Effects of dietary intervention and quadriceps strengthening exercises on pain and function in overweight people with knee pain: randomised controlled trial

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ABSTRACT

Objective To determine whether dietary intervention or knee strengthening exercise, or both, can reduce knee pain and improve knee function in overweight and obese adults in the community.

Design Pragmatic factorial randomised controlled trial.

Setting Five general practices in Nottingham.

Participants 389 men and women aged 45 and over with a body mass index (BMI) of ≥28.0 and self reported knee pain.

Interventions Participants were randomised to dietary intervention plus quadriceps strengthening exercises; dietary intervention alone; quadriceps strengthening exercises alone; advice leaflet only (control group). Dietary intervention consisted of individualised healthy eating advice that would reduce normal intake by 2.5 MJ (600 kcal) a day. Interventions were delivered at home visits over a two year period.

Main outcome measures The primary outcome was severity of knee pain scored with the Western Ontario McMaster (WOMAC) osteoarthritis index at six, 12, and 24 months. Secondary outcomes (all at 24 months) included WOMAC knee physical function and stiffness scores and selected domains on the SF-36 and the hospital anxiety and depression index.

Results 289 (74%) participants completed the trial. There was a significant reduction in knee pain in the knee exercise groups compared with those in the non-exercise groups at 24 months (percentage risk difference 11.61, 95% confidence interval 1.81% to 21.41%). The absolute effect size (0.25) was moderate. The number needed to treat to benefit from a ≥30% improvement in knee pain at 24 months was 9 (5 to 55). In those randomised to knee exercise improvement in function was evident at 24 months (mean difference −3.64, −6.01 to −1.27). The mean difference in weight loss at 24 months in the dietary intervention group compared with no dietary intervention was 2.95 kg (1.44 to 4.46); for exercise versus no exercise the difference was 0.43 kg (−0.82 to 1.68). This difference in weight loss was not associated with improvement in knee pain or function but was associated with a reduction in depression (absolute effect size 0.19).

Conclusions A home based, self managed programme of simple knee strengthening exercises over a two year period can significantly reduce knee pain and improve knee function in overweight and obese people with knee pain. A moderate sustained weight loss is achievable with dietary intervention and is associated with reduced depression but is without apparent influence on pain or function.

Trial registration Current Controlled Trials ISRCTN 93206785.

WHAT IS ALREADY KNOWN ON THIS TOPIC

Knee pain is highly prevalent in the community and is often associated with knee osteoarthritis in middle aged and older people

Exercise (both aerobic and strengthening) can reduce pain and improve physical function and mobility in people with knee osteoarthritis

Current osteoarthritis guidelines also support weight loss for overweight and obese people with knee osteoarthritis, despite the paucity of clinical trials

WHAT THIS STUDY ADDS

A simple home based programme of knee strengthening exercise significantly reduces knee pain and improves mobility in overweight and obese adults with knee pain, with a number needed to treat of nine

Long term improvement is confirmed over 24 months

Dietary intervention did not have an effect on knee symptoms or function but was associated with an improvement in depression

INTRODUCTION

Obesity is an established risk factor for the development and progression of both structural knee osteoarthritis[1-4] and knee pain.[5] It usually predates the development of knee osteoarthritis, supporting cause rather than consequence.[6]

All international recommendations emphasise the central role of non-pharmacological management of knee pain and osteoarthritis.[7-10] There is sufficient evidence to recommend weight reduction as an intervention for knee osteoarthritis[11 12] and convincing evidence that exercise reduces pain and disability from knee osteoarthritis.[13-16] Only one randomised trial has assessed the effect of weight loss and exercise specifically in overweight and obese people with knee osteoarthritis.[17] That trial reported that the combination of modest weight loss plus moderate exercise provides

better overall improvements in function and pain compared with either intervention alone.

We used a randomised controlled trial to determine whether interventions of diet and quadriceps strengthening exercise reduce knee pain in overweight and obese adults aged 45 and over. We also examined the effects of these interventions on knee stiffness, physical function, and quality of life.

METHODS

Recruitment of participants—All men and women aged 45 and over with a body mass index (BMI) of ≥28.0 and knee pain who were registered at one of five general practices in Nottingham were eligible for inclusion. In addition, a small number of people were recruited after publicity in local media. General practices sent a questionnaire to all registered patients aged 45 and older. The questionnaire assessed frequency of knee pain, use of analgesics, and physical activity. It incorporated the SF-36,[18] and the hospital anxiety and depression rating scale.[19] Knee pain was defined as knee pain on most days of the past month. Respondents were invited to participate in the study.

Randomisation procedure—Participants were randomised to one of four groups: dietary intervention plus quadriceps strengthening exercises; dietary intervention alone; quadriceps strengthening exercises alone; and advice leaflet only (control group). Participants and those delivering the interventions were not blind to allocation.

Interventions—All participants in the dietary groups completed the EPIC seven day food diary[20] before the first home visit. The dietary intervention consisted of individualised dietary advice that would help to create a deficit of 2.5 MJ (600 kcal) a day and achieve a weight loss of 0.5-1.0 kg a week. For participants randomised to the diet and exercise group the trial dietitian taught the programme of exercises at the initial home visit. The exercise programme comprised a series of simple self managed exercises, designed to strengthen the quadriceps muscle.[15 16] The advice leaflet was based on the Arthritis Research Campaign (UK) leaflet for osteoarthritis of the knee. Participants in the dietary groups were visited at home once a month for the first six months and then every other month for the duration of the 24 months of follow-up. Those in the exercise only or control groups were visited every four months.

Outcomes—The primary outcome was a reduction in pain score from baseline of ≥30% at 24 months with knee pain severity scored with the pain subscale of the Western Ontario and McMaster Universities (WOMAC) osteoarthritis index.[21] We compared mean knee pain scores at six, 12, and 24 months between treatment arms as a secondary outcome. Additional secondary outcome measures comprised mean change in WOMAC stiffness subscale, WOMAC physical function subscale, hospital anxiety and depression rating scale, and mean change in the bodily pain and physical function domains of the SF-36.

Statistical analysis—We had four treatment groups: (1) dietary intervention + quadriceps strengthening exercises; (2) dietary intervention only; (3) quadriceps strengthening exercises only; and (4) advice leaflet. We were interested primarily in the main effects of diet (1 + 2 *v* 3 + 4) and exercise (1 + 3 *v* 2 + 4) with respect to the mean change in WOMAC primary and secondary outcomes. Analyses adopted the intention to treat principle.[22 23] Each analysis of the primary and secondary outcomes included the stratification variables of age, sex, BMI, and baseline outcome as covariates as well as indicators for each intervention to calculate estimates of the risk difference and change in mean outcome values. The primary analysis also tested the diet by exercise interaction. The time course of treatment effects was estimated by a linear model incorporating time × treatment interactions. Secondary outcomes at 24 months are presented as differences in mean WOMAC stiffness, WOMAC physical function, hospital anxiety and depression, and SF-36 subscales of bodily pain and physical function.

