Maintenance treatment with quetiapine versus discontinuation after one year of treatment in patients with remitted first episode psychosis: randomised controlled trial

Eric Y H Chen,[1] Christy L M Hui,[1] May M L Lam,[1] Cindy P Y Chiu,[1] C W Law,[2] Dicky W S Chung,[3] Steve Tso,[4] Edwin P F Pang,[3] K T Chan,[4] Y C Wong,[3] Flora Y M Mo,[3] Kathy P M Chan,[5] T J Yao,[6] S F Hung,[5] William G Honer[7]

EDITORIAL by Craig et al

[1]Department of Psychiatry, University of Hong Kong, Hong Kong
[2]Department of Psychiatry, Queen Mary Hospital, Hong Kong
[3]Department of Psychiatry, Tai Po Hospital, Tai Po, Hong Kong
[4]Department of Psychiatry, Castle Peak Hospital, Tuen Mun, Hong Kong
[5]Department of Psychiatry, Kwai Chung Hospital, Kwai Chung, Hong Kong
[6]Clinical Trials Centre, University of Hong Kong, Queen Mary Hospital, Hong Kong
[7]University of British Columbia, Centre for Complex Disorders, BCMHARI, A3-127, Vancouver, BC, Canada
Correspondence to: E Y H Chen
eyhchen@hku.hk

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STUDY QUESTION How does discontinuation of maintenance treatment affect relapse in patients with first episode psychosis who have completed at least one year of maintenance therapy and have no previous relapses or residual symptoms?

SUMMARY ANSWER Discontinuation of maintenance treatment led to a substantially increased risk of relapse in the following year, even in these asymptomatic, high functioning patients.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS After first episode psychosis, the decision on whether to discontinue maintenance treatment is a common clinical problem. The findings support maintenance treatment after one year and in patients with no positive symptoms of psychosis.

Design

We randomised participants into discontinuation (placebo) or maintenance (quetiapine 400 mg/day) groups in a 12 month double blind trial.

Participants and setting

We assessed eligibility in consecutive patients enrolled in a territory-wide early psychosis service in Hong Kong. We included 178 patients with first episode non-affective psychosis who had completed at least one year of antipsychotic drug treatment. We excluded patients with previous relapses or residual psychotic symptoms.

Primary outcome(s)

Relapse (reappearance of definite psychotic symptoms beyond ratings of "questionable" or "within limits of normal experience" on PANSS scale) monthly for 12 months.

Main results and the role of chance

Twenty-seven of 89 patients in the quetiapine group and 56/89 patients in the placebo group relapsed. The Kaplan-Meier estimate of the risk of relapse at 12 months was 41% (95% confidence interval 29% to 53%) for the quetiapine group and 79% (68% to 90%) for the placebo group (P<0.001 by log-rank). In a planned post-transition subgroup analysis excluding patients who relapsed within 60 days after randomisation, fewer patients in the quetiapine group (32%, 19% to 45%) than in the placebo group (75%, 62% to 89%) relapsed (^{2}=19.17, df=1; P<0.001). We did two sensitivity analyses with more stringent criteria for relapse; the quetiapine group showed a significantly lower relapse rate than did the placebo group in both analyses.

Harms

Patients taking quetiapine had more side effects (sleepiness or sedation, reduced salivation, and constipation) than did those taking placebo.

Bias, confounding, and other reasons for caution

Factors such as expressed emotion and illicit substance use also contribute to relapse. The study design required patients to switch to the study drug; a post-transition subgroup analysis that excluded patients who relapsed within two months of the switch period supported the main findings. Our design does not consider the relative advantages or disadvantages of quetiapine compared with other antipsychotics.

Generalisability to other populations

This study excluded patients with previous relapses and residual symptoms of psychosis. Risk of relapse would probably be higher if these patients were included.

