Individualised pelvic floor muscle training in women with pelvic organ prolapse (POPPY): a multicentre randomised controlled trial

*Suzanne Hagen, Diane Stark, Cathryn Glazener, Sylvia Dickson, Sarah Barry, Andrew Elders, Helena Frawley, Mary P Galea, Janet Logan, Alison McDonald, Gladys McPherson, Kate H Moore, John Norrie, Andrew Walker, Don Wilson, on behalf of the POPPY Trial Collaborators**

Lancet 2014; 383: 796–806

Published Online November 28, 2013 http://dx.doi.org/10.1016/S0140-6736(13)61977-7

This online publication has been corrected. The corrected version first appeared at thelancet.com on July 4, 2014

See **Comment** page 760

*Listed in the appendix

Nursing, Midwifery and Allied Health Professions Research Unit, Glasgow Caledonian University, Glasgow, UK (Prof S Hagen PhD, S Dickson BSc, J Logan MA); **Clinic 2, Balmoral Building, Leicester Royal Infirmary, Leicester, UK** (D Stark BSc); **Health Services Research Unit** (Prof C Glazener FRCOG, A Elders MSc) **and Centre for Healthcare Randomised Trials, Health Services Research Unit** (A McDonald MSc, G McPherson PhD, Prof J Norrie MSc), **Third Floor Health Sciences Building, University of Aberdeen, Aberdeen, UK; Robertson Centre for Biostatistics, University of Glasgow, Boyd Orr Building, Glasgow, UK** (S Barry PhD, A Walker PhD); **Department of Physiotherapy, Melbourne School of Health Sciences** (H Frawley PhD) **and Department of Medicine–Royal Melbourne Hospital** (Prof M P Galea PhD), **University of Melbourne, VIC, Australia; Pelvic Floor and Bladder Unit, Department of Urogynaecology, St George Hospital, NSW, Australia** (K H Moore FRACOG); **and Department of Obstetrics and Gynaecology, Dunedin School of Medicine, Dunedin, New Zealand** (Prof D Wilson FRCOG)

Correspondence to: Prof Suzanne Hagen, Nursing, Midwifery and Allied Health Professions Research Unit, Glasgow Caledonian University, Glasgow, UK
s.hagen@gcu.ac.uk

Summary

Background Pelvic organ prolapse is common and is strongly associated with childbirth and increasing age. Women with prolapse are often advised to do pelvic floor muscle exercises, but evidence supporting the benefits of such exercises is scarce. We aimed to establish the effectiveness of one-to-one individualised pelvic floor muscle training for reducing prolapse symptoms.

Methods We did a parallel-group, multicentre, randomised controlled trial at 23 centres in the UK, one in New Zealand, and one in Australia, between June 22, 2007, and April 9, 2010. Female outpatients with newly-diagnosed, symptomatic stage I, II, or III prolapse were randomly assigned (1:1), by remote computer allocation with minimsation, to receive an individualised programme of pelvic floor muscle training or a prolapse lifestyle advice leaflet and no muscle training (control group). Outcome assessors, and investigators who were gynaecologists at trial sites, were masked to group allocation; the statistician was masked until after data analysis. Our primary endpoint was participants' self-report of prolapse symptoms at 12 months. Analysis was by intention-to-treat analysis. This trial is registered, number ISRCTN35911035.

Findings 447 eligible patients were randomised to the intervention group (n=225) or the control group (n=222). 377 (84%) participants completed follow-up for questionnaires at 6 months and 295 (66%) for questionnaires at 12 months. Women in the intervention group reported fewer prolapse symptoms (ie, a significantly greater reduction in the pelvic organ prolapse symptom score [POP-SS]) at 12 months than those in the control group (mean reduction in POP-SS from baseline 3·77 [SD 5·62] *vs* 2·09 [5·39]; adjusted difference 1·52, 95% CI 0·46–2·59; p=0·0053). Findings were robust to missing data. Eight adverse events (six vaginal symptoms, one case of back pain, and one case of abdominal pain) and one unexpected serious adverse event, all in women from the intervention group, were regarded as unrelated to the intervention or to participation in the study.

Interpretation One-to-one pelvic floor muscle training for prolapse is effective for improvement of prolapse symptoms. Long-term benefits should be investigated, as should the effects in specific subgroups.

Funding Chief Scientist Office of the Scottish Government Health and Social Care Directorates, New Zealand Lottery Board, and National Health and Medical Research Council (Australia).

Introduction

Pelvic organ prolapse is a common disorder in women—40% of women older than 50 years have some degree of prolapse on examination.[1] About 11% of women undergo surgery for urinary incontinence or prolapse in their lifetime, and 7% for prolapse alone.[2] In England, about 29 000 prolapse repairs were done between 2010 and 2011,[3] at a cost of around £60 million, and numbers of women undergoing surgery are likely to increase substantially as the population ages.[4] Increasing age and parity, and a family history of prolapse, are the main risk factors for prolapse, although factors such as obesity, heavy lifting, and constipation can also have a role.[5] One study reported a total population-attributable risk for prolapse of 46%, which was associated with women having prolapse symptoms during pregnancy, a mother with prolapse, and undertaking heavy physical work.[6] Prolapse is characterised by symptomatic descent of the vaginal walls, apex, or vault from the normal anatomical position.[7] Women with prolapse might present with vaginal, bladder, bowel, back, abdominal, and sexual symptoms. The disorder can affect daily activity and quality of life. Treatment options include surgery and conservative management, of which the latter is used commonly if the prolapse is low in severity or the woman is not a candidate for surgery. Conservative interventions include physical interventions to improve the function and support of the pelvic floor muscles via pelvic floor muscle training; mechanical interventions (eg, use of vaginal pessaries) to support the prolapse; and lifestyle interventions (eg, weight loss and avoiding of heavy lifting) to avoid exacerbation of the prolapse by decreasing intra-abdominal pressure.

Many physiotherapists who specialise in women's health offer women with prolapse individualised pelvic floor muscle training.[8] The aim of muscle training is to improve the function of the pelvic floor muscles—ie, strength, endurance, and coordination—and to ultimately increase the structural support for the pelvic organs. A Cochrane review[9] showed that training of the pelvic floor muscles was effective for treatment of urinary incontinence. Evidence for the management of prolapse is less clear. A separate Cochrane review[10] identified four trials (including two pilot trials) comparing individuals undergoing pelvic floor muscle training with control groups; two of which were at significant risk of bias. Symptoms, although measured differently in different studies, were improved in the short term in three trials, and pooled data for severity from two trials showed an improvement in prolapse after treatment due to muscle training. The review concluded that reliable evidence is needed about the medium-term and long-term effectiveness and cost-effectiveness of pelvic floor muscle training.

We did the Pelvic Organ Prolapse PhysiotherapY (POPPY) trial to assess whether one-to-one pelvic floor muscle training would reduce the symptoms of prolapse and the need for further prolapse treatment in women with stage I–III prolapse, and whether it would be a cost-effective option, compared with a prolapse lifestyle advice leaflet.