RESULTS

Recruitment began in May 2003 and ended in March 2005. The last participant completed the trial in February 2007. Of the 728 men and women who had knee pain and a BMI ≥28.0, information packs were sent to 491 eligible people (67%), of whom 389 returned an initial consent form and were randomised: 109 to dietary intervention and quadriceps strengthening exercises, 122 to dietary intervention only, 82 to quadriceps strengthening exercises only, and 76 to advice leaflet (control group).Two hundred and eighty four participants (73%) completed the trial. The baseline characteristics of participants were similar between the groups (mean age 61, median BMI 33.6, 66% women).

Over the course of the trial, 74 participants (19%) withdrew, most because of personal or medical problems, family commitments, and lack of time. Withdrawals were significantly greater from the exercise groups (52, 27%) than from the non-exercise groups (21, 11%). We excluded 26 (7%) participants. There was no evidence of an interaction between diet and exercise (estimated coefficient =−0.084, 95% confidence interval −0.28 to 0.12; P=0.407).

Primary outcome

At 24 months, 38 (47%) of the exercise only group achieved ≥30% reduction in pain from baseline compared with 23 (30%) of the advice leaflet group. Mean pain scores were 5.70 and 7.04, respectively (estimated numbers of successes include values derived from multiple imputation) (table 1).

There was a significant reduction in knee pain in the knee exercise groups compared with those in the non-exercise groups at 24 months (percentage risk difference 11.61, 95% confidence interval 1.81% to 21.41%; P=0.020). The difference in risk of a good response (defined as a ≥30% reduction in pain from baseline) represents an absolute benefit of 11.6 percentage points and corresponds to a number needed to treat

Table 1 | Percentage with successful outcome and mean WOMAC pain score at 24 months by treatment group

Treatment	No of participants*	No (%) with successful outcome†	Mean (SD) pain score‡
Advice leaflet	76	23 (30)	7.04 (4.21)
Diet only	122	42 (35)	6.96 (4.33)
Exercise only	82	38 (47)	5.70 (3.96)
Diet + exercise	109	46 (43)	6.39 (4.15)

*As randomised.
†≥30% reduction in pain score. Number with successful outcome includes those estimated from multiple imputation.
‡Unadjusted for covariates, but allowing for multiple imputation.

with knee exercise of nine (5 to 55). Those exposed to knee exercise were more likely to experience a ≥30% reduction in pain (relative risk 1.36, 1.05 to 1.76; P=0.022). The absolute effect size (0.25) is only just within the moderate range. There was no evidence of an effect of dietary intervention on pain. Improvement in the mean WOMAC pain score was evident in the exercise group at six months, not evident at 12 months, and significant at 24 months, with a net treatment effect (all exercise minus all non-exercise) of −0.91 (−1.66 to −0.17; P=0.016). There was no evidence of an effect of dietary intervention over time on the WOMAC pain score.

Secondary outcomes

There was a main treatment effect of knee strengthening exercise with a significant net reduction in the mean change in WOMAC physical function score (−3.64, −6.01 to −1.27; P=0.003) and stiffness (−0.35, −0.66 to −0.03; P=0.030) (table 2). The absolute effect sizes were 0.24 and 0.19, respectively. There was no evidence of an effect of dietary intervention on these WOMAC outcomes.

Analysis of the quality of life outcome data at 24 months (table 2) showed a significant effect of exercise, with improvements in the SF-36 subscales of bodily pain and physical function (absolute effect size for each is 0.22). There was no evidence of an effect of dietary intervention, but there was a reduction in the depression score (absolute effect size=0.19).

Table 2 | Differences in mean change in secondary outcome scores at 24 months

	Difference* Mean (SE)	95% CI	P value
WOMAC physical function			
Exercise	−3.64 (1.21)	−6.01 to −1.27	0.003
Diet	−2.84 (1.48)	−5.88 to 0.19	0.065
WOMAC stiffness			
Exercise	−0.35 (0.16)	−0.66 to −0.03	0.030
Diet	−0.16 (0.17)	−0.50 to 0.19	0.365
HADS anxiety			
Exercise	−0.26 (0.37)	−1.02 to 0.51	0.496
Diet	0.09 (0.35)	−0.62 to 0.79	0.807
HADS depression			
Exercise	0.15 (0.37)	−0.62 to 0.92	0.693
Diet	−0.67 (0.32)	−1.30 to −0.04	0.037
SF-36: bodily pain†			
Exercise	5.62 (2.35)	0.99 to 10.25	0.018
Diet	0.94 (2.83)	−4.89 to 6.78	0.742
SF-36: physical function†			
Exercise	5.32 (2.04)	1.30 to 9.33	0.010
Diet	3.93 (2.68)	−1.64 to 9.49	0.157

*Analyses included age, sex, BMI, and baseline outcome of interest as covariates plus indicators for each intervention.
†Positive values reflect improvement.

We examined mean weight loss at 24 months. The difference in mean weight loss (initial minus final) at 24 months between the dietary and non-dietary groups was 2.95 kg (1.44 to 4.46; P=0.000). There was a non-significant difference in mean weight loss of only 0.43 kg (−0.82 to 1.68; P=0.501) between the exercise group and those not exposed to this intervention. These data are adjusted for treatment, age, BMI, sex, and baseline weight. Those in the dietary groups were twice as likely to experience moderate weight loss (5% of initial weight) compared with non-dietary groups at 24 months (unadjusted relative risk 2.3, 1.42 to 3.74; P<0.001).

DISCUSSION

In overweight and obese adults aged 45 and over, a home based knee strengthening exercise programme reduced knee pain, improved the function of the knee, and reduced knee stiffness over a two year period. These effects were not apparent in people allocated to dietary intervention (without knee exercise), even though weight loss was achieved, but levels of depression were reduced.

Comparison with other studies

Our results add to the substantial evidence, summarised in a recent overview of nine systematic reviews,[24] that exercise interventions for patients with knee osteoarthritis reduce pain and improve physical function but that effect sizes are considered small. Another systematic review and meta-analysis in obese patients with knee osteoarthritis concluded that there is robust evidence that weight reduction improves self reported disability and reduces pain, though only self reported disability and not pain could be predicted by weight loss.[25] We found no evidence of an effect of dietary intervention on knee pain or function. In the review by Christensen et al, three of the four trials showed a significant weight loss in the intervention group, but the pooled mean weight loss (6.1 kg) was higher than that experienced by our dietary participants.[25] The follow-up in these three studies was shorter and participants had a higher mean baseline BMI.

It is reassuring that exercise intervention significantly improved the quality of life outcomes of SF-36 physical function and bodily pain. This concordance strengthens our WOMAC primary and secondary outcome conclusions. Dietary intervention was not associated with these quality of life outcomes but did seem to reduce the depression score. A positive association between BMI and depression was recently reported in a large cohort of primary care patients with osteoarthritis.[26]

Strengths and limitations

This was a pragmatic trial and the factors that improve external validity—for example, ascertainment based on knee pain and not radiographic change—might

have reduced the effect size. A relatively long follow-up period might have reduced efficacy. Contact time with the researcher was limited to a visit once every four months for those in the exercise only group and exercise was self managed, factors that will not have enhanced adherence. Withdrawals were higher from the exercise groups than the dietary intervention group, and the potential selective loss might have resulted in some bias.