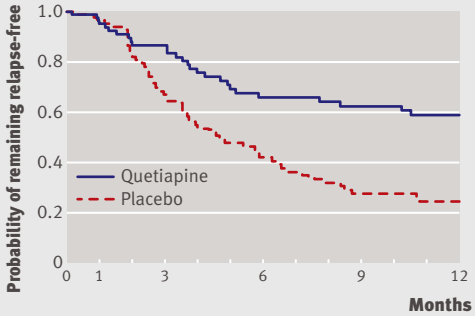
Study funding/potential competing interests

The study was supported by the Research Grants Council of Hong Kong (HKU 7655/05M) and an investigator initiated study award from AstraZeneca Pharmaceuticals. WGH was supported by the Michael Smith Foundation for Health Research and the British Columbia Mental Health and Addictions Services. EYHC, MMLL, DWSC, and WGH have received research funding, educational grants, and fees for participation in advisory boards/lectures and consultation from AstraZeneca, Eli Lilly, In-Silico Biosciences, Janssen-Cilag, Novartis, Otsuka, Pfizer, Sanofi-Aventis, and Wyeth/Solvay. The funders had no role in the design, conduct, or reporting of the study.

Trial registration number

Clinical trials NCT00334035.

KAPLAN-MEIER ANALYSIS OF RELAPSE OF PSYCHOSIS WITH AND WITHOUT MAINTENANCE TREATMENT



No at risk												
Quetiapine	89	71	58	56	49	42	39	38	37	36	36	31
Placebo	89	76	62	49	39	33	29	25	22	19	18	16

No with relapse												
Quetiapine	0	4	10	10	17	21	23	23	24	25	25	27
Placebo	0	3	13	25	35	39	43	47	50	53	53	55

Determinants of disparities between perceived and physiological risk of falling among elderly people: cohort study

Kim Delbaere,[1 2 3] Jacqueline C T Close,[1 4] Henry Brodaty,[5 6] Perminder Sachdev,[5 7] Stephen R Lord[1]

[1]Falls and Balance Research Group, Neuroscience Research Australia, University of New South Wales, Randwick, NSW 2031, Sydney, Australia
[2]Department of Experimental-Clinical and Health Psychology, Faculty of Psychology and Educational Sciences, Ghent University, Belgium
[3]Department of Rehabilitation Sciences and Physiotherapy, Faculty of Medicine and Health Sciences, Ghent University, Belgium
[4]Prince of Wales Clinical School, University of New South Wales, Randwick, Sydney, Australia
[5]School of Psychiatry, University of New South Wales, Prince of Wales Hospital, Randwick, Sydney, Australia
[6]Dementia Collaborative Research Centre, University of New South Wales, Sydney, Australia.
[7]Neuropsychiatric Institute, Prince of Wales Hospital, Randwick, Sydney, Australia

Correspondence to: S R Lord
s.lord@neura.edu.au

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STUDY QUESTION

What are the prevalence and determinants of irrational fear of falling among elderly people, and how does this affect future falls?

SUMMARY ANSWER

Disparities between perceived and physiological fall risk occur in almost a third of people, are primarily associated with psychological measures, and strongly influence the probability of falling.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS

Fear of falling is common in elderly people and is associated with poor balance, depression, and falls. By categorising people in relation to their physiological fall risk and their perceived fall risk, this study shows that many elderly people underestimate or overestimate their risk of falls.

Participants and setting

A total of 500 men and women aged 70–90 years were randomly recruited from a cohort of 1037 living in the community in eastern Sydney, Australia, and participating in the Sydney Memory and Ageing Study.

Design, size, and duration

Prospective cohort study with a one year follow-up for falls.

Main results and the role of chance

The participants' mean age was 77.9 years (SD 4.6), and 270 (54%) were women; 149 (30%) reported one or more falls in the previous year, and 166 (33%) reported at least one injurious fall or multiple non-injurious falls in the follow-up year. Multivariate logistic regression analysis showed that perceived fall risk (estimated with the falls efficacy scale international (FES-I)) and physiological fall risk (estimated with the physiological profile assessment (PPA)) were both independent predictors of future falls. Classification tree analysis was used to split the sample into four groups based on the disparity between physiological and perceived risk—vigorous, anxious, stoic, and aware (see figure). Perceived fall risks in the vigorous and aware groups (144 (29%) and 202 (40%) of the total) were congruent with their physiological fall risks. The anxious group (54 (11%)) had a low physiological but high perceived fall risk, which was related to depressive symptoms (P=0.029), neurotic personality traits (P=0.026), and decreased executive functioning (P=0.01). The stoic group (100 (20%)) had a high physiological but low perceived fall risk, which was protective for falling and mediated through a positive outlook on life (P=0.001) and maintained physical activity and community participation (P=0.048).