Methods

Study design and participants

We did this parallel-group, multicentre, randomised trial between June 22, 2007, and April 9, 2010, in new attendees at outpatient gynaecology clinics who presented with symptomatic prolapse at 25 centres (23 in the UK; one in Dunedin, New Zealand; and one in Sydney, Australia). Centres were a mixture of university teaching hospitals and district general hospitals, and all offered similar specialist pelvic floor physiotherapy services. Eligible women of any age had stage I–III prolapse of any type (anterior, posterior, apical, or a combination) as confirmed by their gynaecologist on vaginal examination with the pelvic organ prolapse quantification (POP-Q) system,[11] and had prolapse as their main presenting complaint. We excluded women who had received previous treatment for prolapse, including surgery; who were pregnant or less than 6 months postnatal; or who were unable to comply with the intervention (ie, if they were not able to attend the clinic for appointments with the physiotherapist). Women who needed treatment for vaginal atrophy were eligible after completing a course of local oestrogens.

We based the trial methods on findings from our pilot trial.[12] Women provided signed informed consent. We did the trial in accordance with the Declaration of Helsinki. Approval was obtained from the Scotland A Research Ethics Committee, the Lower South Regional Ethics Committee, the Human Research Ethics Committees of The University of Melbourne, and from St George Hospital (Kogarah, NSW, Australia). An independent Trial Steering Committee and a separate independent Data Monitoring Committee oversaw the trial. Full details of the study protocol are available online.

See **Online** for appendix

For the **study protocol** see https://w3.abdn.ac.uk/hsru/poppy/Public/DownloadPage.aspx

Randomisation and masking

Patients were randomly assigned (1:1), with the remote-computer-determined randomisation application at the Centre for Healthcare Randomised Trials (University of Aberdeen, UK), to receive an individualised programme of pelvic floor muscle training or a prolapse lifestyle advice leaflet and no muscle training (control group). Randomisation used a minimisation approach to balance group sizes for key prognostic factors at baseline. Factors were centre, stage of prolapse (I, II, or III), and the motivation for prolapse surgery (ie, women not considering surgery versus those considering surgery). Motivation for surgery is a potentially important factor affecting how adherent women will be to pelvic floor muscle training. The university-based trial coordinator accessed the web-based application and then informed the woman, and the physiotherapist as necessary, of the allocated group. The intervention could not be masked from women or treating physiotherapists. The researchers who coordinated data entry and management (SD, JL, GMcP) were remote from the clinical sites and therefore did not have contact with patients. Outcome assessment was by participant-completed questionnaires, thus avoiding assessor bias; data-entry staff were masked to group allocation. The gynaecologists undertaking the POP-Q assessment at 6 months, including those who were investigators (CG, KHM, and DW), were masked to group allocation until after the examination. The statistical analyst (SB) was independent of the research team and was masked to group allocation until after the main analysis had been undertaken.

Procedures

Women allocated to the intervention were invited to attend five one-to-one appointments for pelvic floor muscle training over 16 weeks (at weeks 0, 2, 6, 11, and 16) with a women's health physiotherapist. The duration of 16 weeks was chosen on the basis of muscle physiology (15 weeks of specific muscle training is needed to gain muscle hypertrophy[13]) and UK clinical guidelines for the management of urinary incontinence, which recommend muscle training for "at least 3 months".[14] Appointment frequency was based on present practice within the UK National Health Service (NHS)—ie, first appointments close together to allow reinforcement of correct exercise technique and understanding of all advice given, later appointments becoming further apart to encourage independent home exercise.

At the first appointment an explanation of types of prolapse, anatomy and function of pelvic floor muscles was given with use of diagrams and a model pelvis. Internal assessment of the pelvic floor muscles was done

to correct exercise technique and assess muscles (using the PERFECT Scheme).[15] An individualised home exercise programme was prescribed on the basis of examination findings. Women were encouraged to progress exercises, with an aim of ten times 10 s maximum holds and up to 50 fast contractions three times per day, and to record all exercises in a diary. Furthermore, women were taught how to precontract the pelvic floor muscles against increases in intra-abdominal pressure (so-called the Knack exercise) and were encouraged to use this technique daily. The home exercise programme was modified at each appointment on the basis of examination findings and diary recordings. Use of electromyography biofeedback, pressure biofeedback, and electrical stimulation were not permitted. Trial physiotherapists attended training before their involvement in intervention delivery within the trial. No additional training was given to physiotherapists during intervention delivery.

Participants received a prolapse lifestyle advice leaflet that gave advice about weight loss, constipation, avoidance of heavy lifting, coughing, and high-impact exercise; women in the control group received this leaflet by post, whereas women in the intervention group received it at their first appointment. The leaflet contained no information about pelvic floor muscle exercises or techniques. Women attended a review appointment with their gynaecologist 6 months after trial entry, at which time they could be referred for further treatment if desired.

We used postal questionnaires to collect data at baseline, and 6 months and 12 months after trial entry. Our primary endpoint was prolapse symptoms at 12 months as measured by the pelvic organ prolapse symptom score (POP-SS),[16] a validated, patient-completed method with seven items relating to frequency of prolapse symptoms in the previous 4 weeks; each item is scored from 0 (never) to 4 (all of the time), with a possible total score ranging from 0 to 28. Secondary outcomes were women's perceived change in prolapse since the start of the study (same, better, or worse); quality of life, measured as interference of prolapse symptoms with everyday life (scored 0 [not at all] to 10 [a great deal]); number of days with prolapse symptoms in the previous 4 weeks; uptake of further prolapse treatment (surgery, pessary, referral to physiotherapy, referral to dietitian, oestrogen cream or tablets, or hormone replacement therapy); severity of incontinence (International Consultation on Incontinence Questionnaire—Urinary Incontinence Short Form, scored from 0 to 21, with higher values showing greater severity);[17] bowel symptoms (early short form version of International Consultation on Incontinence Questionnaire—bowels module, as provided by the developers); sexual symptoms (Pelvic Organ Prolapse/Urinary Incontinence Sexual Questionnaire);[18] general health (12-Item Short Form Health Survey);[19] use of health services in primary and secondary care; and frequency of the practice of pelvic floor muscle exercises in the past 4 weeks (a few times only, once a week, a few times a week, once a day, a few times a day; and contractions per day less than five, five to ten, 11–20, 21–30, 31–60, >60). Intervention adherence was measured in terms of attendance at appointments and the amount of exercise women recorded in their daily exercise diary. Additionally, at each appointment, the physiotherapists delivering the intervention collected data about women's adherence to the prescribed exercise.

The clinics' gynaecologists used the POP-Q system to assess prolapse type and stage in all women before group allocation and at the 6 month review appointment.[11] Formal POP-Q training was given at each trial centre initiation visit. This training included a verbal explanation of the POP-Q system; observation of the American Urogynecological Society POP-Q training DVD; information about standardisation of conditions for POP-Q examination (eg, examination position, bladder emptying, and equipment use); and use of the recording form and a question and answer session. Each centre was given a copy of the DVD and the publication describing the POP-Q.[11] Centres were encouraged to undertake further in-house training, and additional centre visits were offered if necessary.

Statistical analysis

We estimated a mean difference between groups in POP-SS of 2·5 (SD 8) as our effect size, on the basis of findings from our pilot trial.[12] With 253 women per group, the trial had 80% power at a 5% significance level to detect a difference of 2·5 points in the primary outcome measure, assuming a common SD of 8 points.[20] This calculation allowed for a 10% overall loss to follow-up, and 15% of the control group receiving all the benefit of muscle training by undertaking exercises with their own initiative.

