Managing urinary incontinence in elderly village women in rural Bangladesh: a cluster randomized trial.

Protocol incorporated into a research proposal submitted to the Canadian Institutes for Health Research, submitted April 2014. The trial is registered at ClinicalTrials.gov with registration number NCT02453100

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PLEASE NOTE:

There were two amendments to the protocol during the trial.

1) Disclosure of the intervention occurred before rather than, as per protocol, after consent.

2) In every village with an exercise intervention the research paramedic lead an exercise group for participants in weeks 13 to 24. The protocol required that she encourage continued exercise but did not envisage an organised exercise group.

2. Trial protocol

2.1 Trial design

The study is a cluster randomized trial of a behavioural intervention in which villages, paired geographically on size and socioeconomic structure, are randomly allocated within pair to active or control intervention

2.2 Recruitment protocol (common to both intervention and control villages)

In 2013 GK completed a periodic census of residents of all the villages under its care (the first since 2005). For each village identified for inclusion in the study, a list will be compiled of all women estimated, from the 2013 census, to be aged 60-75 years at the time the protocol is to be implemented in the village. Population records held at the local GK health centre will be used to check for any changes in the census lists (deaths, movements in or out of the village).

The female village paramedic will approach, at home, all listed women aged 60-75 years to determine whether they have urinary incontinence ('yes' to screening questions 2, 3 or 4 on the Urinary Distress Index (appendix 1)) and, if so, whether they would meet the inclusion criterion for the trial (see below). The numbers reporting involuntary leakage will determine the number of 'paras' (sections of the village) to be included if a large number is identified at this stage. Eligible women will be invited to a village meeting at which promotion of healthy lifestyle habits for elderly women will be discussed (without focus on urinary incontinence).

Following the village meeting eligible women will be visited at home by the village and research paramedic together. The village paramedic will introduce her colleague and then withdraw while the research paramedic explains the study and asks for consent. The baseline questionnaires (appendices 1-4) including a demographic questionnaire developed for this study (appendix 5) will be completed. Weight and height will be measured and a urine sample tested for pyuria/leucocytes: those testing positive for infection will commence a 7 day course of antibiotics, following standard GK procedures: women receiving antibiotics will not be excluded from participation in the trial. Allocation of the village to intervention or control group will be disclosed to the research paramedic and physiotherapist after recruitment but before a further training meeting of all women who have consented. During this meeting women will be given training on research procedures (use of the 3 day continence record (3DCR), appendix 6) and education about the healthy bladder including information on how the urinary system works and how to maintain good bladder habits (appendix 7). The first 3DCR belt will be attached with demonstration of how this can be tucked up so that it is not generally visible.

2.3 Protocol specific to intervention villages

1) In the intervention villages the training meeting will be extended to introduce the physiotherapist who will lead the exercise classes. She will explain the pelvic floor muscle training using visual aids and describe the arrangements for the exercise classes.
2) Three days after the attachment of the baseline 3DCR the research paramedic will visit the woman at home with the community physiotherapist, to collect the 3DCR and reinforce the healthy bladder education. The physiotherapist will give individual training to each woman on the pelvic floor exercises.

3) Women will then be included in group mobility and pelvic floor exercise classes for one and a half hours twice weekly for 12 weeks and encouraged to carry out independent exercises each day when there is no group session. The progressive exercise regime is described in detail in appendix 8.
4) Two weeks after the initial pelvic floor training (and after 4 group exercise classes) the physiotherapist will visit the woman in her home to identify and help overcome any obstacle to independent exercise between classes and to reinforce the earlier training in pelvic floor muscle training. If the woman feels the need for further coaching the physiotherapist may offer to check that woman is carrying out the exercise correctly by inserting one finger into the vagina while the woman contracts her pelvic floor muscles. Should the internal examination show that pelvic floor exercises are not being performed optimally, the physiotherapist will make a further attempt at explaining what is required. Inability to successfully demonstrate a pelvic floor contraction will not result in exclusion from the study. Experience from the feasibility study indicated that such an examination was acceptable to only 42% (appendix 9) and it will be made clear that such internal checking is entirely voluntary. A separate witnessed consent (signature or thumb print) will be obtained prior to this procedure. If a previously unsuspected 3rd degree uterine prolapse is discovered at this time the woman will be removed from the study and, if medically indicated, offered surgical repair through GK at no cost.
5) At the end of 12 weeks, immediately after the last scheduled group exercise class, two short questionnaires will be completed (the 7 item depression scale and the Sandvik index).
6) The research and/or the village paramedics will meet with the woman each month for six months from the initial training session to encourage her continued participation and adherence to the individual exercise program, to reinforce healthy bladder habits and to deliver, and collect, the 3DCR.
7) At 6 months, on the day she collects the final 3DCR, the research paramedic will repeat the questionnaire measures of continence, quality of life and depression used at baseline and repeat the measurement of weight.

2.4 Protocol specific to the control villages

This protocol is identical to that in the intervention village, but without pelvic floor muscle training or group exercise classes.

1) Three days after the attachment of the baseline 3DCR the research paramedic will visit the woman at home to collect the first 3DCR and reinforce the healthy bladder education.
2) Two weeks after the training meeting the research paramedic will visit the woman at home to reinforce the healthy bladder message and will offer to examine the woman for uterine prolapse. This will be entirely voluntary. A separate witnessed consent, signed or with thumb print will be obtained prior to this procedure. If a previously unsuspected 3rd degree uterine prolapsed is discovered during this checking the woman will be removed from the study and if medically indicated offered surgical repair through GK at no cost.
3) At the end of 12 weeks two short questionnaires will be completed (the 7 item depression scale and the Sandvik index).
4) The research and/or village paramedic will meet with the woman each month for 6 months from the initial training session to encourage her continued participation and adherence to the 3DCR. The paramedic will reinforce the healthy bladder habits education at each visit.
5) At 6 months, on the day she collects the final 3DCR, the research paramedic will repeat the questionnaire measures of continence, quality of life and depression used at baseline and repeat the measurement of weight.