Bias, confounding, and other reasons for caution

Dichotomising the FES-I and PPA scores provided a parsimonious way of assessing disparities between perceived and physiological fall risks, but the cut-points derived for these measures should be considered estimates only.

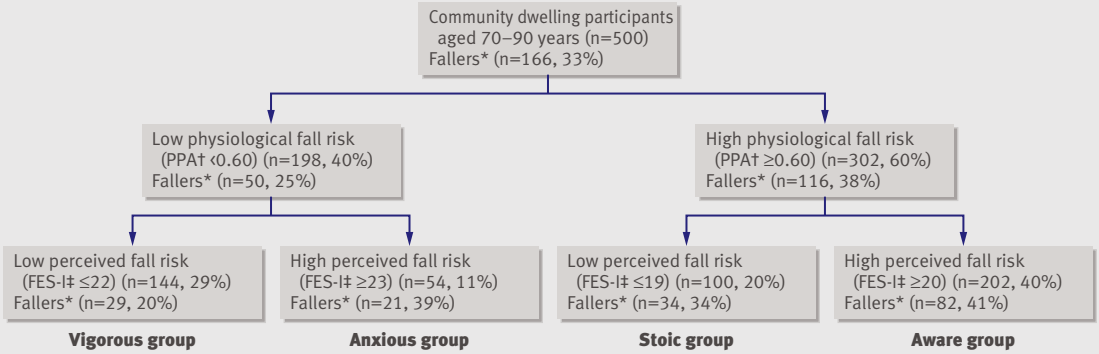
Generalisability to other populations

Our sample—largely healthy, community dwelling elderly adults—should be generalisable towards other community populations considering it had similar demographic, medical, and falls characteristics to those of other studies. Further studies are necessary to investigate whether the same disparity categorisation can be found in elderly people at increased risk of falls, including those with cognitive impairment and Parkinson's disease.

Study funding/potential competing interests

This work was funded by grants from the Australian National Health and Medical Research Council. The physiological profile assessment is commercially available through Neuroscience Research Australia.

CLASSIFICATION TREE OF PARTICIPANTS BY THEIR PHYSIOLOGICAL AND PERCEIVED RISKS OF FALLING



*Defined as ≥1 injurious fall or ≥2 non-injurious falls in follow-up year †PPA = physiological profile assessment ‡FES-I = falls efficacy scale international

Effect of interpregnancy interval on outcomes of pregnancy after miscarriage: retrospective analysis of hospital episode statistics in Scotland

Eleanor R Love,[1] Siladitya Bhattacharya,[1] Norman C Smith,[2] Sohinee Bhattacharya[3]

EDITORIAL by Shelley

[1]University of Aberdeen, Aberdeen
[2]Department of Obstetrics and Gynaecology, Aberdeen Maternity Hospital, Aberdeen
[3]Dugald Baird Centre for Research on Women's Health, Aberdeen Maternity Hospital, Aberdeen AB25 2ZD
Correspondence to: Sohinee Bhattacharya **sohinee.bhattacharya@abdn.ac.uk**

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STUDY QUESTION

After an initial miscarriage what is the optimum interpregnancy interval for the best outcomes in the second pregnancy?

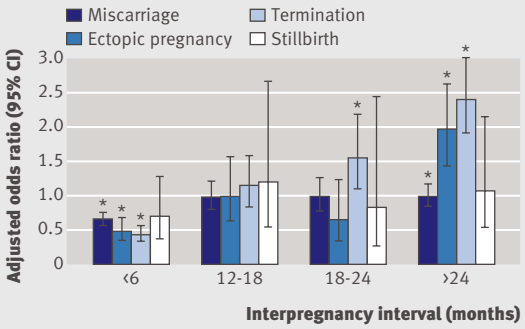
SUMMARY ANSWER

In a Scottish population, women who conceived within six months of an initial miscarriage had the best reproductive outcomes and lowest complication rates in a subsequent pregnancy.

WHAT IS ALREADY KNOWN AND WHAT THIS PAPER ADDS

Little is known about the effect of the intervals between pregnancies after an initial miscarriage.
After an initial miscarriage, women from a developed country had the best outcomes in a subsequent pregnancy if they conceived again within six months.