We tabulated descriptive statistics, reporting baseline demographics and clinical characteristics with means and SDs, or medians and IQRs as appropriate. We used intention-to-treat analyses to compare the primary outcome at 12 months by fitting a linear mixed-effects model to change from baseline in POP-SS at 6 months and 12 months, with a random intercept for patient within centre, and a random slope for time within patient, and adjusted for baseline POP-SS score and the minimisation variables. Such models implicitly adjust the model estimates when data are missing, with an assumption that data are missing at random, according to reported values.[21] We included women who had observations at baseline and at least one follow-up timepoint in the model. We present the difference between the intervention and control groups in estimated mean change from baseline for 6 months and 12 months with 95% CIs and p values. We also used multiple imputation to assess the assumption of data missing at random and the corresponding effect of

missing responses on the primary outcome.[22] Model assumptions were checked with residual plots and were shown to hold.

We compared POP-Q stage between groups in an ordinal regression model with 6 month POP-Q stage as the dependent variable and baseline POP-Q stage and minimisation variables as covariates. The pooled odds ratio (OR) from the ordinal model was calculated with a 95% CI and p value. Stage II prolapse was subdivided into two groups dependent on whether the prolapse was above the hymen or at the hymen or below. Change in POP-Q stage between baseline and 6 months was also presented. Other secondary outcomes were compared between groups with the Mann-Whitney *U* test for continuous and ordinal variables and the χ^2 or Fisher's exact test for categorical variables.

With planned subgroup analyses we explored the effect of prolapse stage and type, age, and motivation for surgery on the primary outcome, with stricter levels of significance (two-sided p<0·01) than those used for other analyses.

Analyses were done according to a pre-specified statistical analysis plan using the R programming package (version 2.15.0)[23] and the mi package in R (version 0.09-17)[24] for post-hoc multiple imputation analysis.

Our economic assessment was a within-trial analysis 12 months after recruitment, with a cost perspective of the UK NHS. We used direct health-service costs to generate the total cost for each participant. On the basis of the number of physiotherapy appointments attended during the trial, we estimated the amount of physiotherapy time involved in the delivery of the intervention and the associated costs of clinic space. All women were asked in follow-up questionnaires about their use of health services (consultations with their family doctor or a practice nurse) and any further prolapse treatment they had received. Costs were attributed to these items with UK data from the Personal Social Services Research Unit, Unit Costs of Health and Social Care; Scottish Health Service Costs; British National Formulary; and C&G Medicare.[25–28] The costs were balanced against changes in the primary clinical outcome. We assumed that differences between trial groups in rates of subsequent treatments, such as, surgery at the end of the trial follow-up period represented savings. We did sensitivity analyses to assess the possible effects of varying of the intervention effect size and the uptake of subsequent prolapse treatment.

This trial is registered, number ISRCTN35911035.

Role of the funding source

The sponsor of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. GM, JN, SB, AE, SH, and AW had access to all the data in the study and all authors had final responsibility for the decision to submit for publication.

Results

The figure shows the trial profile. 447 eligible patients were randomised to the intervention group (n=225) or the control group (n=222). 377 (84%) participants completed follow-up for questionnaires at 6 months and 295 (66%) for questionnaires at 12 months (figure); 365 (82%) women attended for 6 month review. Non-responders at 12 months were significantly younger and had a higher body-mass index (BMI) than did responders (data not shown). We noted no evidence of differential dropout between the trial groups (figure). Table 1 shows baseline clinical and demographic characteristics. The mean age of participants was 56·8 years (SD 11·5); the median number of births per woman was two (range zero to seven); 412 (93%) of 445 women had had at least one vaginal birth, 28 (6%) of 447 had had at least one caesarean section, 118 (26%) of 445 had had at least one forceps delivery, and 9 (2%) of 447 had had a vacuum extraction. Two (<1%) patients were missing the delivery type for a total of three births between them, explaining the denominator of 445 for these calculations. Women were on average overweight (mean BMI 27 [SD 5·1]). The most common presentation was combined anterior, posterior, and upper compartment

For the **R programming package** see http://www.R-project.org/

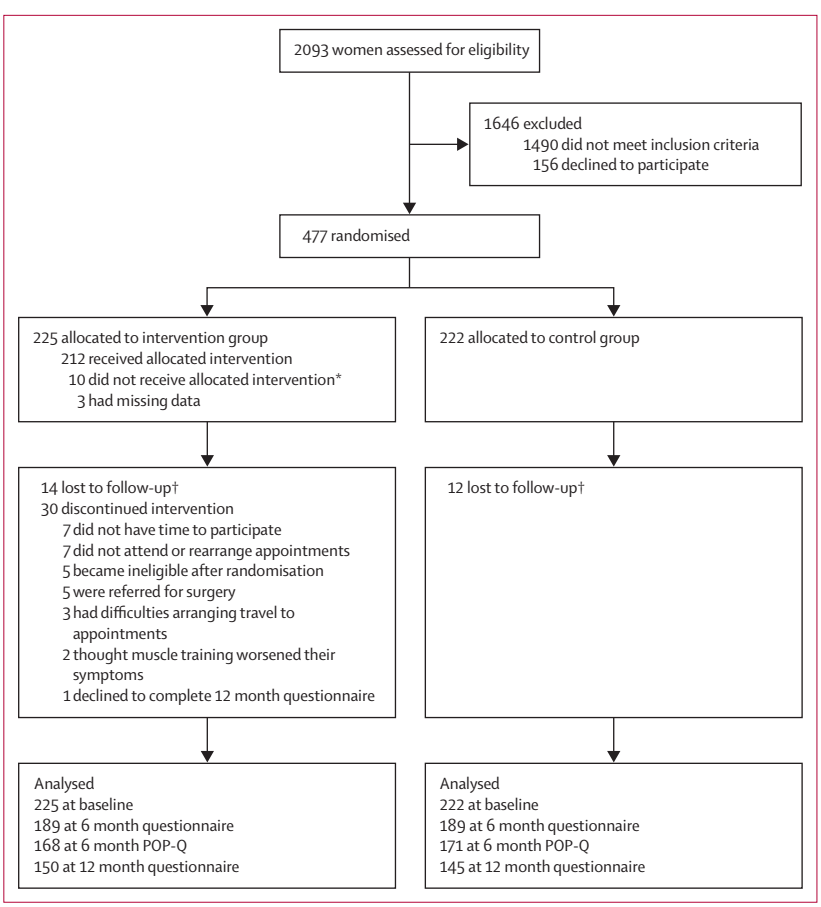

Figure: **Trial profile**
POP-Q=pelvic organ prolapse quantification. *Did not attend any appointments. †Withdrew from questionnaire follow-up.