2.5 Allocation procedures

Within each of the 4 Divisions of Bangladesh in which GK has a substantial presence, villages with 120 or more women aged 60-75 years in the 2013 GK census will be listed, together with the proportion of households classified, by GK administrative criteria (independent of this study), as poor or very poor. Villages within Division will be paired matching on size and socioeconomic structure, with the proviso that the matched pairs are in different GK projects (i.e. do not share a common health centre) to minimize the possibility of contamination. Only one village will be chosen from each 'project'. In each of the 4 Division the four pairs of villages most closely matched (first on size, then socio-economic composition) will be chosen for the study, with random selection of pairs if more than 4 pairs are equally eligible. Within each pair the intervention village will be randomly allocated by the study statistician (based in Canada) with the status revealed to the field team only after the initial recruitment phase is completed (see paragraph 2.2 above).

2.6 Protection from bias

It is not possible to blind the field team or participants as to the nature of the intervention beyond initial recruitment but concealment to that point will minimize any difference in recruitment strategies in intervention and control villages. The proviso that pairs of villages come from different 'projects' implies that the villages within a pair will be at least 30 km apart. In the feasibility study (appendix 9) women were asked at the final (6 month) contact whether they had discussed the intervention with anyone (in person or by phone) and, if so, how far away that person lived: the greatest distance reported was 2 km.

The primary outcome measure is the change in the number of 'red knots' (indicating urinary incontinence episodes over 3 days) between baseline and the 6 month follow-up. Use of this semi-objective measure does not require subjective interpretation by the survey team and will minimize observer bias, but it is nevertheless possible that the closer attention paid to participants in the intervention villages may influence the assiduousness with which they report episodes.

In both intervention and control villages, women will be offered physical examination for uterine prolapse during the first two weeks of the trial. In the intervention villages the uptake may be higher as the examination will include feedback on the training for pelvic floor exercises. However the prevalence of these conditions is low (only 1/39 women examined in the intervention villages in the feasibility study was found to have a 3rd degree prolapse) and it is unlikely that such a differential exclusion would bias the outcome importantly.

2.7 Inclusion/exclusion criteria

Participation will be limited to those aged 60-75 years at the start of recruitment, who are assessed by the research paramedics to have both sufficient cognitive capacity to give informed consent and reasonable mobility to take part in the exercise program. The paramedic responsible for the village and trained for this study will assess whether a potential participant can stand from a seated position and walk unaided for 3 meters within 15 sec and is able to demonstrate her understanding of the 3 day continence record under supervision of the paramedic. Women meeting both these criteria will be eligible for inclusion. While this requirement will exclude those with dementia or who are bed-ridden, for example, the study requirements make low intellectual and mobility demands in an attempt to make the results generalizable to the great majority of elderly women in these circumstances. In this phase (unlike the feasibility study) recruitment will be restricted to those who declare themselves to be incontinent at baseline (2.2 above).

Women found at 2 weeks into the trial to have a stage 3 or greater uterine prolapse will also be excluded.

2.8 Treatment duration

In the intervention villages the period of physiotherapist supervised exercise will be 12 weeks followed by a further 12 week paramedic-monitored maintenance period for a total of 24 weeks. In the control villages paramedics will monitor the whole 24 week period. The data collection will be spread over 36 months.

2.9 Frequency and duration of follow-up

The 3 day continence record (3DCR) will be completed at baseline then every 4 weeks for a total of 7 recordings. Questionnaires reflecting troublesomeness of urinary symptoms (appendix 1), severity of urinary symptoms (appendix 2), depression (appendix 3) and quality of life (appendix 4) will be completed at baseline and at 24 weeks: the severity and depression scales will also be completed at 12 weeks.

2.10 Outcome measures: primary and secondary

The primary outcome will be change in frequency of involuntary leakage of urine between baseline and 24 weeks as indicated by the 3DCR. Secondary outcomes include change from baseline in frequency of micturition, severity of urinary symptoms, and depression at 3 and 6 months and in level of distress caused by urinary symptoms and in quality of life measured at 6 month.

2.11 Measurement at follow-up

All proposed measures (appendices 1-6) have been piloted during the feasibility study (appendix 9) and psychometric properties examined in prior test-retest studies (appendix 10).

2.12 Health research issues – health economics and quality of life

As no treatment for incontinence is currently offered to incontinent village women the cost of physiotherapist and paramedic time to provide the proposed intervention cannot be discounted against savings in the cost of existing treatment. However the study has been designed to use only facilities currently available within the GK field force and as such the marginal cost is low. No incontinence specific quality of life scale has been developed and validated for the Bangladeshi population but the EQ-5D has been used in Bangladeshi rural populations and we have agreement to use the 'approved' Bangladeshi version for this project. The power of such a measure to detect a meaningful difference on this scale as well as the sample size required is discussed below.

2.13 Sample size calculations (including non-compliance/drop-out)

It is proposed to identify 30 eligible incontinent women in each of 32 villages. Based on the feasibility we anticipate that at least 24 of these will agree to take part. In the feasibility study 80.3% of those recruited provided end-of-study 3DCR.

Using the feasibility study data from five villages, we calculated study power based on the sample size formula for cluster randomized trials for the primary outcome of change in urinary incontinence between baseline and follow-up and for the secondary outcome of EQ-5D, both as continuous variables. The power/sample size calculation was based on 16 pairs of villages, each pair containing one intervention village and one control village, with 20 participants in each village. Based on the results of Diehr *et al.*, we will match in design but break the matches in analysis to increase the power: unless the matching is highly effective, this strategy has as high or higher power than the matched design and analysis in cluster randomized design. While the intra-class correlation (ICC) estimated from the feasibility data was nearly zero for both outcomes, we assumed conservatively ICC=0.15 in the calculation to cover unexpectedly higher levels of correlation than the feasibility data among participants from the same village.