ADJUSTED† ODDS RATIOS OF ADVERSE PREGNANCY OUTCOMES FOR DIFFERENT INTERPREGNANCY INTERVALS



Reference category was interpregnancy interval of 6-12 months.
Interaction terms interpregnancy interval x year of admission in five year bands were entered into the model, but only that for miscarriage was statistically significant.
*P<0.05.
†Adjusted for maternal age at first pregnancy, Carstairs social deprivation category, and year of first pregnancy.

Participants and setting

From the Scottish hospital discharge records (1991-2000), we identified 30 937 women who had a miscarriage in their first recorded pregnancy and subsequently became pregnant.

Design, size, and duration

A retrospective cohort study design was used to assess the effects of increasing interpregnancy intervals in six monthly bands up to two years. We grouped together women with an interpregnancy interval greater than two years. An interpregnancy interval of 6-12 months was the reference category.

Main results and the role of chance

Compared with women with an interpregnancy interval of 6-12 months, those who conceived again within six months were less likely to have another miscarriage (adjusted odds ratio 0.66, 95% confidence interval 0.57 to 0.77), termination (0.43, 0.33 to 0.57), or ectopic pregnancy (0.48, 0.34 to 0.69). Women with an interpregnancy interval of more than 24 months were more likely to have an ectopic second pregnancy (1.97, 1.42 to 2.72) or termination (2.40, 1.91 to 3.01).

Bias, confounding, and other reasons for caution

As parity is not routinely recorded in the Scottish morbidity records for women who have early pregnancy loss, we were unable to confirm if the earliest miscarriages recorded were indeed the first pregnancy event. Further problems are potential inaccuracies in estimation of interpregnancy intervals due to misclassification of hospital admissions that could have been the result of the same event. This study spans a long period during which the routine use of ultrasound for diagnosis, increasing availability of assisted reproduction techniques, and the formation of dedicated early pregnancy units for the management of pregnancy loss are likely to affect outcomes. However, as the women in all the interpregnancy interval groups were identified from the same period, and the year of occurrence of the first pregnancy event was included as a covariate in the model, this is unlikely to have had a significant effect on the results.

Generalisability to other populations

The Scottish population is a relatively homogeneous population with uniform healthcare access. While the findings may be generalisable to similar populations, that may not be the case for heterogeneous populations with different access to antenatal care. Additionally, this study examined miscarriages that led to hospital contact only, and results therefore cannot be generalised to all women with a miscarriage.

Study funding/potential competing interests

This research was partially funded by the Chief Scientist's Office in Scotland (project No CZG_2_283). SB and SohB were employed by the University of Aberdeen at the time of doing this research and are independent from the funders. ERL is a medical student and NCS is employed by NHS Grampian. The findings and their interpretation in this study are the authors' own, and neither the funders nor the sponsors played any part in arriving at the conclusions. We have no competing interests.

Equity in access to total joint replacement of the hip and knee in England: cross sectional study

Andy Judge,[1 2] Nicky J Welton,[3] Jat Sandhu,[1 4] Yoav Ben-Shlomo[1]

EDITORIAL by Bowling and McKee

[1]Department of Social Medicine, University of Bristol, Bristol BS8 2PS
[2]NIHR Musculoskeletal Biomedical Research Unit, Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, University of Oxford, Headington, Oxford OX3 7LD
[3]Department of Community Based Medicine, University of Bristol, Bristol BS6 6JL
[4]School of Population and Public Health, University of British Columbia, 8th Floor - 601 West Broadway, Vancouver, British Columbia, Canada V5Z 4C2
Correspondence to: A Judge, NIHR Musculoskeletal Biomedical Research Unit, Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, University of Oxford, Headington, Oxford OX3 7LD
Andrew.Judge@ndorms.ox.ac.uk

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STUDY QUESTION Does equity in access to hip and knee replacement surgery in England vary?

SUMMARY ANSWER Equity in access to hip and knee replacement varies by age, sex, deprivation, rurality, and ethnicity.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS Joint replacement is a common elective procedure that makes a substantial contribution to public health, hence is an important equity indicator. There was evidence of inequity by age, sex, deprivation, rurality, and ethnicity, which varied by geography; hospital and distance variables did not explain the observed inequities.