	Intervention (N=225)	Control (N=222)
Age (years)	56·20 (11·60)	57·50 (11·39)
BMI (kg/m^2)	27·15 (4·99), n=214	27·42 (4·57), n=210
Parity	2 (2–3), n=223	2 (2–3), n=217
Stage of prolapse*		
Stage I	23 (10%)	18 (8%)
Stage II (above the hymen)	48 (21%)	47 (21%)
Stage II (at or below the hymen)	116 (52%)	127 (57%)
Stage III	38 (17%)	29 (13%)
Stage IV	0	1 (<1%)
Type of prolapse		
Anterior	23 (10%)	25/220 (11%)
Posterior	13 (6%)	11/220 (5%)
Anterior and posterior	54 (24%)	54/220 (24%)
Anterior and upper	27 (12%)	22/220 (10%)
Posterior and upper	6 (3%)	8/220 (4%)
Anterior and posterior and upper	102 (45%)	100/220 (46%)
Duration of prolapse symptoms in months	12 (6–24), n=196	12 (6–24), n=201
Baseline POP-SS†	10·04 (6·0), n=224	9·51 (5·64), n=222
Symptom reported in last 4 weeks		
Something coming down	193/219 (88%)	195/219 (89%)
Discomfort worse when standing	140/221 (63%)	147/220 (67%)
Abdominal pain when standing	153/222 (69%)	145/217 (67%)
Lower-back heaviness	131/222 (59%)	125/216 (58%)
Strain to empty bladder	138/221 (62%)	109/218 (50%)
Feel bladder not empty	159/221 (72%)	152/218 (70%)
Feel bowel not empty	154/221 (70%)	140/222 (63%)
Faecal urgency‡	138/223 (62%)	135/221 (61%)
Faecal incontinence‡	60/223 (27%)	55/222 (25%)
Urinary incontinence	145/225 (64%)	156/221 (71%)
Urinary incontinence score (ICIQ-UI SF§)	4 (0–7), n=218	4 (0–7), n=216

Data are mean (SD), median (IQR), n (%), or n/N (%), unless otherwise indicated. BMI=body-mass index. POP-SS=pelvic organ prolapse symptom score. ICIQ-UI SF=International Consultation on Incontinence Questionnaire Urinary Incontinence Short Form. *Pelvic organ prolapse quantification (POP-Q) stage reported here was calculated at the analysis stage with a specially developed programme that used the nine individual POP-Q measurements recorded by the gynaecologist. On occasion this stage differed from that assigned by the gynaecologist that identified women's trial eligibility. †POP-SS: 0=no symptoms, 28=all seven symptoms all the time. ‡We defined faecal urgency as a sudden, irresistible need to have a bowel movement; faecal incontinence was any involuntary loss of faecal material. §ICIQ-UI SF score: 0=no incontinence, no interference with everyday life; 21=maximum leakage and interference.

Table 1: **Baseline characteristics**

	Number of women attending (N=222*)
0	10 (5%)
1	9 (4%)
2	10 (5%)
3	15 (7%)
4	22 (10%)
5	156 (70%)

Data are n (%), unless otherwise indicated. *Missing data for three women from the intervention group.

Table 2: **Number of physiotherapy appointments attended by women in the intervention group**

prolapse, followed by combined anterior and posterior (table 1). Stage II prolapse was the most common type and most women had stage II prolapse at or below the hymen (table 1). Median duration of prolapse symptoms was 12 months (table 1). As expected for a trial of this size, the clinical and demographic factors at baseline were similar between groups (table 1).

178 (80%) of 222 women in the intervention group attended four or five of the possible five physiotherapy appointments during the 16 week intervention period (table 2). Mean interappointment adherence to the prescribed number of sets of exercise or greater was 72% (range 53–79). Women in the intervention group were more likely than those in the control group, although not significantly so, to report undertaking of pelvic floor exercises in the last 4 weeks at 12-month follow-up (115 [78%] of 147 *vs* 95 [69%] of 138 women; risk difference 9·4%, 95% CI –0·8 to 19·6, p=0·07; risk ratio 1·13, 95% CI 0·96–1·34, p=0·15).

Eight adverse events (six vaginal symptoms, one case of back pain and one of abdominal pain) and one unexpected serious adverse event (a skiing injury), defined as affecting normal daily life, were reported; all reports were from women in the intervention group. No event was deemed to be related to the intervention or to trial participation.

Women in the intervention group reported greater improvement in prolapse symptoms (a significantly greater reduction in POP-SS) than those in the control group at both 6 months and 12 months (table 3). When we combined the results from refitting of the model to five imputations of the missing POP-SS scores, estimates of the differences between the groups were very similar to those from the original model (6 months 2·79, 1·91–3·67; 12 months 1·66, 0·74–2·58). The most commonly reported symptom at baseline was "a feeling of something coming down" (table 1); this finding persisted at 6 months and 12 months (table 3). All POP-SS symptoms were significantly less common in the intervention group than the control group at 6 months (table 3); at 12 months "discomfort worse when standing" and "lower abdominal heaviness" were significantly less common (table 3). Women in the intervention group were less likely than those in the control group to report prolapse symptoms in the last 4 weeks, both at 6 months and 12 months (table 3).

When asked "how do you feel your prolapse is now compared to the start of the study?", women in the intervention group were significantly more likely than those in the control group to report that their prolapse was "better", both at 6 months and 12 months (table 3).

After adjustment for baseline POP-Q stage, centre, and whether the woman was motivated to have surgery, the odds of women having a low-severity of prolapse at 6 months were greater in the intervention group than in the control group, although this difference was not significant (OR 1·47, 95% CI 0·97–2·27; p=0·07). A greater proportion of women in the intervention group

	6 months			12 months		
	Intervention (n=225)	Control (n=222)	Adjusted difference in mean change from baseline,* or p value	Intervention (n=225)	Control (n=222)	Adjusted difference in mean change from baseline,* or p value
POP-SS†	6·56 (5·09), n=188	9·17 (5·81), n=189	..	5·74 (4·89), n=145	7·04 (5·43), n=139	..
Reduction in POP-SS from baseline	3·16 (4·78)	0·12 (3·86)	2·84 (2·05–3·63); p<0·0001	3·77 (5·62)	2·09 (5·39)	1·52 (0·46–2·59); p=0·0053
Prolapse symptoms reported in last 4 weeks						
Feeling of something coming down	136/185 (73%)	162/187 (87%)	0·0001	98/139 (70%)	102/138 (74%)	0·09
Discomfort worse when standing	81/184 (44%)	122/185 (66%)	<0·0001	54/141 (38%)	78/137 (57%)	0·0016
Abdominal pain when standing	89/187 (48%)	114/184 (62%)	0·0001	56/143 (39%)	69/135 (51%)	0·0077
Lower-back heaviness	88/187 (47%)	108/182 (59%)	0·0036	63/143 (44%)	68/137 (50%)	0·10
Strain to empty bladder	87/185 (47%)	106/185 (57%)	0·0325	67/143 (47%)	64/136 (47%)	0·95
Feel bladder not empty	109/187 (58%)	129/184 (70%)	0·0009	80/144 (56%)	85/137 (62%)	0·56
Feel bowel not empty	111/187 (59%)	134/184 (73%)	0·0014	85/140 (61%)	91/137 (66%)	0·41
Days with prolapse symptoms in the last 4 weeks‡	137/185 (74%)	162/186 (87%)	0·0001	95/143 (66%)	104/139 (75%)	0·0233
How prolapse is now compared with at the start of the study						
Better	98/187 (52%)	32/189 (17%)	<0·0001	83/145 (57%)	63/141 (45%)	0·0125
The same	77/187 (41%)	114/189 (60%)	..	49/145 (34%)	52/141 (37%)	..
Worse	12/187 (6%)	43/189 (23%)	..	13/145 (9%)	26/141 (18%)	..