Based on the feasibility data, there was a mean change of 3.23 with an SD of 4.50 in women not dry at baseline in the control village. With 16 pairs of villages our study has 81% power, with ICC of 0.15, to detect a mean 2 point difference between intervention and control villages in improvement between baseline and end-of-trial leakage episodes over 3 days. A reduction of episodes of this order is perceived by incontinent women to be a significant improvement. For the secondary outcome of EQ-5D, the pilot data indicated a mean change of 7.2 on the visual analogue scale with standard deviation of 17.9 in the control subjects. Our study design has 83% power to detect a 7.0 point difference in the mean change of EQ-5D VAS scores between the intervention and control villages. Thus, for both outcomes, we have sufficient power to detect clinically-significant changes associated with the intervention (see also appendix 11).

2.14 Compliance

In the feasibility study (appendix 9) not all women were contacted but among those that were there were 17 refusals recorded (82.3% acceptance among those contacted). Once in the study compliance was high with >80% completing the end of study 3DCR and questionnaires. Where compliance is not complete, the most recent continence record will be used as exit value.

2.15 Loss to follow-up

Follow-up is completed at 6 months after recruitment and, as such, is equivalent to compliance (see 2.14).

2.16 Number of centres

The study will be carried out only in villages in which health care is provided by GK and the study will be coordinated centrally through the GK research office.

2.17 Analysis

The analyses will be by intention-to-treat. Matching for village pairs will be broken but the villages will be considered random effects accounting for the cluster randomized design of the study. General Linear Models (GLM) will be used to compare the improvement of urinary incontinence and the mean change in the VAS quality of life, EQ-5D, from baseline to the follow-up between the intervention and control villages. These GLMs will be fitted using the restricted maximum likelihood method implemented in Stata. Statistical inference on the intervention-effect parameter will be made using the standard inference method of GLMs.

2.18 Frequency of analysis

No interim analysis is planned (unless requested to do so by the statistician of the data monitoring committee (DMC) - see below).

2.19 Subgroup (and mediation) analyses

We consider the following a-priori hypothesized potential differences across subgroups. The analysis of the primary outcome (urinary incontinence improvement) will be carried out stratifying by age and severity of incontinence at baseline. Changes in depression score and quality of life will be examined stratified by improvement (if any) in incontinence.

2.20 Pilot study

Preliminary work has included both qualitative and quantitative pilot studies to test the acceptability and comprehension of the proposed measures and their psychometric properties (appendix 10). A 4

week trial of the intervention was carried out immediately following training of the field staff and prior to the comprehensive feasibility study reported in appendix 9.

Trial steering committee and data monitoring committee

A data monitoring committee (DMC) of four members will be established with two Bangladeshi and two North American members including a DMC statistician with extensive knowledge of cluster randomized trials. The committee will receive and review periodic (12 monthly) reports of trial progress and immediate report of any untoward incident that might impinge on the safety of participants. In such an event, the committee will recommend any change that may be necessary to preserve the safety of participants or, if such changes cannot be made, the termination of the trial. Should the DMC request an interim analysis they will consider the result and recommend whether any extension of the trial is indicated to increase power or whether the trial should be stopped early because either a clear answer has already been obtained or because there appears to be little prospect of achieving sufficient power.

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Appendix 1

Urinary Distress Index

Urogenital distress Inventory version 6 – short form

1. Do you usually experience frequent urination? ☐ Yes ☐ No

   If yes, how much does this bother you? ☐Not at all ☐Somewhat ☐Moderately ☐Quite a bit

2. Do you usually experience urine leakage associated with a feeling of urgency; that is, a strong sensation of needing to go to the bathroom? ☐ Yes ☐ No

   If yes, how much does this bother you? ☐Not at all ☐Somewhat ☐Moderately ☐Quite a bit

3. Do you usually experience urine leakage related to coughing, sneezing, or laughing? ☐Yes ☐ No

   If yes, how much does this bother you? ☐Not at all ☐Somewhat ☐Moderately ☐Quite a bit

4. Do you experience small amounts of urine leakage (that is, drops)? ☐ Yes ☐ No

   If yes, how much does this bother you? ☐Not at all ☐Somewhat ☐Moderately ☐Quite a bit

5. Do you experience difficulty emptying your bladder? ☐ Yes ☐ No

   If yes, how much does this bother you? ☐Not at all ☐Somewhat ☐Moderately ☐Quite a bit

6. Do you usually experience pain or discomfort in the lower abdomen or genital region? ☐ Yes ☐ No

   If yes, how much does this bother you? ☐Not at all ☐Somewhat ☐Moderately ☐Quite a bit

   If yes, then is your pain relieved after emptying your bladder? ☐ Yes ☐ No

No= 0, Not at all= 1, Somewhat= 2, Moderately= 3, Quite a bit= 4

Note: Screening for incontinence as an inclusion criterion will be a ‘yes’ answer to Q2 , Q3 or Q4.

Appendix 2

Sandvik Severity Index

How often do you experience urinary leakage?

I never have leakage of urine Check box here [ ], stop, and go on to next form

1. Less than once a month
2. A few times a month
3. A few times a week
4. Every day and/ or night

How much urine do you lose each time?

1. Drops
2. Small splashes
3. More

The severity index is created by multiplying the results of questions 1 and 2
The four level severity index is based on the following index values (1 – 12)

1 – 2 = slight

3 – 6 = moderate

8 – 9 = severe

12 very severe

Appendix 3:

Center for Epidemiologic Studies Short Depression Scale (CES-D -10)

Please indicate how often you have felt this way during the past week by checking the appropriate box for each question.