We did not ask participants to stop taking painkillers during the trial, a factor that has the potential to confound the pain outcomes. There were no differences between the four randomisation groups with respect to self reported use of analgesics at the start of the trial, but those in an exercise group reported less use and lower doses during the trial than those in a dietary group.

Conclusions and policy implications

Our findings support the long term effectiveness of quadriceps strengthening exercise as an intervention for knee pain in overweight and obese adults aged 45 and over. Such exercise might act by reducing the muscle weakness and impaired balance that occur with knee pain and osteoarthritis. Although the effect size is moderate, it compares favourably with drug based approaches to the long term management of osteoarthritis. Our results give strong support to published recommendations,[7-12] including from NICE,[15] for the management of people with knee osteoarthritis. We have also shown that lifestyle interventions have an impact on the psychological wellbeing and quality of life. This underlines the need for breaking the vicious circle of increase in body weight-decrease in physical activity-increase in osteoarthritis related pain and depression. Further work is needed to establish factors that might indicate which participants are most likely to benefit from these interventions and the best way to deliver them in primary care.

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Competing interests: None declared.

Ethical approval: The study was approved by Nottingham research ethics committee (Q1090219), and informed consent was given by all participants.

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Lifestyle interventions for knee pain in overweight and obese adults aged ≥45: economic evaluation of randomised controlled trial

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ABSTRACT

Objective To estimate the cost effectiveness of four different lifestyle interventions for knee pain.
Design Cost utility analysis of randomised controlled trial.
Setting Five general practices in the United Kingdom.
Participants 389 adults aged ≥45 with self reported knee pain and body mass index (BMI) ≥28.
Interventions Dietary intervention plus quadriceps strengthening exercises, dietary intervention, quadriceps strengthening exercises, and leaflet provision. Participants received home visits over a two year period.
Main outcome measure Incremental cost per quality adjusted life year (QALY) gained over two years from a health service perspective.
Results Advice leaflet was associated with a mean change in cost of −£31, and a mean QALY gain of 0.085. Both strengthening exercises and dietary intervention were more effective (0.090 and 0.133 mean QALY gain, respectively) but were not cost effective. Dietary intervention plus strengthening exercises had a mean cost of £647 and a mean QALY gain of 0.147 and was estimated to have an incremental cost of £10 469 per QALY gain (relative to leaflet provision), and a 23.1% probability of being cost effective at a £20 000/QALY threshold.
Conclusion Dietary intervention plus strengthening exercises was estimated to be cost effective for individuals with knee pain, but with a large level of uncertainty.
Trial registration ISRCTN93206785.

INTRODUCTION

Nearly half of people aged >50 report having knee pain at some point in the past year, and, of these, a third report consulting their general practitioner.[1] Previous economic evaluations for people with knee pain have estimated only the cost effectiveness of different exercise programmes and have not focused on those who are overweight.[2 3] A recent study found that there was an early reliance on pharmacological treatments at the expense of non-pharmacological treatments such as weight loss and exercise.[4] This occurred despite the fact that these two treatments have been recommended as first line treatments for people with knee pain.[5] The value of a quadriceps strengthening exercise programme has been estimated indicating that a home based exercise programme can help improve self reported knee pain and function.[6 7]

We investigated the cost effectiveness of four interventions designed to alleviate knee pain in overweight and obese adults.

WHAT IS ALREADY KNOWN ON THIS TOPIC

The prevalence of knee pain increases with age and for those who are overweight
No assessment as to the cost effectiveness of dietary intervention or quadriceps strengthening exercises, or both, has been made for overweight individuals

WHAT THIS STUDY ADDS

Provision of dietary intervention plus quadriceps strengthening exercises was estimated to be cost effective at a threshold of £20 000 per QALY, though there was a large level of associated uncertainty

METHODS

Participants

The lifestyle interventions for knee pain study compared the effectiveness[8] and cost effectiveness of four intervention groups: dietary intervention plus quadriceps strengthening exercises, dietary intervention, quadriceps strengthening exercises, and leaflet provision. We sent an ascertainment questionnaire to all registered patients aged ≥45 in five Nottingham general practices. A local media campaign was also conducted to improve recruitment. Recruitment started in May 2003 and ended in March 2005. Responding individuals were recruited into the study if they reported that they had had knee pain on most days of the past month and had a body mass index (BMI) >28.0.

Interventions

Participants in both the dietary intervention groups were visited by a dietitian and received a personalised dietary plan that would create a deficit of 2.5 MJ (600 kcal) a day. They were scheduled to receive visits every month in the first six months and every other month for the remainder of the 24 month intervention period. Participants in the exercise groups were taught exercises designed to strengthen the quadriceps (thigh) muscles. They were asked to repeat these exercises at home twice daily and were visited every four months throughout the intervention period. The leaflet was based on the Arthritis Research Campaign *Osteoarthritis of the Knee* leaflet.

Measuring costs

For each participant we estimated the overall change in cost to the health service over the two year trial period by summing the costs associated with visits by healthcare professionals and the change in the costs associated with analgesic use. All costs were estimated in UK sterling (£) at 2006-7 financial year costs.

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Visit costs—All visits were made to provide advice, with the exception of visits to the leaflet group, where visits were undertaken to record trial outcome information. We assumed that the visit cost for the leaflet intervention was zero. The unit cost of visits was estimated from a previously published source.[9] The cost of providing dyno bands was estimated.

Analgesic costs—At baseline, and at 12 and 24 months after randomisation, participants were asked to report analgesic use. These data were combined with unit cost data[10] to estimate the four weekly cost of analgesics.

Use of other resources—We asked a subset of participants (at one year after randomisation) how many visits related to knee pain (in the preceding four weeks) they had made to healthcare professionals or hospital.

Measuring outcomes

To estimate the impact that each intervention had on health related quality of life participants completed the EQ-5D[11] at baseline and at six, 12, and 24 months after randomisation. This enabled us to carry out a cost utility analysis.[12] A utility score was assigned to each of the health state descriptions elicited by the EQ-5D.[13] We used the area under the curve method to estimate, for each participant, the quality adjusted life year (QALY) gain/loss that accrued over the trial period.

Cost effectiveness

We calculated the cost effectiveness of interventions by estimating the incremental cost per QALY gain (incremental cost effectiveness ratio) associated with each intervention group, relative to the next best alternative. Confidence intervals for the incremental cost effectiveness ratio were computed.