Data are difference (95% CI) or n/N (%), unless otherwise indicated. POP-SS=pelvic organ prolapse symptom score. *Adjusted for baseline POP-SS, Pelvic organ prolapse quantification (POP-Q) stage, centre, and whether or not the woman was motivated to have surgery. †POP-SS: 0=no symptoms, 28=all seven symptoms all the time. ‡The question about the number of days with symptoms had a seven-category response, from 0 (none of the time) to 6 (every day). We used the Mann-Whitney *U* test for the number of categories changed since baseline.

Table 3: **Self-reported prolapse symptoms at 6 months and 12 months**

than in the control group had an improvement in their prolapse stage by 6 months (table 4), but this difference was not significant (risk difference 7·5%, 95% CI –1·4 to 16·4, p=0·10; risk ratio 1·39, 95% CI 0·94–2·06, p=0·10).

At 12 months, significantly more women in the control group than the intervention group had received further treatment (table 4; risk difference 25·5%, 14·5–36·0, p<0·0001; risk ratio 2·1, 1·5–2·9, p<0·0001). We noted a similar uptake of surgery, pessary, and other non-trial treatments in the study groups at 12 months, but significantly more women in the control group had had a physiotherapy referral for pelvic floor muscle training (table 4).

Women were asked to report to what extent prolapse interfered with dimensions of their quality of life and about other symptoms (table 5). At 6 months, scores in women in the intervention group were significantly lower (ie, better) than those in women in the control group for all aspects of daily life, and sexual, bladder, and bowel function (except for faecal incontinence), but this finding was not evident at 12 months (table 5). The treatment effect at 12 months was consistent for all prespecified subgroups. We recorded no significant interactions between trial group and any of the subgroup terms in the model: prolapse stage I–III (p=0·38); prolapse type of most descended part anterior, posterior, or upper (p=0·61); age younger than 50 years or 50 years and older (p=0·29); and motivation for surgery as keen or wants to avoid (p=0·89).

	Intervention (n=168)	Control (n=171)	p value
+2 stages	4/168 (2%)	9/171 (5%)	..
+1 stage	26/168 (16%)	29/171 (17%)	..
no change	93/168 (55%)	100/171 (58%)	..
–1 stage	34/168 (20%)	25/171 (15%)	..
–2 stages	11/168 (7%)	8/171 (5%)	..
Further treatment received by 12 months			
Any further treatment received	35/145 (24%)	71/143 (50%)	<0·0001
Surgery	16/145 (11%)	14/143 (10%)	0·84
Pessary	8/145 (5%)	16/143 (11%)	0·13
Physiotherapy referral	2/145 (1%)	38/143 (27%)	<0·0001
Oestrogen, drugs, or other	14/145 (10%)	15/143 (11%)	0·85

Table 4: **Change in prolapse (pelvic organ prolapse quantification) stage at 6 months, and uptake of further prolapse treatment by 12 months**

The cost of the physiotherapy intervention was £170·24 on the basis of an hourly cost of £30·67 for a band 6 physiotherapist.[25] Trial physiotherapists reported that initial appointments took 80 min (60 min face-to-face plus 20 min of administration); follow-up appointments (maximum of four) took 40 min. For overheads such as the cost of the examination room, a figure of £16 per appointment was used.[26] On average women attended for 4·2 sessions of the possible five; therefore, we applied an 84% uptake rate. On the basis of the questionnaire responses regarding further treatment received, and of published cost estimates of the various treatment courses (surgery £1044,[26] pessary £229·45,[27,28] referral for

	6 months			12 months		
	Intervention (n=225)	Control (n=222)	p-value	Intervention (n=225)	Control (n=222)	p-value
Interference of prolapse symptoms with:*						
Everyday life	1 (0–3), n=188	3 (1–6), n=189	0·001	1 (0–3), n=145	1 (0–4), n=138	0·095
Physical activity	2 (0–5), n=187	3 (0–6), n=189	0·010	1 (0–3), n=128	1 (0–4), n=124	0·251
Social activity	0 (0–3), n=187	1 (0–4), n=189	0·012	0 (0–1), n=128	0 (0–2), n=123	0·173
Personal hygiene	0 (0–2), n=188	1 (0–5), n=189	0·003	0 (0–2), n=128	1 (0–3), n=124	0·079
Interference of prolapse symptoms with sex life						
Not at all	75/146 (51%)	53/145 (37%)	0·033†	52/95 (55%)	47/95 (50%)	0·510†
A little	35/146 (24%)	46/145 (32%)	..	25/95 (26%)	29/95 (31%)	..
Somewhat	19/146 (13%)	30/145 (21%)	..	11/95 (12%)	10/95 (10%)	..
A lot	17/146 (12%)	16/145 (11%)	..	7/95 (7%)	9/95 (9%)	..
Bladder symptoms						
Urine leakage	103/188 (55%)	129/189 (68%)	0·01	72/132 (54%)	77/128 (60%)	0·430
ICIQ-UI SF score‡	3 (0–5), n=183	4 (0–7), n=181	<0·0001	3 (0–5), n=126	3 (0–6), n=126	0·118
Bowel symptoms*						
Faecal urgency§	96/188 (51%)	114/189 (60%)	0·041	63/130 (49%)	71/126 (56%)	0·120
Faecal incontinence	42/188 (22%)	47/189 (40%)	0·479	23/130 (18%)	34/127 (27%)	0·072

Data are median (IQR) or n/N (%), unless otherwise indicated. Women were asked to answer questions in relation to the last 4 weeks. ICIQ-UI SF=International Consultation on Incontinence Questionnaire Urinary Incontinence Short Form. *Prolapse-related interference scores range from 0 (not at all) to 10 (a great deal). †Mann-Whitney *U* test done on the ordinal response. ‡ICIQ-UI SF score: 0=no incontinence, no interference with everyday life; 21=maximum leakage and interference. §We defined faecal urgency as sudden, irresistible need to have a bowel movement; faecal incontinence was any involuntary loss of faecal material.

Table 5: **Self-reported effect of prolapse symptoms, and prevalence of urinary and bowel symptoms at 6 months and 12 months**

physiotherapy £170·24, oestrogen or HRT £195·51[27]), the difference between the groups in mean cost of subsequent treatment was £38·63 (95% CI –41·95 to 126·41; p=0·34). The mean cost per woman in the control group was £306·86 (250·74–368·29) and per woman in the intervention group was £268·23 (210·35–333·59). Overall, the net cost of the intervention per woman was £170·24–£38·63=£131·61. This cost is set against a significant difference between groups for the primary outcome. The net cost per one-point improvement in POP-SS was £131·61/1·52, or £86·59. When we consider the 95% CI around the difference in change in POP-SS from baseline (0·46–2·59), the cost per point improvement in POP-SS ranges from £51·81 to £286·11. When we consider the 95% CI around the net costs (£170·24–£126·41 to £170·24+£41·95) the cost per point improvement on POP-SS ranges from £28·84 to £139·60.