	Rarely or none of the time (less than 1 day)	**Some or a little of the time** (1-2 days)	**Occasionally or a moderate amount of the time** (3-4 days)	**All of the time** (5-7 days)
1. I was bothered by things that usually don't bother me.	☐	☐	☐	☐
2. I had trouble keeping my mind on what I was doing.	☐	☐	☐	☐
3. I felt depressed.	☐	☐	☐	☐
4. I felt that everything I did was an effort.	☐	☐	☐	☐
5. I felt hopeful about the future.	☐	☐	☐	☐
6. I felt fearful.	☐	☐	☐	☐
7. My sleep was restless.	☐	☐	☐	☐
8. I was happy.	☐	☐	☐	☐
9. I felt lonely.	☐	☐	☐	☐
10. I could not "get going."	☐	☐	☐	☐

Appendix 4: EQ-5D Quality of Life Questionnaire

By placing a tick in one box in each group below, please indicate which statements best describe your own health state today.

Mobility

I have no problems in walking about	❑
I have some problems in walking about	❑
I am confined to bed	❑

Self-Care

I have no problems with self-care	❑
I have some problems washing or dressing myself	❑
I am unable to wash or dress myself	❑

Usual Activities (*e.g. work, study, housework, family or leisure activities)*

I have no problems with performing my usual activities	❑
I have some problems with performing my usual activities	❑
I am unable to perform my usual activities	❑

Pain/Discomfort

I have no pain or discomfort	❑
I have moderate pain or discomfort	❑
I have extreme pain or discomfort	❑

Anxiety/Depression

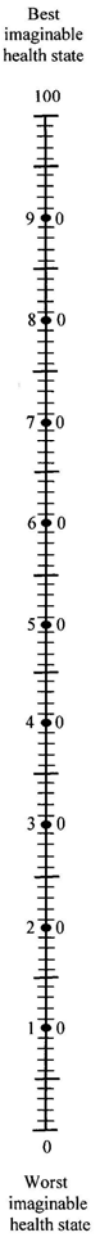
I am not anxious or depressed	❑
I am moderately anxious or depressed	❑
I am extremely anxious or depressed	❑

2

To help people say how good or bad a health state is, we have drawn a scale (rather like a thermometer) on which the best state you can imagine is marked 100 and the worst state you can imagine is marked 0.

We would like you to indicate on this scale how good or bad your own health is today, in your opinion. Please do this by drawing a line from the box below to whichever point on the scale indicates how good or bad your health state is today.

Your own health state today



Appendix 5

Demographic Questionnaire

Medical History and Medication

How old is the subject now? (use standard GK age decision algorithm)

_____ years

What is the subject's weight (measured using scale)?

_____kg

What is the subject's height (measured using rod)?

_____ metres

Please tick the box if the subject reports any of the following conditions

Heart problems	
Breathing problems	
Depression	
Diabetes	
Joint problems	
One sided paralysis	
Visual Impairment (even with glasses)	

Does the subject regularly take any medications or supplements? Yes No

If yes: What does she take?

How many pregnancies has the subject had? _____

How many deliveries has the subject had? _____

Does the subject suffer from troublesome constipation?

Yes No

Does the subject ever suffer with urination that is painful, frequent and cloudy/smells unpleasant?

Yes No

Does she suffer from this more than 3 times in a year?

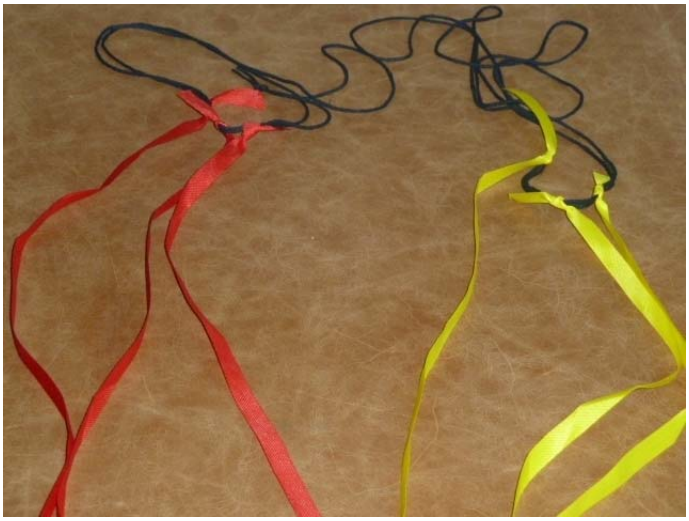
Yes No

Appendix 6

3-Day Bladder Incontinence Record

The 3 day bladder continence record (3DCR)

As there was no existing continence diary for illiterate people, one was devised that was thought to be culturally appropriate and acceptable. Following discussions in Bangladesh and with Bangladeshi women resident in Edmonton, a belt was devised (see photo) in which a cord was strung round the waist, beneath clothing, and worn for 3 days on each occasion a record was to be made. The woman was instructed to use one yellow and one red ribbon on each of the 3 days. She was asked to tie a knot in the yellow ribbon (on right in the picture below) each time she urinated and a knot in the red ribbon (left below) each time she was wet from urine leakage.



This method of recording was included pre- and post- intervention in the 4 week pre-test and every 4 weeks for 24 months in the feasibility study. It was highly related to UDI score (appendix 1) at baseline.