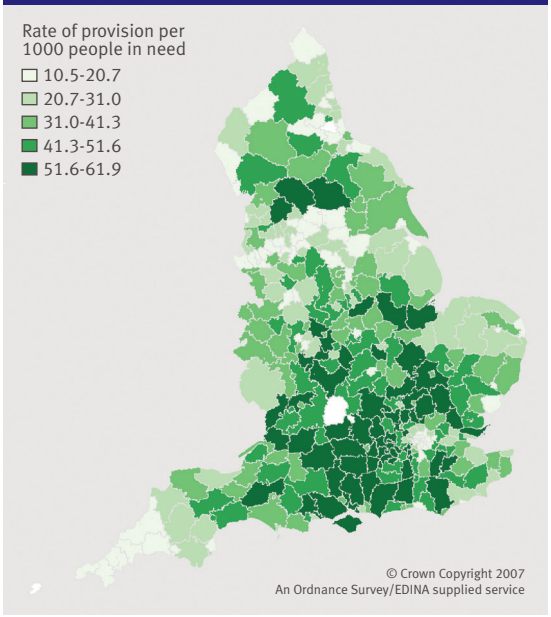
Participants and setting

We used data from the Somerset and Avon Survey of Health and English Longitudinal Study of Ageing and the hospital episode statistics database to determine need for and provision of total hip and knee replacement in English census wards.

Design

This cross sectional study used multilevel Poisson regression modelling to compare the log of the rate ratio of provision relative to need and produce equity rate ratios. Overall rates of equity were produced for each of the 354 districts in England.

EQUITY IN ACCESS TO TOTAL KNEE REPLACEMENT ACROSS THE 354 DISTRICTS IN ENGLAND



Primary outcomes

Equity rate ratios comparing rates of provision relative to need by sociodemographic, hospital, and distance variables.

Main results and the role of chance

For both operations there was an "n" shaped curve by age. Compared with people aged 50-59, those aged 60-84 got more provision relative to need, while those aged ≥85 received less total hip replacement (adjusted rate ratio 0.68, 95% confidence interval 0.65 to 0.72) and less total knee replacement (0.87, 0.82 to 0.93). Compared with women, men received more provision relative to need (1.08, 1.05 to 1.10, for hip replacement, and 1.31, 1.28 to 1.34, for knee replacement). Compared with the least deprived, residents in the most deprived areas got less provision relative to need (0.31, 0.30 to 0.33, for hip replacement, and 0.33, 0.31 to 0.34, for knee replacement). Adjustment for hospital characteristics did not attenuate the effects. The overall rate of provision relative to need (equity) varied geographically across England. For example, for total knee replacement the level of equity was worse for people living in the north, West Midlands, and London. People living in southern England fared best (with the exception of London), with those in need of surgery being more likely to get an operation than in other areas of the country.

Bias, confounding, and other reasons for caution

The lack of data from the private sector could explain the low rates of provision in London, where up to 30% of patients go privately, leading to an overestimate of unmet need. We found evidence of a strong gradient for deprivation, whereby people in affluent areas get most provision relative to need. Incorporating data from the private sector could strengthen this further so we are probably underestimating the deprivation effect. A further limitation is in trying to identify where in the care pathway the inequities occur. We considered whether hospital variables explained observed inequities but found no evidence of importance, suggesting causes of inequity might lie further down the care pathway at the level of the patient or primary care.

Generalisability to other populations

The study is representative of patients treated in English NHS hospitals.

Study funding/potential competing interests

This study was part of a PhD studentship, funded by the MRC HSRC, Department of Social Medicine, University of Bristol. JS received funding from a National Coordinating Centre for Research Capacity Development (NCCRCD) Department of Health Public Health Initiative 2003.

Delivering the diabetes education and self management for ongoing and newly diagnosed (DESMOND) programme for people with newly diagnosed type 2 diabetes: cost effectiveness analysis

M Gillett,[1] H M Dallosso,[2] S Dixon,[1] A Brennan,[1] M E Carey,[2] M J Campbell,[1] S Heller,[3] K Khunti,[4] T C Skinner,[5] M J Davies[6]

[1]School of Health and Related Research (ScHARR), University of Sheffield, Sheffield
[2]DESMOND Project Office, University Hospitals of Leicester NHS Trust, Leicester
[3]Academic Unit of Diabetes, Endocrinology and Metabolism, School of Medicine and Biomedical Sciences, University of Sheffield, Sheffield
[4]Department of Health Sciences, University of Leicester, Leicester
[5]Combined Universities Centre for Rural Health, Geraldton, Australia
[6]Department of Cardiovascular Medicine, University of Leicester, Leicester Royal Infirmary, Leicester

Correspondence to: M Gillett
m.gillett@sheffield.ac.uk

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STUDY QUESTION

What is the long term cost effectiveness of the diabetes education and self management for ongoing and newly diagnosed (DESMOND) intervention, a six hour structured group education programme, compared with usual care newly diagnosed type 2 diabetes?