Discussion

Our findings show a greater reduction in prolapse symptoms at 12 months in women who underwent pelvic floor muscle training than in the control group. This difference was both statistically significant and of a magnitude that would be important to women, because it exceeded the minimally important change for the POP-SS.[29] This finding was supported by an increase in uptake of supplementary treatments (mainly pelvic floor muscle training) in the control group after 6 months, showing a residual need; a reduced prevalence of each individual prolapse symptom, and of bladder, bowel, and sexual symptoms; and a better quality of life in the intervention group after 6 months of muscle training. Furthermore, women in the intervention group were more likely to report that their prolapse was "better" at both 6 months and 12 months. Although more women in the intervention group had improvement in prolapse stage, this result did not differ significantly between the groups. Subgroup analyses showed that these findings of effectiveness held irrespective of prolapse stage or type, or the woman's age or attitude towards having surgery. Because of the high degree of uptake of some form of pelvic floor muscle training in the control group before the primary outcome assessment at 12 months, and the absence of evidence of differential use of other non-training interventions, the intention-to-treat treatment effect estimate could be an underestimate of the benefit associated with pelvic floor muscle training at 12 months. Therefore, we are confident that the significant treatment effects reported represent real effects that are of importance to women and clinicians. The finding that at 12 months, women in the control group were as likely to be exercising as were those in the intervention group might partly be explained by the uptake of physiotherapy in the control group. That almost 80% of women in the intervention group were still exercising at 12 months is encouraging, because long-term adherence is an important consideration for the effectiveness of this intervention.

The net cost of the intervention was about £130 per woman. The main determinant of the net cost of the intervention is its provision. The main area of uncertainty is the longer-term effect of pelvic floor muscle training on the need for subsequent treatments such as pessaries,

physiotherapy, and surgery; our results are based on the trial follow-up period and we cannot exclude the possibility that treatments have been delayed rather than avoided. Our sensitivity analyses showed plausible ranges around our results; however, reasons exist for believing that the increased costs are unlikely—namely that expenditure on the intervention is a once-only event, as such all costs have been incurred and the benefits in terms of reduced symptoms and treatments avoided are likely to continue to accrue over time. In the assumption that women in the intervention group gained 10% on their quality of life for a year because of the intervention, the cost per quality-adjusted life-year (QALY) gained is about £16 000. This level of cost per QALY is commonly accepted as worthwhile by organisations such as the National Institute for Health and Clinical Excellence in the UK.

The main strengths of our trial were its size, rigour, and pragmatic design, with the intervention being relevant to UK NHS practice, and potentially to other similar health systems worldwide; furthermore, the outcomes were woman-centred. Participants' compliance with trial processes and the intervention were generally high. Unlike other trials in this specialty, our main focus was the prolapse symptoms that led women to seek treatment, and which we used to measure treatment success.

In terms of limitations, we achieved 88% of our target sample size of 506, and noted a lower rate of questionnaire response than expected at 12 months, despite postal and telephone reminders. However, because the SD of the POP-SS was smaller than originally assumed, we nevertheless had sufficient power to identify important differences. We noted no evidence of differential dropout because the response rate was similar in both groups, and results were also robust to missing data. Not all women had a prolapse assessment at 6 months; therefore there was also attrition in the POP-Q responses. This attrition might have contributed to the non-significant POP-Q finding. We noted significant crossover of women in the control group to the intervention group due to their uptake of pelvic floor muscle training after 6 months, which makes interpretation of the findings more challenging. A further limitation is the short follow-up period of 12 months. Because of natural fluctuation in prolapse symptoms and the effect of different treatment modalities, clinical and cost differences between the groups might be expected to change with time. Included women were treatment-naive and presented for treatment for the first time. However, pelvic floor muscle training might also be effective for enhancement of surgical or pessary treatment, or for use after surgical failure, or shortly after childbirth, and these situations need further research. In the economic analysis we did not estimate QALYs gained because findings from our pilot work showed that the SF-12 was insensitive to meaningful changes in prolapse symptoms in this population. Therefore, decision makers should interpret the results on the basis of a careful reading of the symptoms women suffered and the extent to which these symptoms were relieved. The paucity of other economic studies in this specialty makes comparing of results difficult; we look forward to future studies that provide comparisons for these results.

Six other randomised studies have been published to date comparing pelvic floor muscle training with a control intervention.[12,30–34] Three of these trials are pilot trials, which makes the drawing of conclusions from their findings problematic on the basis of their developmental nature and small sample sizes.[12,30,31] Three other full-sized trials have been published.[32–34] The Piya-Anant trial[32] had methodological limitations and a high risk of bias, and cannot reliably contribute to the evidence base. No information was provided about the processes of random sequence generation or allocation concealment, the investigators did not report about attrition and selectively reported about only a subgroup of the women randomised, and uncertainty existed as to whether the analysis was intention to treat. Of the remaining two trials, the Brækken single-centre trial[33] of pelvic floor muscle training versus control randomly assigned 109 women with stage I–III prolapse, of which a subgroup of only 69 (63%) women were symptomatic and hence similar to our population. The very intensive training regimen consisted of weekly appointments for 3 months, followed by bi-weekly appointments for 3 months—a treatment model that would not be possible to deliver in the UK and many other countries because of the restricted availability of specialist physiotherapy resource within their health services. Kashyap and colleagues[34] reported a single-centre trial in women with stage I–III prolapse, which compared taught pelvic floor muscle training plus a self-instruction manual (n=70) with the self-instruction manual alone as the control intervention (n=70). One person delivered the training intervention to all women. The content of the manual was not described and therefore what written instruction the control group received is unclear. More importantly, four women transferred from the control group to the training plus manual group; in which group these women were analysed is unclear. Until this point is clarified, the results have restricted use.

Both Braekken and colleagues[33] and Kashyap and colleagues[34] reported symptom benefit from pelvic floor muscle training. Braekken and colleagues analysed the subgroup of women with symptoms at baseline and reported that women who had received muscle training were more likely than women in the control group to have reduced frequency of prolapse symptoms (74% *vs* 31%) and reduced bother of symptoms (67% *vs* 42%). Kashyap and colleagues reported a significantly greater mean reduction in POP-SS score after the intervention for the muscle training plus manual group compared with the control group (2·99 *vs* 1·25). Neither trial sought evidence about longer term outcomes or the effect on the uptake of other treatments.

Braekken and colleagues[33] also reported that pelvic floor muscle training improved POP-Q stage: 19% of

women in the intervention group had an improved stage versus 8% in the control group (11% risk difference). Our finding for POP-Q was non-significant, but of a similar size. The most likely reason for the non-significant finding in our trial is that the study was not powered to show a difference for this outcome. Data for change in the POP-Q or prolapse stage in Kashyap and colleagues' trial were not adequately reported to allow comparison.[34]

We chose symptom change as our primary outcome measure. This endpoint is usually the driver for individuals seeking treatment for prolapse and is hence the most important outcome for women. That little correlation exists between stage of prolapse and the prolapse symptoms ascribed to it is increasingly recognised.[35,36] Therefore, and as we recorded, that an improvement in symptoms does not necessarily correspond to an improvement in stage is not surprising. 45% of women in the control group in our study reported that their prolapse was better at 12 months. This finding is partly because about half of these women had received further treatment for prolapse by this timepoint. Although significantly more women in the intervention group than the control group reported that their prolapse was better, the remaining participants reported no change or worse prolapse. Thus, a substantial group of women did not benefit. One potential reason for this finding is that a more intensive intervention might be needed for some women. Another reason is that some types or stages of prolapse do not respond to pelvic floor muscle training as well as do others, and hence, improved selection of women for training might be needed. Although our subgroup analyses did not support these hypotheses, the analyses were exploratory and underpowered to draw firm conclusions.