Decision uncertainty

To estimate the level of uncertainty associated with the decision as to which intervention was most cost effective we used probabilistic methods to estimate the cost effectiveness acceptability curve for each intervention group.[14 15]

Estimates of mean change in cost (£) and mean (SD) QALY gain associated with each intervention and their component parts

	Dietary intervention plus strengthening exercises	Dietary intervention	Strengthening exercises	Leaflet provision
Analgesic costs:				
Baseline	6.23 (6.19)	6.59 (5.72)	6.60 (6.22)	7.86 (7.12)
12 month	5.14 (5.53)	5.62 (5.79)	5.80 (6.60)	6.26 (6.58)
24 month	5.88 (6.05)	5.75 (5.05)	6.76 (6.45)	6.15 (5.09)
Change in cost (over two years)	−16.22 (118.00)	−17.62 (102.74)	−9.17 (94.37)	−31.07 (136.17)
Visit costs (over two years)	631.86 (324.41)	753.19 (246.01)	223.83 (115.10)	0.00 (0.00)
Overall change in cost	615.64 (323.20)	735.57 (260.13)	214.66 (128.02)	−31.07 (129.78)
EQ-5D score:				
Baseline	0.542 (0.274)	0.531 (0.305)	0.587 (0.245)	0.555 (0.281)
6 month	0.643 (0.211)	0.603 (0.275)	0.649 (0.254)	0.591 (0.251)
12 month	0.608 (0.255)	0.612 (0.267)	0.626 (0.250)	0.617 (0.260)
24 month	0.642 (0.245)	0.609 (0.279)	0.649 (0.260)	0.601 (0.266)
QALY gain	0.147 (0.340)	0.133 (0.415)	0.090 (0.388)	0.085 (0.349)
Incremental cost (*v* leaflet)	646.71	766.64	245.73	—
Incremental effect (*v* leaflet)	0.062	0.048	0.005	—
ICER	10 649	Dominated	ED	—

ICER=incremental cost effectiveness ratio; ED=extended dominance.

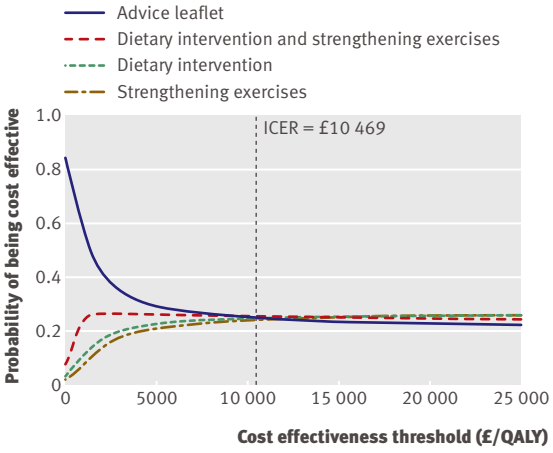
RESULTS

Participants—Questionnaires were returned by 8004 of the 12 408 individuals (65%). Of these, 320 were eligible to take part and randomised to one of the four interventions. An additional 69 participants were recruited via the media campaign. In total, 109 participants were randomised to receive dietary intervention plus quadriceps strengthening exercises, 122 to dietary intervention, 82 to quadriceps strengthening exercises, and 76 to leaflet provision. The mean age of the 389 participants was 61.3 and 257 (66%) were women. According to BMI, 90 (23%) were classified as overweight (BMI 25-<30), 196 (50%) as class I obese (30-<35), 65 (17%) as class II obese (35-40), and 38 (10%) as class III obese (≥40).

Costs—The mean number of visits received by participants randomised to dietary intervention plus quadriceps strengthening exercises was 11.19 (range 0-16), compared with 13.46 for dietary intervention alone (range 0-17), 4.95 for quadriceps strengthening exercises (range 0-7), and 6.05 (range 0-7) for those who received the leaflet. The estimated unit cost per home visit was £54.60 for both the dietary intervention groups, and £44.60 for those who received the quadriceps strengthening exercises; the dyno bands cost £5.50. Over the two year trial period the estimated mean visit cost for those who received dietary intervention plus quadriceps strengthening exercises was £615.64 compared with £735.57 for the dietary intervention, £214.66 for the quadriceps strengthening exercises, and £0.00 for the leaflet (table). At baseline, 12 months, and 24 months the associated question on analgesic costs was completed by an average of 287 (74%) participants. Estimated analgesic costs were lower at follow-up than baseline (table). The overall change in cost to the health service ranged between an increase in mean cost of £735.57 (for the dietary intervention) and a decrease in mean cost of £31.07 (for the leaflet). There was no significant difference across each of the four intervention groups in the number of knee pain related visits to healthcare professionals in the preceding four weeks.

Outcomes—At baseline, six, 12, and 24 months an average of 3369 (87%) participants completed the EQ-5D. Leaflet provision was associated with the lowest QALY gain (0.085 QALYs), and dietary intervention plus quadriceps strengthening exercises was associated with the largest gain (0.147 QALYs) (table).

Cost effectiveness—Comparison of the mean change in cost and mean QALY gain (table) across the four intervention groups showed that dietary intervention alone was dominated by dietary intervention plus quadriceps strengthening exercises. Similarly, quadriceps strengthening exercises was not cost effective as it was subject to extended dominance. Compared with leaflet provision, dietary intervention plus quadriceps strengthening exercises was both more costly (mean incremental cost £646.71, 95% confidence interval £578.15 to £709.62) and more effective (mean incremental effect



0.062, −0.035 to 0.167), with an estimated incremental cost per QALY gain (incremental cost effectiveness ratio) of £10 469.44 (£3738.28 to dominated) (table). Thus, dietary intervention plus quadriceps strengthening exercises is likely to be deemed cost effective as it has an incremental cost effectiveness ratio that is more favourable than a threshold of £20 000-£30 000 per QALY.

Decision uncertainty—The cost effectiveness acceptability curves indicate that for threshold values ≥£5000 per QALY the probability of cost effectiveness was <30% for all four interventions, showing that there is a large level of uncertainty associated with the decision as to which intervention is the most cost effective (figure). The probability that dietary intervention plus quadriceps strengthening exercises was the most cost effective intervention was 23.1% at λ=£20 000 per QALY.

Decision uncertainty: plots of cost effectiveness acceptability curves for four intervention groups (ICER=incremental cost effectiveness ratio)

DISCUSSION

In this randomised controlled trial of four interventions for knee pain in overweight and obese adults, dietary intervention plus quadriceps strengthening exercises was associated with the highest mean gain in QALYs. It was also more costly, with an estimated incremental cost effectiveness ratio of £10 469. As this value falls below a threshold value of £20 000-£30 000 per QALY, the provision of dietary intervention plus quadriceps strengthening exercises represents a cost effective use of scarce healthcare resources. The probability that this was the most cost effective intervention, however, was only 23.1% when λ=£20 000/QALY.

Strengths and weaknesses

Though our two year follow-up period was longer than in many other clinical trials, we did not estimate the long term costs and benefits of these interventions. Similarly, we did not evaluate the provision of group exercise programmes, which others have shown to be effective,[3] and might be more cost effective.

Comparison with other studies

Our results are in contrast with those of Hurley et al, who found that the provision of a rehabilitation programme by a physiotherapist was less effective, in terms of QALYs gained, than usual primary care.[3] Thomas et al found that, compared with either telephone contact or no intervention, an exercise programme was estimated to be more effective but also more costly and was not associated with a reduction in other health costs.[2] Hurley et al found that, compared with usual care, a greater proportion of those who received rehabilitation by a physiotherapist had a clinically meaningful improvement but that this was also more costly.[3]

Future research

Further research might focus on the value of personalised knee pain interventions given the high level of variation in the benefit received from the dietary intervention plus quadriceps strengthening exercises. One might also consider a more thorough investigation of the impact that these interventions have on the number of visits to other healthcare professionals related to knee pain.