SUMMARY ANSWER

The DESMOND intervention is likely to be cost effective compared with usual care, especially with respect to the current "real world" cost of the intervention to primary care trusts, with reductions in weight and smoking being the main benefits delivered.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS

A previous multicentre randomised controlled trial of the DESMOND intervention reported significant benefits in weight loss, smoking cessation, illness beliefs, and depression at 12 months. The cost of the intervention per quality adjusted life year (QALY) gained is £2092 using intervention costs based on current practice and £5387 using costs taken from the previous trial. Using current real world costs, the DESMOND intervention is 70% likely to be cost effective when assessed against both the £20000 (€23982; $31191) per QALY and £30000 per QALY cost effectiveness acceptability thresholds typically used by the National Institute for Health and Clinical Excellence.

Design

Cost-utility analysis using the Sheffield type 2 diabetes model to estimate the long term use of therapies, incidence of complications, mortality, and associated impact on costs and health related quality of life.

Sources of effectiveness

A 12 month, multicentre, cluster randomised controlled trial comparing the DESMOND intervention with usual care in people with newly diagnosed type 2 diabetes, as well as "real world" costs estimated for a hypothetical primary care trust with a population of 329 550 patients.

Data sources

The cost per patient of delivering the DESMOND intervention in the trial was obtained by aggregating individual cost components, such as costs of training educators and venue costs. This exercise was repeated using estimated real world costs. Separately, use of drugs and healthcare resources was calculated and unit costs estimated.

Main results

On the basis of the previous trial of the programme, the estimated incremental lifetime cost of patients receiving the DESMOND intervention per person is £209 (95% confidence interval −£704 to £1137), the incremental gain in QALYs is 0.0392 (−0.0813 to 0.1786), and the incremental cost per QALY gained is £5387. Using real world intervention costs, the lifetime incremental cost is £82 (−£831 to £1010) and the mean incremental cost per QALY gained is £2092. Probabilistic sensitivity analysis indicates that, at an acceptability threshold of £20 000 per QALY, the likelihood that the DESMOND intervention is cost effective in the long term is 66% on the basis of the 12 months costs of delivering the intervention from the trial and 70% on the basis of real world costs.

Results of sensitivity analysis

Adopting more conservative assumptions regarding the durability of the effects observed at the end of the trial and a lesser effect of smoking on other cause mortality did not change the results substantially.

Limitations

The main uncertainties concern the effect of smoking on mortality and the durability of benefits such as improved rates of smoking and weight loss. Differences between treatment groups in some biomedical measures at the end of the trial were relatively small or were not statistically significant, but were economically significant when evaluated against the low cost of the intervention.

Study funding and potential competing interests

The study was funded by a grant from Diabetes UK secured by the University Hospitals of Leicester NHS Trust. The authors have no competing interests to declare.

ECONOMIC EVALUATION OF THE DESMOND INTERVENTION COMPARED WITH USUAL CARE USING ESTIMATED "REAL WORLD" COSTS

	Usual care	DESMOND intervention	Difference
Intervention costs up to month 12	—	£76	£76
Other resource use (for example, medication use, use of NHS resources)	£244	£260*	£16
Remaining lifetime discounted costs (for example, drug costs, monitoring, costs of complications)	£15 836	£15 826	−£10
Total lifetime costs (including intervention)	£16 080	£16 162	£82
Combined total QALYs gained in lifetime	9.9634	10.0026	0.0392
Incremental cost per QALY gained	—	—	£2092

DESMOND, diabetes education and self management for ongoing and newly diagnosed; QALY, quality adjusted life year.
*Other resource use shown as actual cost in usual care arm plus £16 for the cluster adjusted difference between study arms.