Prolapse can regress with time, which could partly explain the improvement we noted. Three studies of the epidemiology of prolapse concluded that prolapse can both progress and regress.[37–39] Handa and colleagues'[37] and Bradley and colleagues'[38] studies assessed change in severity of prolapse, but in populations older than our own. The study by Miedel and colleagues[39] is most relevant for comparison because it examined both symptoms and stage of prolapse over time in women with a mean age of 56 years. Their findings show that 44% of stage I prolapses had regressed to stage 0, 24% of stage II showed regression, and 64% (95% CI 56–72) of women had a reduction in symptoms by 5 years. However, the study population was mainly non-consulting women identified by a positive questionnaire response to "a feeling of a vaginal bulge", rather than women who were actively seeking treatment for prolapse. As the investigators mentioned, results cannot be automatically generalised to patients who present to health-care services. Therefore, we do not know to what extent women in our trial naturally improved. However, we would expect that any natural regression or progression would happen equally in both groups by virtue of the group allocation, and hence the noted significant differences between the groups must be due to the intervention.

Our trial is the largest, rigorous, pragmatic multicentre trial of pelvic floor muscle training for prolapse, with the longest follow-up, and as such provides the necessary evidence to support changes in clinical practice (panel). However the resource implications of implementation of these findings should be considered. The physiotherapists delivering the trial intervention were specialists in women's health; their numbers are few and their workload is large, presently consisting of mainly the management of urinary incontinence. With the establishment of an evidence-base for pelvic floor muscle training for the management of prolapse, health-care providers will need to invest in extra resources to ensure that a similar service can be provided for women with prolapse. Additionally, beyond the clinical arena, the role of pelvic floor muscle exercises for alleviation of prolapse symptoms is an important public health message that should be shared widely among women of all ages.

We conclude that pelvic floor muscle training should be recommended for the conservative management of prolapse. Effectiveness of such training in the long term, in women who have had previous prolapse surgery, in conjunction with pessary use, and within populations of women with different types or combinations of prolapse, should be investigated further.

***Panel:* Research in context**

Systematic review

The Cochrane review on the topic of conservative management of prolapse was updated in 2011 by two of the investigators, before completion of the analysis of the present trial. We searched the Cochrane Incontinence Group Specialised Trials Register (May 6, 2010) with the search strategy developed for the Cochrane Incontinence Review Group, and CINAHL (between Jan 1, 1982, and May 10, 2010), PEDro (January, 2009), the UK National Research Register (January 2009), ClinicalTrials.gov (April 2009), Current Controlled Trials register (April, 2009), and ZETOC (January, 2009) with the search terms: cystocele, urethrocele, rectocele, vault prolapse, uterine prolapse, vaginal prolapse, pelvic organ prolapse, pelvic floor. We did not impose any language or other restrictions in any of the searches. Four included trials compared pelvic floor muscle training with a control intervention,[12,30,32,33] but two were at significant risk of bias;[30,32] of the remaining two trials, one was the pilot study preceding the current trial.[12] Prolapse symptoms were measured differently in the three trials where this was reported;[12,30,33] however, all three reported greater improvement in symptoms in the training group than the control group. Restricted data from the two trials with low risk of bias[12,33] suggested that pelvic floor muscle training increases the chance of an improvement in prolapse stage compared with no training.

Interpretation

Our trial is the largest, rigorous, pragmatic trial of pelvic floor muscle training versus control for prolapse, and as such provides important robust evidence to inform clinical practice. Our findings confirm those of other smaller or less rigorous studies that such training is beneficial in terms of reducing women's prolapse symptoms. These findings have implications for a range of health-care professionals who care for women with prolapse and for women themselves. Long-term benefits should be investigated, as should the effects in specific subgroups.

Contributors

SH was the chief investigator of the study; had complete involvement in and oversight of the study design, execution, and data collection; and was responsible for writing the final manuscript. DS contributed to the design of the trial overall and the physiotherapy intervention specifically, was responsible for training of the physiotherapists delivering the trial intervention, centre initiation visits, and writing the associated sections of the manuscript. CG contributed to the design of the study, its delivery, and writing of the manuscript, and also to the development, choice, and design of the outcomes measures. SD (the UK trial coordinator) was responsible for the day-to-day management of all aspects of the trial, centre initiation visits, and the trial office, and also contributed to writing of the final manuscript. SB did the statistical analysis of the trial data and contributed to the write-up of the methods and results sections. HF was project manager for the trial in Australia, was a member of the the trial steering committee, and contributed to the final manuscript. MPG was Principal Investigator for the trial in Australia, overseeing its overall management, and contributed to the final manuscript. JL assisted with day-to-day trial management, liaised with centre staff, undertook data reporting, and contributed to the final manuscript. AMcD gave guidance on trial management throughout, and contributed to the final manuscript. GMcP designed the programming of the study database and group allocation system; was involved in the data reporting, including CONSORT; and contributed to the final manuscript. KM was local Principal Investigator in Sydney, was responsible for local set up and delivery of the trial, and contributed to the final manuscript. JN contributed to the study design, and the development and implementation of the statistical analysis plan and its implementation. AW designed and analysed the health economics component of the study and wrote the health economics sections in collaboration with the Chief Investigator DW contributed to the overall study development, oversight of the trial delivery in New Zealand, and guidance on the final manuscript writing. AE developed the programme that calculated prolapse stage from the individual POP-Q measurements, and contributed to the statistical analysis and reporting.

Conflicts of interest

We declare that we have no conflicts of interest.

Acknowledgments

The UK component of the trial was funded by the Chief Scientist Office (CSO) of the Scottish Government (project number CZH/4/377) and is summarised online. The Nursing, Midwifery and Allied Health Professions Research Unit and the Health Services Research Unit are also funded by the CSO. The views expressed in this publication are those of the investigators and not necessarily those of the CSO. We also acknowledge funding for the international components from the National Health and Medical Research Council (Australia) and the New Zealand Lottery Board. We accept full responsibility for the research. We thank all the women who willingly participated in the POPPY trial and completed their questionnaires and attended physiotherapy and gynaecology appointments; the staff at each of our centres for recruiting, motivating and treating our participants; the POPPY trial office staff in the UK (Kim Stewart and Lucy Pyart); those who administered the trial in Dunedin (Gaye Ellis) and Sydney (Wendy Allen) and members of the trial steering committee and data monitoring committee for giving their time in advising the trial team throughout the work.

References

1 Hendrix SL, Clark A, Nygaard I, Aragaki A, Barnabei V, McTiernan A. Pelvic organ prolapse in the Women's Health Initiative: gravity and gravidity. *Am J Obstet Gynecol* 2002; **186:** 1160–66.

2 Olsen AL, Smith VJ, Bergstrom JO, Colling JC, Clark AL. Epidemiology of surgically managed pelvic organ prolapse and urinary incontinence. *Obstet Gynecol* 1997; **89:** 501–06.

3 Health and Social Care Information Centre. Hospital episode statistics, admitted patient care—England, 2010–11. Nov 2, 2011. http://www.hscic.gov.uk/pubs/hesadmitted1011 (accessed June 22, 2013).

4 Wu JM, Kawasaki A, Hundley AF, Dieter AA, Myers ER, Sung VW. Predicting the number of women who will undergo incontinence and prolapse surgery, 2010 to 2050. *Am J Obstet Gynecol* 2011; **205**: 230.e1–5.

5 Miedel A, Tegerstedt G, Maehle-Schmidt M, Nyrén O, Hammarström M. Nonobstetric risk factors for symptomatic pelvic organ prolapse. *Obstet Gynecol* 2009; **113:** 1089–97.