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Soluble or insoluble fibre in irritable bowel syndrome in primary care? Randomised placebo controlled trial

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ABSTRACT

Objective To determine the effectiveness of increasing the dietary content of soluble fibre (psyllium) or insoluble fibre (bran) in patients with irritable bowel syndrome.

Design Randomised controlled trial.

Setting General practice.

Participants 275 patients aged 18-65 years with irritable bowel syndrome.

Interventions 12 weeks of treatment with 10 g psyllium (n=85), 10 g bran (n=97), or 10 g placebo (rice flour) (n=93).

Main outcome measures The primary end point was adequate symptom relief during at least two weeks in the previous month, analysed after one, two, and three months of treatment to assess both short term and sustained effectiveness. Secondary end points included irritable bowel syndrome symptom severity score, severity of abdominal pain, and irritable bowel syndrome quality of life scale.

Results The proportion of responders was significantly greater in the psyllium group than in the placebo group during the first month (57% *v* 35%; relative risk 1.60, 95% confidence interval 1.13 to 2.26) and the second month of treatment (59% *v* 41%; 1.44, 1.02 to 2.06). Bran was more effective than placebo during the third month of treatment only (57% *v* 32%; 1.70, 1.12 to 2.57), but this was not statistically significant in the worst case analysis (1.45, 0.97 to 2.16). After three months of treatment, symptom severity in the psyllium group was reduced by 90 points, compared with 49 points in the placebo group (P=0.03) and 58 points in the bran group (P=0.61 versus placebo). No differences were found with respect to quality of life. Fifty four (64%) of the patients allocated to psyllium, 54 (56%) in the bran group, and 56 (60%) in the placebo group completed the three month treatment period. Early dropout was most common in the bran group; the main reason was that the symptoms of irritable bowel syndrome worsened.

Conclusions Psyllium offers benefits in patients with irritable bowel syndrome in primary care.

Trial registration Clinical trials NCT00189033.

WHAT IS ALREADY KNOWN ON THIS TOPIC

Increasing dietary fibre (either insoluble or soluble) is almost universally advocated for the treatment of irritable bowel syndrome

No trial has assessed its effects in the primary care setting, where the vast majority of these patients are managed

WHAT THIS STUDY ADDS

The addition of soluble fibre (psyllium) but not insoluble fibre (bran) was effective in the clinical management of patients with irritable bowel syndrome in primary care

The benefit of psyllium may be somewhat greater in patients who fulfil the Rome II criteria for irritable bowel syndrome

Bran may worsen symptoms of irritable bowel syndrome, especially at the beginning of treatment, and should be advised only with caution

INTRODUCTION

In the management of irritable bowel syndrome, most general practitioners recommend an increase in fibre intake, through the addition of insoluble fibre in the form of bran.[1] Approximately half of patients with irritable bowel syndrome receive drug treatment, often including psyllium based supplements.[2] However, pooled analyses show limited evidence that fibre alleviates symptoms of irritable bowel syndrome, and insoluble fibre may even worsen the symptoms.[3-5] Most available studies on fibre treatment have severe methodological limitations, such as inadequate outcome assessment and lack of placebo control, and all trials were done in secondary care. In contrast, most patients with irritable bowel syndrome are treated in primary care, and this patient group may benefit more from fibre treatment than do those in secondary care.[1 6-8]

We did a randomised placebo controlled trial in primary care patients with irritable bowel syndrome to assess the effectiveness of treatment with either psyllium or bran on symptoms and quality of life.

METHODS

Setting, participants, and randomisation

We recruited patients in the practices of the Utrecht and Maastricht primary care research networks. Patients aged between 18 and 65 years who had been diagnosed as having irritable bowel syndrome in the previous two years were invited to participate. The inclusion period lasted from April 2004 to October 2006.

Patients were randomly allocated to a 12 week treatment regimen with 10 g psyllium (soluble fibre), 10 g bran (insoluble fibre), or placebo (rice flour) in two daily dosages. The average intake of dietary fibre in an adult Dutch population aged 25-65 years is estimated to be 24.0 (SD 6.9) g/day. An addition of 10 g fibre to the diet (total dietary fibre content 30-40 g) is usually considered adequate.[9] The study was blinded at three levels (patient, doctor, and research personnel), but the practice nurse was aware of the treatment allocated.

Outcomes measures

We used the adequate relief question ("Did you have adequate relief of irritable bowel syndrome related abdominal pain or discomfort in the past week?") as the primary outcome.[10 11] We assessed the primary outcome after one, two, and three months of treatment and defined responders as those patients who reported adequate relief of symptoms during at least two out of the previous four weeks.[12] Patients were asked to keep

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Table 1 | Adequate relief of abdominal pain or discomfort (at least two weeks every four weeks): intention to treat analysis

Follow-up assessment and treatment	Responders (%)	Relative risk (95% CI)	% treatment difference (95% CI)	Number needed to treat
Month 1				
Psyllium	45/79 (57)	1.60 (1.13 to 2.26)	22 (7 to 38)	4.5
Bran	31/77 (40)	1.13 (0.81 to 1.58)	5 (−10 to 21)	16.7
Placebo	27/78 (35)	NA	NA	NA
Month 2				
Psyllium	39/66 (59)	1.44 (1.02 to 2.06)	18 (14 to 35)	5.6
Bran	32/63 (51)	1.22 (0.86 to 1.72)	10 (−7 to 27)	10.0
Placebo	27/66 (41)	NA	NA	NA
Month 3				
Psyllium	25/54 (46)	1.36 (0.90 to 2.04)	14 (−4 to 32)	7.1
Bran	31/54 (57)	1.70 (1.12 to 2.57)	25 (7 to 43)	4.0
Placebo	18/56 (32)	NA	NA	NA

NA=not applicable.

a weekly diary during the 12 weeks of treatment and to measure adherence to treatment. We calculated the primary outcome from weekly assessments.

Secondary outcome measurements included severity of symptoms of irritable bowel syndrome, severity of abdominal pain, and quality of life. Severity of symptoms was assessed with the irritable bowel syndrome symptom severity score. The severity of abdominal pain was measured by means of the first question of this score.[13] Disease specific quality of life was monitored with the irritable bowel syndrome quality of life scale.[14] Fibre intake was monitored every month during the trial with a food frequency questionnaire. The secondary outcomes were recorded during one, two, and three months.

Data analysis

Statistical analyses were based on the intention to treat principle. We calculated the proportion of responders in the three groups and compared them at one, two, and three months. Relative risks and risk differences compared with placebo were calculated. Changes in the secondary outcomes at one, two, and three months after the baseline measurements were also compared. To correct for possible differences in relevant baseline characteristics between the three groups, we did multiple logistic regression analyses.

