted in 0.5% and 0.3% false negative cases for the age dependent and conventional cut-off values, respectively. The increase in exclusion rate with the age dependent value was highest in the oldest age groups of patients. Of 62 patients older than 80 years, DVT could be safely excluded in 22 (35.5%) using the age dependent cut-off value compared with 13 (21.0%) using the conventional cut-off value (increase 14.5%, 6.8% to 25.8%). Compared with the age dependent value, the cut-off value of 750 µg/L had a similar exclusion rate (47.4%) and false negative rate (0.3%).

### Bias, confounding, and other reasons for caution

Since only dichotomised D-dimer values were available, we excluded 712 of the earliest included participants. Analyses that imputed the missing D-dimer values yielded the same results. Furthermore, we used two different laboratory techniques (VIDAS and Tinaquant). After stratifying for type of assay, we found no differences in safety between the two tests, irrespective of the applied cut-off value. We also caution the interpretation for our findings in patients older than 80, since the number of this subgroup was small.

### Study funding/potential competing interests

The study received financial support from the Netherlands Organization for Scientific Research. The funding source had no influence on any aspect of this study.

**Proportion of patients with Wells score ≥1 in whom deep vein thrombosis could be excluded, by age group**

| | All ages | 60-70 years | 70-80 years | >80 years |
|---|---|---|---|---|
| No (%) of patients | 647 (100) | 107 (16.5) | 111 (17.2) | 62 (9.6) |
| Conventional cut-off value (500 µg/L) (no (%, 95% CI)) | | | | |
| Below value | 272 (42.0, 38.2 to 46.0) | 35 (32.7, 24.0 to 42.5) | 34 (30.6, 22.2 to 40.1) | 13 (21.0 11.7 to 33.2) |
| With false negative result | 2 (0.3, 0.04 to 1.1) | 1 (0.9, 0.02 to 5.1) | 0 | 0 |
| Age dependent cut-off value (no (%, 95% CI)) | | | | |
| Below value | 309 (47.8, 43.9 to 51.7) | 42 (39.3, 30.0 to 49.2) | 50 (45.0, 35.6 to 54.8) | 22 (35.5, 23.7 to 48.7) |
| With false negative result | 3 (0.5, 0.01 to 1.3) | 1 (0.9, 0.02 to 5.1) | 0 | 0 |
| Cut-off value (750 µg/L) (no (%, 95% CI)) | | | | |
| Below value | 307 (47.4, 43.5 to 51.4) | 45 (42.1, 32.6 to 52.0) | 51 (45.9, 36.4 to 55.7) | 21 (33.9, 22.3 to 47.0) |
| With false negative result | 2 (0.3, 0.04 to 1.1) | 1 (0.9, 0.02 to 5.1) | 0 | 0 |
| Absolute increase in efficiency (% (95% CI)) | | | | |
| Using age dependent cut-off value | 5.7 (4.1 to 7.8) | 6.5 (2.7 to 13.0) | 14.4 (8.5 to 22.3) | 14.5 (6.8 to 25.8) |
| Using cut-off value (750 µg/L) | 5.4 (3.8 to 7.4) | 9.3 (4.6 to 16.5) | 15.3 (9.2 to 23.4) | 12.9 (5.7 to 23.9) |