Instructions for the continence diary belt

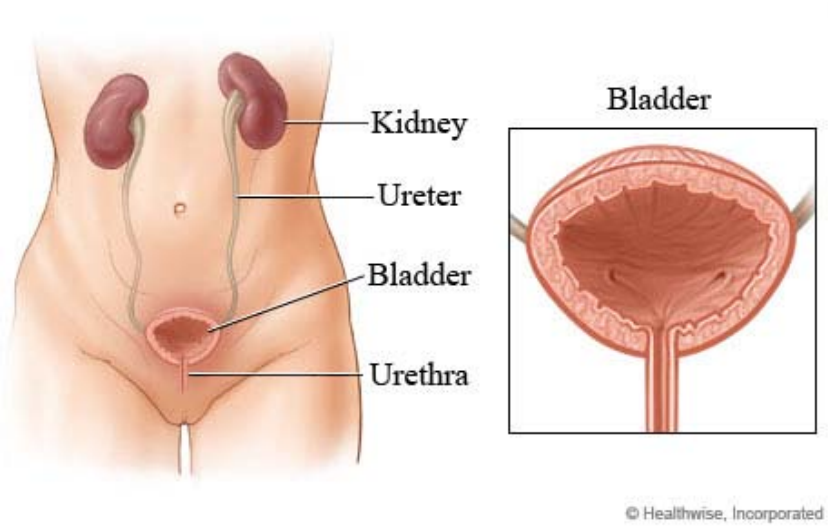
1. The belt is tied on by paramedic at start of 3 days, under the woman's clothing.
2. The belt has 3 yellow ribbons on one side, three red ribbons on the other.
3. The first red and yellow ribbons – closest to the centre/each other are for the first day.
4. From the time the paramedic ties the belt on until the same time the next day the woman ties a knot in the first yellow ribbon each and every time she goes to urinate.
5. From the time the paramedic ties on the belt until the same time the next day the woman ties a knot in the red ribbon every time she is wet as/before she goes to pass urine she ties a knot in both red and yellow ribbons. If she is wet (after coughing or sneezing for example) and does not then go to pass urine she ties a knot in the red but not the yellow.
6. The next day, from the time the paramedic tied on the belt, she uses the second yellow ribbon to record every time she goes to pass urine for the next 24 hours and the red ribbon for every time she is wet whether or not she goes to pass urine.
7. On the third day she uses the third yellow and third red ribbon from the time of day that the paramedic first tied on the belt until the paramedic comes to remove the belt
8. The paramedic removes the belt and puts it in a plastic bag, seals it and labels it with the woman's name, village and date.

Appendix 7

Healthy Bladder Educational Script

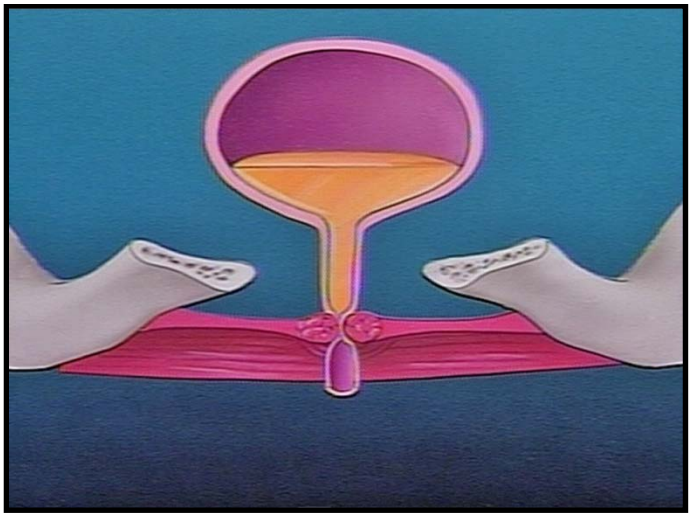
Healthy Bladder Teaching Tool

The kidneys filter blood and collect waste products and produce urine

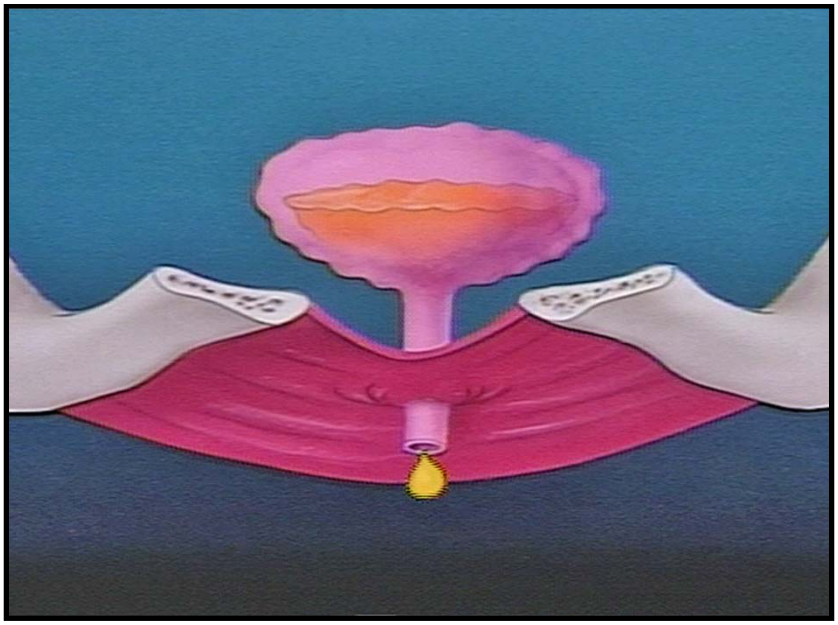


The Bladder collects urine

A normal bladder holds up to 1 ½ to 2 cups of urine.

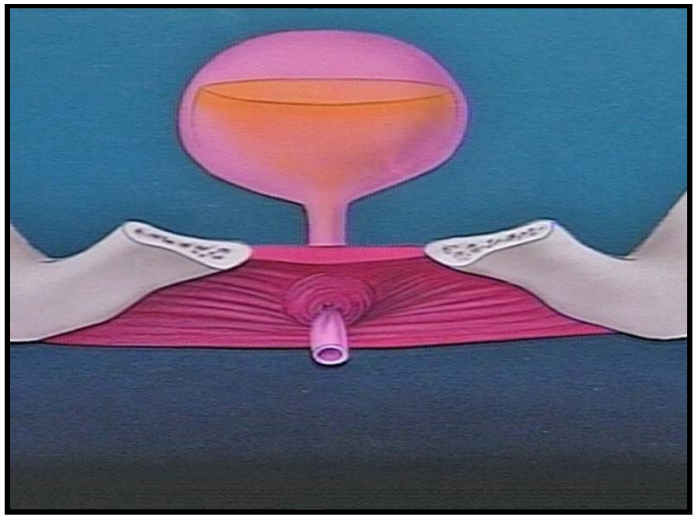


The bladder gets rid of urine through the tube at the bottom of the bladder



The bladder empties 4 – 7 times each day, depending on how much you drink. If it is hot, you will pee less.