6 Slieker-ten Hove MC, Pool-Goudzwaard AL, Eijkemans MJ, Steegers-Theunissen RP, Burger CW, Vierhout ME. Symptomatic pelvic organ prolapse and possible risk factors in a general population. *Am J Obstet Gynecol* 2009; **200**: 184.e1–7.

7 Abrams PH, Cardoza L, Khoury AE, Wein A. Incontinence, 5th edn. Plymbridge, UK: Health Publication Ltd, 2013.

8 Hagen S, Stark D, Cattermole D. A United Kingdom-wide survey of physiotherapy practice in the treatment of pelvic organ prolapse. *Physiotherapy* 2004; **90:** 19–26.

9 Dumoulin C, Hay-Smith J. Pelvic floor muscle training versus no treatment, or inactive control treatments, for urinary incontinence in women. *Cochrane Database Syst Rev* 2010; **1:** CD005654.

10 Hagen S, Stark D. Conservative prevention and management of pelvic organ prolapse in women. *Cochrane Database Syst Rev* 2011; **12:** CD003882.

11 Bump RC, Mattiasson A, Bø K, et al. The standardization of terminology of female pelvic organ prolapse and pelvic floor dysfunction. *Am J Obstet Gynecol* 1996; **175:** 10–17.

12 Hagen S, Stark D, Glazener C, Sinclair L, Ramsay I. A randomized controlled trial of pelvic floor muscle training for stages I and II pelvic organ prolapse. *Int Urogynecol J Pelvic Floor Dysfunct* 2009; **20:** 45–51.

13 Bo K. Pelvic floor muscle exercise for the treatment of stress urinary incontinence: an exercise physiology perspective. *Int Urogynecol J* 1995; **6:** 282–91.

14 National Institute for Health and Clinical Excellence. Urinary incontinence: the management of urinary incontinence in women. Clinical guidance 40. London: NICE, 2006.

15 Laycock J, Jerwood D. Pelvic floor muscle assessment: the PERFECT scheme. *Physiotherapy* 2001; **87:** 631–42.

16 Hagen S, Glazener C, Sinclair L, Stark D, Bugge C. Psychometric properties of the pelvic organ prolapse symptom score. *BJOG* 2009; **116:** 25–31.

17 Avery K, Donovan J, Peters TJ, Shaw C, Gotoh M, Abrams P. ICIQ: a brief and robust measure for evaluating the symptoms and impact of urinary incontinence. *Neurourol Urodyn* 2004; **23:** 322–30.

18 Rogers RG, Coates KW, Kammerer-Doak D, Khalsa S, Qualls C. A short form of the Pelvic Organ Prolapse/Urinary Incontinence Sexual Questionnaire (PISQ-12). *Int Urogynecol J Pelvic Floor Dysfunct* 2003; **14:** 164–68.

19 Ware JE Jr, Kosinski M, Keller SD. A 12-Item Short-Form Health Survey: construction of scales and preliminary tests of reliability and validity. *Med Care* 1996; **34:** 220–33.

20 Allahdin S, Glazener C, Bain C. A randomised controlled trial evaluating the use of polyglactin mesh, polydioxanone and polyglactin sutures for pelvic organ prolapse surgery. *J Obstet Gynaecol* 2008; **28:** 427–31.

21 Diggle PJ, Heagerty P, Liang K-Y, Zeger SL. Analysis of longitudinal data, 2nd edn. Clarendon: Oxford University Press Inc, 2002.

22 Rubin DB. Multiple imputation for nonresponse in surveys. New York: John Wiley & Sons, 1987.

23 R Development Core Team. R: a language and environment for statistical computing. Vienna: R Foundation for Statistical Computing, 2012.

24 Su Y-S, Gelman A, Hill J, Yajima M. Multiple imputation with diagnostics (mi) in R: opening windows into the black box. *J Stat Softw* 2011; **45:** 1–31.

25 Curtis L. Unit costs of health and social care 2009. Kent: University of Kent, 2009.

26 Information Services Division. Scottish health service costs year ended 31 March 2010. Edinburgh: NHS National Services Scotland, 2010.

27 Joint Formulary Committee. British National Formulary, 61st edn. London: British Medical Association and Royal Pharmaceutical Society of Great Britain, 2011.

28 C&G Medicare. Club pessary. 2010. http://www.incoshop.co.uk/club-pessary-238-p.asp/ (accessed June 25, 2012).

For a **summary of the POPPY trial** see http://www.cso.scot.nhs.uk/Publications/ExecSumms/JuneJuly11/HagenNeeds.pdf

29 Hagen S, Glazener C, Cook J, Herbison P, Toozs-Hobson P. Further properties of the pelvic organ prolapse symptom score: minimally important change and test-retest reliability. *Neurourol Urodyn* 2010; **29:** 1055–56.

30 Ghroubi S, Kharrat O, Chaari M, Ben Ayed B, Guermazi M, Elleuch MH. Effect of conservative treatment in the management of low-degree urogenital prolapse. *Ann Readapt Med Phys* 2008; **51:** 96–102 (in French).

31 Stüpp L, Resende AP, Oliveira E, Castro RA, Girão MJ, Sartori MG. Pelvic floor muscle training for treatment of pelvic organ prolapse: an assessor-blinded randomized controlled trial. *Int Urogynecol J* 2011; **22:** 1233–39.

32 Piya-Anant M, Therasakvichya S, Leelaphatanadit C, Techatrisak K. Integrated health research program for the Thai elderly: prevalence of genital prolapse and effectiveness of pelvic floor exercise to prevent worsening of genital prolapse in elderly women. *J Med Assoc Thai* 2003; **86:** 509–15.

33 Brækken IH, Majida M, Engh ME, Bø K. Can pelvic floor muscle training reverse pelvic organ prolapse and reduce prolapse symptoms? An assessor-blinded, randomized, controlled trial. *Am J Obstet Gynecol* 2010; **203:** 170e1–7.

34 Kashyap R, Jain V, Singh A. Comparative effect of 2 packages of pelvic floor muscle training on the clinical course of stage I–III pelvic organ prolapse. *Int J Gynaecol Obstet* 2013; **121:** 69–73.

35 Ellerkmann RM, Cundiff GW, Melick CF, Nihira MA, Leffler K, Bent AE. Correlation of symptoms with location and severity of pelvic organ prolapse. *Am J Obstet Gynecol* 2001; **185:** 1332–37.

36 Mouritsen L, Larsen JP. Symptoms, bother and POPQ in women referred with pelvic organ prolapse. *Int Urogynecol J Pelvic Floor Dysfunct* 2003; **14:** 122–27.

37 Handa VL, Garrett E, Hendrix S, Gold E, Robbins J. Progression and remission of pelvic organ prolapse: a longitudinal study of menopausal women. *Am J Obstet Gynecol* 2004; **190:** 27–32.

38 Bradley CS, Zimmerman MB, Qi Y, Nygaard IE. Natural history of pelvic organ prolapse in postmenopausal women. *Obstet Gynecol* 2007; **109:** 848–54.

39 Miedel A, Ek M, Tegerstedt G, Mæhle-Schmidt M, Nyrén O, Hammarström M. Short-term natural history in women with symptoms indicative of pelvic organ prolapse. *Int Urogynecol J* 2011; **22:** 461–68.