Table 2 | Absolute and relative change in severity of symptoms, severity of abdominal pain, and quality of life from baseline by one, two, and three months of treatment

Follow-up assessment and treatment	IBS symptom severity score (0-500)			Abdominal pain score (0-100)			IBS quality of life scale (0-100)		
	Mean	%	P value	Mean	%	P value	Mean	%	P value
Month 1									
Psyllium	−69	26	0.19	−8	19	0.95	5	7	0.95
Bran	−61	22	0.47	−12	23	0.61	4	5	0.93
Placebo	−49	18	NA	−9	15	NA	3	4	NA
Month 2									
Psyllium	−69	26	0.92	−10	24	0.58	6	8	0.58
Bran	−53	20	0.32	−11	20	0.63	5	7	0.85
Placebo	−71	25	NA	−14	26	NA	5	7	NA
Month 3									
Psyllium	−90	34	0.03	−14	32	0.79	7	10	0.79
Bran	−58	22	0.61	−12	21	0.98	4	5	0.07
Placebo	−49	18	NA	−12	21	NA	4	6	NA

IBS=irritable bowel syndrome; NA=not applicable.

RESULTS

Participants

A total of 296 patients agreed to participate in the trial. In total, 275 patients attended the baseline visit and were randomised; 85 were allocated to psyllium, 97 to bran, and 93 to placebo. More than half (56%) of the patients had constipation predominant irritable bowel syndrome. The mean intake of dietary fibre before participation was 26.9 (SD 11.8) g/day, and patients used on average 2.4 (1.0) l/day of fluids. At baseline, patients allocated to psyllium reported less severe abdominal pain associated with irritable bowel syndrome than did those in the bran and placebo groups.

Two hundred and thirty four (85%) patients attended the second visit at one month, 195 (71%) attended the visit at two months, and 164 (60%) attended the final visit at the end of the three month treatment period. In total, 111 (40%) patients were lost to follow-up during the treatment period: 31 (36%) in the psyllium group, 43 (44%) in the bran group, and 37 (40%) in the placebo group. Reasons given were non-medical (n=15), presumed lack of benefit (n=10), symptom free (n=2), and intolerance of trial treatment (n=34; 7 patients allocated to psyllium, 18 patients allocated to bran, and 9 patients allocated to placebo).

Primary outcome

Rates of response were significantly higher with psyllium than with placebo during the first month of treatment (45/79 (57%) *v* 27/78 (35%); relative risk 1.60, 95% confidence interval 1.13 to 2.26), with a risk difference of 22% (95% confidence interval 7% to 38%). The number needed to treat was four. We saw a similar positive effect during the second month of treatment (39/66 (59%) *v* 27/66 (41%); relative risk 1.44, 1.02 to 2.06). During the third month of treatment the difference between psyllium and placebo—25/54 (46%) *v* 18/56 (32%)—was not statistically significant (relative risk 1.36, 0.90 to 2.04). Only in the third month of treatment was bran more effective than placebo (31/54 (57%) *v* 18/56 (32%); relative risk 1.70, 1.12 to 2.57) (table 1).

Adjustment for baseline symptom severity in the multivariate logistic regression analysis only increased the observed beneficial effect—in the first month of treatment the relative risk for adequate relief in the psyllium group versus the placebo group was 2.70 (1.33 to 5.46). In the worst case analysis (considering patients lost to follow-up as non-responders), psyllium remained more effective than placebo during the first two months of treatment, but bran was no longer superior to placebo during the third month (1.45, 0.97 to 2.16).

Secondary outcomes

The reduction in severity of symptoms in the psyllium group was higher than that in the placebo group, with a significant mean reduction of 90 versus 49 points (P=0.03) only after three months of treatment, whereas the change in severity of symptoms in the bran group was comparable to that in the placebo group. We found no significant differences between the three groups with respect to changes in the severity of abdominal pain related to irritable bowel syndrome or in quality of life (table 2).

Adherence

Adherence to the trial treatment did not differ between the psyllium and bran groups. Patients allocated to psyllium added on average 7.1 (SD 3.1) g/day, bringing their total intake of dietary fibre to 35.1 (14.9) g/day. Patients allocated to bran added on average 6.5 (3.3) g/day and consumed 34.1 (17.2) g/day dietary fibre in total. Fibre intake did not change during the treatment period. Total fluid intake, on average 2.5 (SD 0.8) l/day, did not differ between the groups.

DISCUSSION

In this randomised trial in primary care patients with irritable bowel syndrome, psyllium resulted in a significantly greater proportion of patients reporting adequate relief of symptoms compared with placebo supplementation. Patients receiving psyllium also reported a significant reduction in severity of symptoms of irritable bowel syndrome. We found no differences between the treatment groups in abdominal pain or health related quality of life. Bran showed no clinically relevant benefit, and many patients seemed not to tolerate bran.

Potential limitations

The selection process may have affected the generalisability of the results. A detailed comparison of randomised patients with eligible but non-randomised patients with irritable bowel syndrome (n=371) and non-eligible patients with irritable bowel syndrome (n=724) is reported elsewhere and showed that randomised patients had a higher intensity of abdominal pain, a higher consultation rate, and a longer history of irritable bowel syndrome.[15]

Successful blinding of dietary interventions in research is difficult to achieve, but we took maximum precautions to guarantee that the treatments looked identical. Clinical staff involved were kept blinded to treatment allocation. However, in retrospect approximately three quarters of patients correctly guessed which treatment they were given. We have no clear explanation for this.

Forty per cent of the patients in this study stopped participation before the final visit. The main reason was that they felt worse when taking the fibre supplement. Although this dropout rate is considerable, it is comparable to that in other trials of this nature.[16-18] Obviously, a high dropout rate is going to contribute negatively to the overall result of the study. Although this "worst case scenario" is the most appropriate way of analysing the effectiveness of treatment, it may underestimate the true effectiveness of fibre treatment.[11]

The dropout rate was highest among those patients randomised to bran. This was mainly attributed to worsening of symptoms of irritable bowel syndrome. This has also been reported in secondary care.[19 20]

Implications of findings

The results of this large scale trial in primary care support the addition of soluble fibre, such as psyllium, but not bran as an effective first treatment approach in the clinical management of patients with irritable bowel syndrome.

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Competing interests: None declared.

Ethical approval: The medical ethics committee of the University Medical Center Utrecht approved the study protocol. All patients gave written informed consent.

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Risk of ovarian cancer in women with symptoms in primary care: population based case-control study

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STUDY QUESTIONS What are the symptoms of ovarian cancer presented to primary care and how well do they predict cancer?

SUMMARY ANSWER Seven symptoms independently predicted ovarian cancer: abdominal distension, postmenopausal bleeding, loss of appetite, urinary frequency, abdominal pain, rectal bleeding, and abdominal bloating, with positive predictive values from 0.2% to 2.5%.

Participants and setting
Women aged over 40 with a diagnosis of primary ovarian cancer, from 39 general practices in Devon, England, and five controls matched by age and general practice.

Design, size, and duration
This was a case-control study of 212 women with a diagnosis of ovarian cancer in 2000-7, plus 1060 matched controls. We identified the cases from the general practice computer systems. We coded all entries in the primary care records present in the year before diagnosis of cancer in the case, using the international classification of primary care-2.