A normal bladder empties fully every time you pee and does not leak.



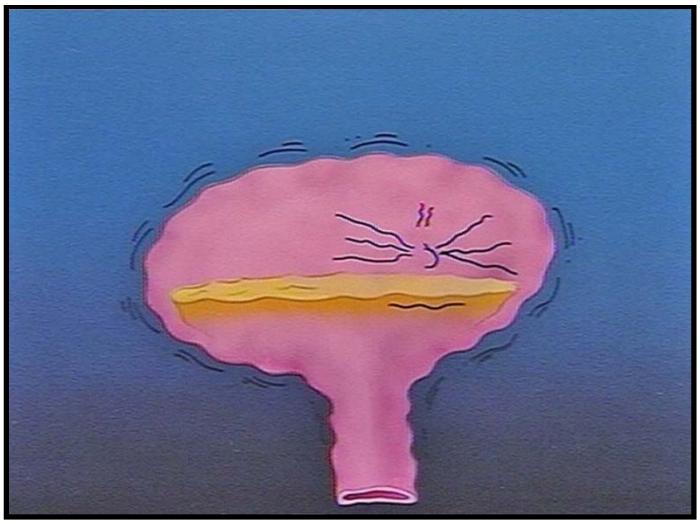
There are muscles wrapped around the tube to keep it closed until you are ready to go to the toilet.

FLUIDS

It is important to drink enough fluid everyday.

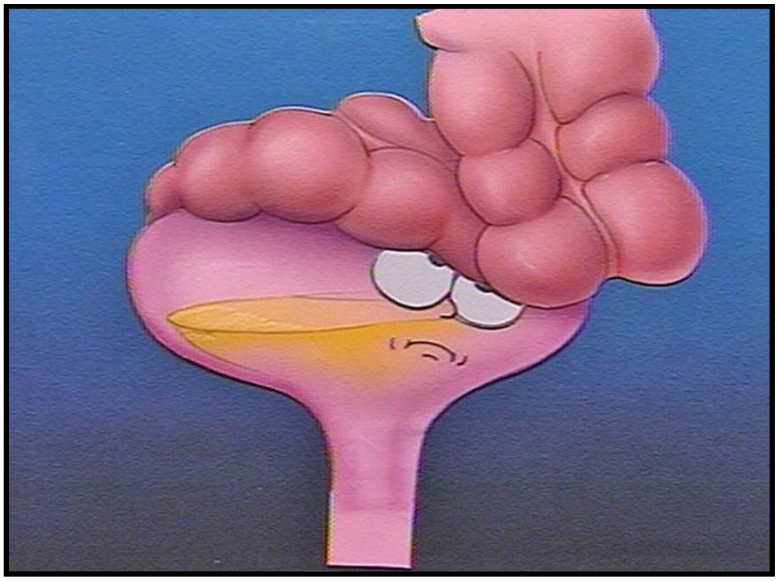
You will get enough fluid if you drink ½ cup regularly throughout the day

DO NOT cut back on drinking so you won't leak.



Your bladder may get irritated and not hold as much urine if you don't drink enough. The urine gets strong and this may cause the bladder to want to empty frequently.

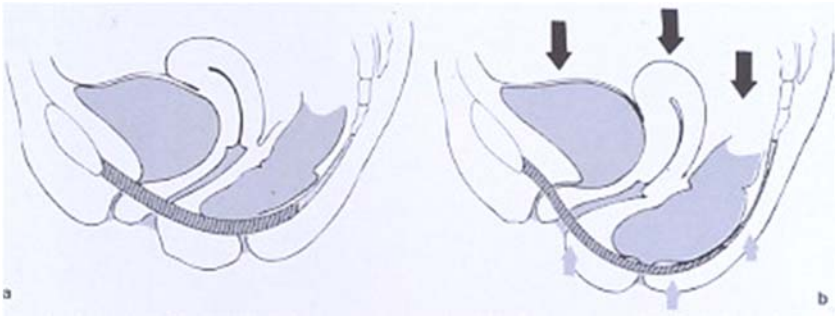
Constipation



You should avoid constipation. This is bowel movements that are infrequent (3 times or fewer per week) or hard to pass.

When the bowel does not empty properly it will swell up and push down onto the bladder.

Pushing down to have a bowel movement



Having to always push down to get out hard stool pushed down on your organs and muscles.

Try to eat a healthy diet of fruits and vegetables

Appendix 8

Details of the Exercise Intervention

The intervention will be a series of exercises performed in a group setting and consisting of a 60 minute twice weekly exercise class held at sites selected by the local investigators and easily accessed by participant. Each session will be followed by a supervised 30 minute group walk at a pace moderately challenging to the participants. Participants will be asked to perform the same exercises individually at home the other days of the week. Exercises for month 1 are given in detail as an example below, following a summary of the procedures.

These exercises were successfully implemented in the 4 week pre-test and for 12 weeks in intervention villages during the feasibility study. The instruments used by the physiotherapists to record attendance and variations adopted are also appended.

Warm up and Stretching Exercises.
Five to ten minutes of warm up and stretching exercises will be performed at the beginning of classes. These include shoulder and waist rotations, walking on the spot and other stretches.

Pelvic Floor Muscle (PFM) Exercises.
At the beginning of the training participants will be taught to contract the PFM by the community physiotherapist. They will be taught to identify the PFM and to not use any accessory muscles (abdominals, buttocks or legs) when performing the contractions. The exercise regimen will be designed to strengthen both fast and slow twitch muscle fibres using both fast and sustained contractions. During the exercise sessions the number of fast contractions will be gradually increased to 10 fast contractions in a row in 10 seconds and 10 sustained contractions held for 10 seconds. There will be at least 20 seconds rest between the contractions. The exercises will be performed in lying, sitting, and standing positions. They will be inserted between the fitness exercises.

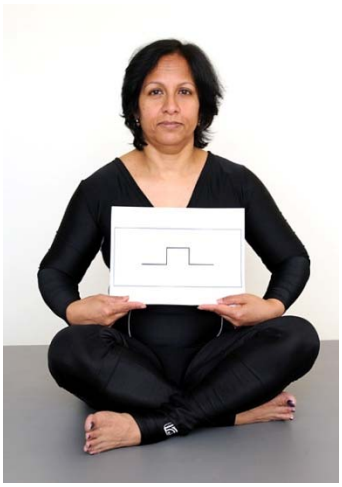
Fitness Exercises. Body awareness, breathing, relaxation, strengthening of the thigh, abdominal and back muscles and balance training will be performed between the PFM exercises. A rolled up cloth may be used as a prop for some exercises if needed. The exercises will be done in lying, sitting and standing positions.

Walking. Thirty minute walks at a brisk pace







Exercise List

PF = pelvic floor muscle contraction

Month 1

Arm circles, one way then the other X 5

Shoulder shrugs then push back and then down X 5

Hip circles, one way then the other X 10

Marching, 30 seconds

Sit PF, 3 quick ones X 4 sets

Sit, side bend holding for 30 seconds both sides X 3

Lying knees up, posterior pelvic tilt X 4, progress to 12

Lying knees up, straighten one knee and lower, do with the other knee X 4, progress to 12

Lying on tummy one knee bent up, 3 quick ones X 4 sets

Up on all fours

- stretch back up, hold for 10 seconds, X4, progress to 12

- then straight back

- curve back down, hold for 10 seconds, X4, progress to 12

Sit PF, hold X 4 seconds, 4 times

Push ups on the wall X 4, progress to 12

Stand back against the wall and squat, sliding down the wall, 4 second hold, 4 times, progress to 12

Stand leaning against the wall, PF hold X 4 seconds, 4 times

Stand on one leg, hand on wall for support hold 4 seconds, do with other leg , 4 times each leg

Stand leaning on the wall and do gastronomies stretch hold 30 seconds X 3

Appendix 9

Report of the feasibility study conducted August 2012-September 2013.

During this period 122 women from 5 villages were enrolled. This included 93 women recruited in 4 intervention villages, and 29 women in one control village. In each village, women were identified as age 60-75 years using data from the 2005 GK census, and attempts were made to contact each of them: reasons for not recruiting were recorded (death, incapacity, refusal, not found). In addition, in each village, women came forward who had not been identified but were in the age group and who wished to take part. In the first village women identified *a priori* (Group A) and those who volunteered (Group B) initially formed separate exercise groups but these were soon amalgamated in this and all subsequent villages.

Information on which to evaluate the study came from 4 sources.

1) Both paramedics and physiotherapists kept records of participation. Paramedics carried out questionnaires at baseline (week zero) and 6 months. They collected 3 day continence records (3DCR) (see appendix 4) at baseline and every 4 weeks for the duration of the study. Physiotherapists kept a record of each woman's attendance at each exercise class, to a maximum of 24 classes over 12 weeks. We are thus able to estimate protocol adherence for the main study.

2) The 3DCR and questionnaires completed at baseline and six months allowed us to estimate variance in change between baseline and end of intervention and so estimate the sample size needed to achieve adequate power in the main study.

3) Open-ended interviews carried out by graduate students of Professor Ainoon Naher at Jahangirnagar University who attempted to interview all refusals and drop-outs and a sample of women completing the 6 month study in either intervention or control villages.

4) A debriefing meeting in English, facilitated by Professor Ainoon Naher, of Canadian and Bangladeshi researchers, physiotherapists and paramedics, supplemented by one-to-one interviews in Bangla with paramedics.

Results

Recruitment and adherence.

A target population of 139 women was identified as eligible from the 2009-10 disability survey. Of these 8 were found to have died and one was not eligible because of paralysis. There were 17 recorded as refusals, of which 7 were noted as being forbidden by a male family member, 6 refused because of religious barriers to participation and 4 refused from their own choice. There were 34 listed but not found: of these 10 were in the first intervention village where the team was not fully aware of the need to visit all listed women and 15 from the rather large list of 52 in the control village. The response rate among those believed to be alive and eligible was thus 60.7% (79/130) or 82.3% (79/96) of those contacted and eligible. In each village eligible women not on the initial lists asked to be included and these were recruited. The total study included 79 listed women and 43 volunteers. Among the women in the intervention villages 39 (41.9%) agreed to manual vaginal feedback during training for pelvic floor exercises.

In the first intervention village, 9 of the 23 women recruited dropped out within the first month and 6 did not attend any exercise class. Only 10 women in this village took part in the exit evaluation. The dropout rate in other villages was much lower with only one (of 21) woman in the second intervention village not completing the exit assessment, together with 6 /24 in the third intervention village, 0/24 in the fourth village and 4/29 in the control village. In the intervention groups the median number of exercise classes attended was 17 (of a possible 24): in all villages except the first at least 75% attended 16 or more classes.

A six month 3DCR was collected for 98/122 women. For the rest the most recent record was taken. This was baseline for 14 women and from subsequent months for a further 10. First 3DCR for one woman was approximated by the month 2 record.

Changes in scores between baseline and exit.

Two thirds of the women (83/122: 68.0%) recorded at least one episode of wetness over 3 days on the baseline 3DRC. At exit 68/122 (55.7%) recorded at least one episode. Among those wet at baseline there was a mean improvement of 2.35 episodes ($p<0.001$). The mean incontinence in those wet at baseline was higher in the single control village (9.7 episodes) than in any of the four intervention villages (range 2.7-7.9) and the mean improvement greater (3.23 in control, 0.67-4.75 in the 4 intervention villages. These differences were consistent with chance and he power and sample size calculation (appendix 12) was calculated with estimates of change from the control village.