Primary outcome(s), risks, exposures
All symptoms present in at least 5% of cases or controls entered univariable conditional logistic regression analyses. We entered the 99 symptoms significantly associated with ovarian cancer into multivariable regressions to identify symptoms independently associated with cancer. For each of these a positive predictive value for a patient consulting in primary care was derived from the likelihood ratio and national incidence statistics.

Main results and the role of chance
The median age of women with ovarian cancer was 67 (interquartile range 58.5-77.5). Staging data were available for 164 (77%), with 53 (32%) of those with staging having FIGO stage I or II, and 111 (68%) stage III or IV. Of the seven symptoms associated with ovarian cancer after multivariable analyses, the odds ratio (95% confidence interval) was 240 (46 to 1200) for abdominal distension, 24 (9.3 to 64) for postmenopausal bleeding, 17 (6.1 to 50) for loss of appetite, 16 (5.6 to 48) for increased urinary frequency, 12 (6.1 to 22) for abdominal pain, 7.6 (2.5 to 23) for rectal bleeding, and 5.3 (1.8 to 16) for abdominal bloating. In 181 (85%) cases and 164 (15%) controls at least one of these seven symptoms was reported to primary care before diagnosis. Symptom reporting was similar in stages I and II, compared with stages III and IV. The figure shows positive predictive values for ovarian cancer for these symptoms individually, in combination with another symptom, and when the same symptom was reported a second time (shown on diagonal).

Bias, confounding, and other reasons for caution
This study relied on good recording of symptoms by doctors. Some bias might have been introduced by more recording of symptoms in those suspected to have cancer; this would cause our positive predictive values to be overestimated. There will have been some overlap between the variables of abdominal distension (generally regarded as a progressive symptom) and abdominal bloating (usually intermittent).

Generalisability to other populations
The ages of affected women and their histological findings are similar to national figures, suggesting that this was a representative population. Thus the results can be used as a basis for primary care decisions about whether to investigate possible ovarian cancer in a symptomatic woman. They can also help in revision of national guidelines.

Study funding/potential competing interests
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POSITIVE PREDICTIVE VALUES (95% CI) FOR OVARIAN CANCER FOR INDIVIDUAL RISK MARKERS AND FOR COMBINED PAIRS

	Abdominal bloating	Abdominal pain	Urinary frequency	Loss of appetite	Abdominal distension
Positive predictive value as single symptom	0.3 (0.2 to 0.6)	0.3 (0.2 to 0.3)	0.2 (0.1 to 0.3)	0.6 (0.3 to 1.0)	2.5 (1.2 to 5.9)
Abdominal bloating	2.0	0.8 (0.4 to 2.2)	1.2	3.3	3.0
Abdominal pain	–	0.7 (0.4 to 1.1)	0.4 (0.2 to 0.8)	1.0 (0.4 to 2.3)	3.1
Urinary frequency	–	–	0.2 (0.1 to 0.8)	NC	2.2
Loss of appetite	–	–	–	0.5 (0.2 to 1.4)	>5
Abdominal distension	–	–	–	–	4.3

Positive predictive value >1% | Positive predictive value >2% | Positive predictive value >5%

COMMENTARY

Diagnosing ovarian cancer—more problems than answers

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The primary care based case-control study by Hamilton and colleagues identified seven symptoms associated with ovarian cancer: abdominal distension, urinary frequency, abdominal pain, postmenopausal bleeding, loss of appetite, rectal bleeding, and abdominal bloating. The report of the first three of these symptoms at least six months before diagnosis was significantly associated with ovarian cancer. The positive predictive values were below 1%, except for abdominal distension, which had a positive predictive value of 2.5%. This study adds to the evidence base derived from primary care of red flag symptoms for several cancers.[1] This is important as most patients in the United Kingdom present initially to primary rather than secondary care.

These findings are broadly concordant with the recent UK consensus statement on ovarian cancer regarding symptoms that could indicate ovarian cancer.[2] This proposes that "increased abdominal size/persistent bloating—not bloating that comes and goes"—might indicate ovarian cancer. The study by Hamilton and colleagues, however, also found abdominal bloating to be independently associated with ovarian cancer, though with a positive predictive value of only 0.3%. The difficulty here, as acknowledged by Hamilton and colleagues, is to understand what is meant by "bloating" when it is recorded in the medical record. Is it referring to something that comes and goes (as commonly seen in irritable bowel syndrome) or persistent (increased abdominal girth/abdominal distension)? This is important as referral guidance from the Scottish Intercollegiate Guidelines Network (SIGN)[3] and the National Institute for Health and Clinical Excellence (NICE)[4] currently refer to abdominal bloating but not distension.

Medical records from primary care in the UK are a rich source of data that are used to populate databases—such as the THIN (the health improvement network) and GPRD (the general practice research database)—that have produced several valuable studies. To improve the quality of these data we need to standardise terminology and improve our Read coding in primary care. This has been one of the positive spin-offs of the UK quality and outcomes framework (QOF). This phenomenon was seen in the study of Hamilton and colleagues, whereby the "incidence" of ovarian cancer seemed to increase after the creation of a cancer register became a requirement for the framework.

There is now increasing evidence that ovarian cancer is not a "silent killer" but one that presents with vague symptoms[2] that have a low positive predictive value for cancer. When a woman presents with such on-going symptoms and a careful history and abdominal and pelvic examination have not identified a cause, pelvic ultrasonography should be considered. This has a reasonably high sensitivity and specificity for identifying ovarian cancer.[5] In its key messages for ovarian cancer for health professionals, the Department of Health proposes that women should be tested for CA125 as part of the initial diagnostic investigation,[6] but this is not supported by current SIGN guidelines[3] because of the test's low sensitivity and specificity.[5 7] CA125 concentrations have been used as part of the ongoing UK collaborative trial for ovarian cancer screening,[8] but this involves serial measurements in women without symptoms. In primary care it might be more logical to measure CA125 concentrations in patients with abnormal results on pelvic ultrasonography, pending gynaecological referral.

Competing interests: None declared.

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pico FAST TRACK

Willingness of Hong Kong healthcare workers to accept pre-pandemic influenza vaccination at different WHO alert levels: two questionnaire surveys

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STUDY QUESTION What proportion of hospital based healthcare workers in Hong Kong would accept pre-pandemic influenza vaccination, and was this affected by escalation in the WHO influenza pandemic alert level?

SUMMARY ANSWER Potential acceptance of pre-pandemic influenza vaccines was low, and the change in WHO alert phase had no significant effect.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS The acceptance of seasonal influenza vaccination in healthcare workers worldwide is low. Neither the change in WHO alert levels nor experience of the SARS outbreak affected the intention to accept influenza vaccines among healthcare workers in Hong Kong.

Participants and setting

2255 healthcare workers completed the questionnaires in the surveys conducted at 31 hospital departments of internal medicine, paediatrics, and emergency medicine in Hong Kong from January to March 2009 (during WHO influenza pandemic alert phase 3) and in May 2009 (WHO alert phase 5).

Design

Repeated cross sectional studies using self administered anonymous questionnaires.

Primary outcome(s)

The intention to accept pre-pandemic vaccination for influenza A subtypes H5N1 or H1N1.