Changes in questionnaire scores over the course of the study were considered for the 98 women completing these at both baseline and exit. On the Sandvik severity scale 32/98 (33.0%) were recorded as having no problem at baseline: 17/98 (17.4%) had symptoms classified in clinical use as severe (a score of 12). At exit, the number with no problem had increased to 52/98 (53.1%) and with severe symptoms only 10/98 (10.2%). These corresponded to mean scores of 4.8 at baseline and 2.7 at exit. Scores on the short form of the Urinary Distress Inventory (UDI) also decreased from a mean of 9.4 at baseline to 5.4 at exit. On the quality of life (visual analogue) scale from the EQ-5D scores increased

(life got better) from a score of 5.8 at baseline to 6.7 at exit. All these changes were highly significant ($p<0.001$). On the short geriatric depression scale, where there were difficulties with translation, women were only slightly less depressed at exit (mean score 3.6) than at baseline (4.04) ($p=0.09$).

Qualitative assessments

A verbal report of the qualitative study was given at the debriefing meeting held at Savar in mid-August. The prime results were that women without incontinence felt the study to be of little interest, that the internal (vaginal) examination, requested for all women in the pilot study, was poorly received and that exercise alone (without offer of medications) was seen by some to be uncaring. Discussions with the team revealed a need for greater training in the use of questionnaires, particularly the visual analogue scale of the EQ-5D, and further attention to the translation of the depression scale (now in hand).

Implications for the full trial

The inclusion criteria have been changed to include only those incontinent at baseline. The requirement for an internal examination has been removed and, where undertaken voluntarily, has been moved to week 2.

Appendix 10

Results of the comprehension acceptability and reliability pre-test

Under the supervision of Professor Ainoon Naher, 30 village women aged 60-75 were recruited from a village close to Savar but not part of the GK system. These women were interviewed twice by the same 2 graduate students. At baseline they completed the EQ-5D, the Sandvik severity scale, the Urinary Distress Index, the 7 item geriatric depression scale and the demographic questionnaire developed for this project. The women repeated the EQ5D after 1 week and the rest of the questionnaires after 25-27 days.

For the EQ-5D Cronbach's alpha calculated for the 5 dimensions of health was 0.78 at baseline, suggesting an acceptable inter-item correlation and adequate comprehension of the items. Because of a data entry problem, data on reliability is not available.

For the Sandvik severity scale there was a problem in that the form did not allow a response of 'no incontinence'. However, when coding was adjusted to allow for this, the correlation between first and second severity scales was 0.90, suggesting a comprehensible and reliable measure. At baseline 53.3% of these women had no or slight incontinence, 20% moderate, 10% severe and 16.7% very severe.

On the Urinary Distress Index there was no overall scale but test-retest correlations between 'how much does it bother you' questions ranged from 0.75 for leakage related to coughing, sneezing and laughing to 0.93 for leakage associated with a feeling of urgency.

On the 7 item geriatric depression scale there was a misunderstanding on the part of the graduate students administering the questionnaire, who assumed that if a woman replied that she was 'basically happy with life' the rest of the questions did not apply. This error meant that a Cronbach's alpha could not meaningfully be calculated. However the test-retest correlation on that question was 0.82, suggesting an acceptable reliability.

On the demographic questionnaire the data at test-retest was virtually identical on the two occasions, with almost no-one reported a different set of symptoms, or of age, at baseline or follow-up.

In summary, the test-retest exercise identified some problems with the administration of the questionnaires and of data entry but did not indicate serious problems of comprehension, acceptability or reliability. In informal group discussion, lead by Professor Naher with 7 women aged 63-67 from this village, it appeared that issues might arise in some areas with local terms for medical problems and that interviewers would need to be prepared for this.

Appendix 11

Sample size calculations

A power calculation was carried out by the study statistician.

It was assumed that there were 16 pairs of villages (intervention/control pairs) with 20 fully complying women in each village, none dry at baseline. Thus the total number of women is 16x2x20=640.

The intraclass correlation coefficient (ICC) estimate from the data from the feasibility study was very close to zero for the primary outcome (change in leakage between baseline and exit). The calculated ICC was 0.016. Thus, we conservatively assumed ICC=0.15 in the power calculation. Based on the pilot data, there was a mean change of 3.23 with an SD of 4.50 in women not dry at baseline in the control village. Using the sample size formula for cluster randomization (reference: Donner A, Birkett N, Buck C. Randomization by cluster. Sample size requirements and analysis. Am J Epidemiol. 1981 Dec;114(6):906-14.) :

$$Z_\beta = \sqrt{\frac{nk\Delta^2}{2\sigma^2[1+(n-1)\rho]}} - Z_{\alpha/2}$$

where Δ is a meaningful difference specified in advance by the investigator, n is the number individuals in each cluster, k is the number of clusters, σ^2 is the variance of the outcome, and ρ is the ICC.

Δ is the intervention effect size: it is set to be 1.0, 1.5, 2.0, 2.5 (i.e., Intervention improves by Δ more than the change of women in the control villages).

With a 5% Type I Error probability (2 sided test), the power of the proposed study designs is:
57.6% if Δ = 1.5
81.8% if Δ = 2.0
94.0% if Δ = 2.5

Thus, with 16 pairs of villages with each village having 20 women completing the study, we have 81% or greater power to detect an intervention effect if the intervention adds 2.0 to the average of 3.23 change in the control women.

A similar process was performed on the secondary outcome EQ-5D assuming ICC=0.15. The pilot data indicated a mean change of 7.2 on the visual analogue scale with standard deviation of 17.9 in the control subjects.

With a 5% Type I Error probability (2 sided test), the power of the proposed study designs is:
71.2% if Δ = 7.0
82.1% if Δ = 8.0

Our study design has 82% power to detect an 8 point difference in the mean change of EQ-5D scores between the intervention and control villages.