Main results and the role of chance

Of the 4006 questionnaires distributed for the first survey, 1866 (46.6%) were completed. Of the 42 targeted units, 31 (73.8%) participated; representing 20% of all doctors and nurses working in these units. Of the 810 questionnaires distributed in the second survey in all three specialties of one hospital, 389 (48.0%) were completed.

The overall intention to accept pre-pandemic vaccination (H5N1 vaccine) was only 28.4% in the first survey, at WHO pandemic alert phase 3. The table shows the responses from the three hospital departments where both surveys were conducted: no significant changes in the level of intention to accept were seen in the second survey despite the escalation to alert phase 5. The potential acceptance of pre-pandemic vaccination against H1N1 influenza ("swine flu") was 47.9% at WHO alert phase 5. The respondents who were willing to accept H5N1 vaccine were likely to accept H1N1 vaccine as well (91%), whereas only 23.6% of those who declined the H5N1 vaccine expressed an intention to accept H1N1 vaccination (P<0.0001).

The most common reasons for intending to accept vaccination were "wish to be protected" and "following Health Authority's advice." The major barriers to potential acceptance were fear of side effects and doubts about the vaccines' efficacy. The strongest positive associating factors were history of seasonal influenza vaccination and perceived risk of contracting the infection. More than half of the respondents thought nurses should be the first priority group to receive the vaccines. About half of the respondents wanted their family members to receive the vaccines as well.

WILLINGNESS TO ACCEPT VACCINATION AT TWO DIFFERENT INFLUENZA PANDEMIC ALERT PHASES IN ONE HOSPITAL

Vaccination acceptance	No (%) of respondents		Relative risk (95% CI)	P value
	First survey (alert phase 3)	Second survey (alert phase 5)		
H5N1 vaccine:				
Yes	137 (31.2)	134 (34.8)	1.12 (0.92 to 1.36)	0.30
No	302 (68.8)	251 (65.2)		
H1N1 vaccine:				
Yes	–	182 (47.9)	–	–
No	–	198 (52.1)		

Bias, confounding, and other reasons for caution

The main limitation of this study is the response rate just below 50%, which may have resulted in a biased sample. In addition, the study documented only what people said they would do and thus may not reflect the actual vaccine uptake rates.

Generalisability to other populations

There is no major generic barrier to vaccination in Hong Kong, as the uptake for childhood immunisation is high (84.7-99.6%), and a recent survey indicates a high intention to accept (88%) human papillomavirus vaccine, similar to that recorded in the UK (89%).

The seasonal influenza vaccination rate of 32.9% recorded in the current study is close to the range reported from European countries (13.3-28.9%). The findings of this study can therefore serve as a reference for other countries that are planning to offer pre-pandemic influenza vaccine to their healthcare workers.

Study funding/potential competing interests

This study did not receive any external funding. No competing interests are declared.

pico
FAST TRACK

Monitoring the emergence of community transmission of influenza A/H1N1 2009 in England: a cross sectional opportunistic survey of self sampled telephone callers to NHS Direct

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STUDY QUESTION Would the results from self sampling of NHS Direct callers with influenza-like illness improve ascertainment of the early onset of community transmission of influenza A/H1N1 2009 (swine flu) in England?

SUMMARY ANSWER Testing in Health Protection Agency regional laboratories provided a reliable indication of local community transmission, as these trends were mirrored by the proportions of NHS Direct callers with laboratory confirmed infection.

Participants and setting

Participants were people in six Strategic Health Authorities with cold or flu symptoms, or both; aged 16 years or over; who telephoned the NHS Direct multi-channel health advice and information service; and were advised to self treat or seek pharmacy advice (that is, those for whom primary care management was considered unnecessary) during the early stages of the influenza A/H1N1 2009 epidemic (June 2009) in England.

Design

A cross sectional opportunistic survey.

Primary outcome(s)

The proportion of self sampled NHS Direct callers positive for influenza A/H1N1 2009 infection was compared with the proportion of patients managed through primary care and who tested positive in Health Protection Agency (HPA) regional laboratories.

Main results and the role of chance

The rate of change in the proportion of influenza A/H1N1 2009 infections in the NHS Direct scheme each week within each of the six regions closely matched the rate of increase in the proportion infected reported by HPA regional laboratories. Combining the NHS Direct data for the week ending 23 June and the week ending 30 June, the proportion positive in the two severely affected regions of West Midlands and London was 14% (95% CI 11% to 17%), which was significantly greater than the 3% positive in the mildly affected regions of North East and East Midlands (95% CI 1% to 9%; P=0.009). Comparing the data from both systems showed that local community transmission was happening once HPA regional laboratories began detecting 100 or more influenza A/H1N1 2009 infections, or a proportion positive of more than 20% of those tested, each week.

Bias, confounding, and other reasons for caution

The telephone caller survey was limited to people over 16 and to those who were not advised to seek further medical attention. Self sampling kits were sent and returned using the postal service.

Generalisability to other populations

Such self sampling could be replicated in countries with similar telephone helpline services.

Study funding/potential competing interests

This enhanced surveillance was undertaken as part of the national surveillance function of the HPA.

OVERALL WEEKLY TEST RESULTS OF SELF SAMPLED NHS DIRECT CALLERS AND CLINICAL SAMPLES TESTED BY REGIONAL LABORATORIES FOR INFLUENZA A/H1N1 2009 (SWINE FLU) INFECTION IN REGIONS OF ENGLAND GROUPED BY INCIDENCE, 24 MAY TO 30 JUNE 2009*

	Week ending 2 June		Week ending 9 June		Week ending 16 June		Week ending 23 June		Week ending 30 June		Five week summary	
	x/n	Proportion positive (95% CI)	x/n	Proportion positive (95% CI)	x/n	Proportion positive (95% CI)	x/n	Proportion positive (95% CI)	x/n	Proportion positive (95% CI)	x/n	Proportion positive (95% CI)
Mildly affected												
Self samples†	0/4	0 (0 to 60)	0/23	0 (0 to 15)	0/39	0 (0 to 9)	1/29	3 (0 to 18)	1/38	3 (0 to 14)	2/194	1 (0 to 4)
Clinical samples‡	5/46	11 (4 to 24)	29/156	19 (13 to 26)	14/262	5 (3 to 9)	57/466	12 (9 to 16)	142/732	19 (17 to 22)	247/1662	15 (13 to 17)
Severely affected												
Self samples†	0/23	0 (0 to 15)	2/126	2 (0 to 6)	8/178	4 (2 to 9)	22/243	9 (6 to 13)	35/173	20 (15 to 27)	70/743	9 (7 to 12)
Clinical samples‡	52/330	16 (12 to 20)	133/556	24 (20 to 28)	648/1977	33 (31 to 35)	1827/4986	37 (35 to 38)	2255/5178	44 (42 to 45)	4915/13 027	38 (37 to 39)

The following six regions of England were sampled: the North East; the East Midlands; the East of England; the South East; London; and the West Midlands. Data presented for mildly and severely affected regions only
Exact binomial confidence intervals have been calculated for all data
*NHS Direct self sampling initiated on 28 May 2009 †Results from self obtained samples are by week of self swab ‡HPA regional laboratory results are by week of swab