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Non-speculum sampling approaches for cervical screening in older women: randomised controlled trial

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Abstract

Background

Cervical cancer disproportionately affects women aged 65 years and older, especially those with inadequate previous screening. Speculum use is a key deterrent to screening attendance in older women.

Aim

To assess whether offering non-speculum clinician-taken sampling and self-sampling increase uptake among lapsed attenders aged 50-64.

Design and setting

Pragmatic randomised control trial conducted between August 2018 and November 2019 at 10 general practices in East London, UK.

Method

Participants were 784 women aged 50-64 last screened 6-15years before randomisation. Intervention women received a letter offering the choice of a self-sampling kit or a clinician-taken non-speculum sample. Control women received usual care. Main outcome measure: uptake within 4 months.

Results

Screening uptake 4 months after randomisation was significantly higher in the intervention arm: 20.4% (N=80/393) vs 4.9% (N=19/391, absolute difference=15.5%, 95%CI: 11.0%-20.0%, p<0.001). This was maintained at 12 months; 30.5% (N=120/393) vs 13.6% (N=53/391), respectively (absolute difference=17.0%, 95%CI: 11.3%-22.7%, p<0.001).

Conventional screening attendance within 12 months was very similar for both arms (intervention: 12.7% (N=50/393) vs control: 13.6% (N=53/391)). Ethnic differences were observed in screening modality preference. More white women opted for self-sampling (50.7%, N=38/75) while most Asian and Black women opted for conventional screening.

Conclusions

Offering non-speculum clinician-sampling and self-sampling substantially increases uptake in older women with lapsed screening attendance. Non-speculum clinician sampling appeals to women who dislike the speculum but prefer a clinician to take their sample and who lack confidence in self-sampling. Providing a choice of screening modality may be important for optimising cervical screening uptake.

Keywords

Cervical cancer; screening; Human papillomavirus; self-sampling; older women; general practice

How this fits in

Inadequately screened women aged 50 and older are at a disproportionately higher risk of cervical cancer and dying from it. Speculum use is a major barrier to cervical screening and can become more uncomfortable with ageing and the menopause. Although self-sampling has been hailed as a game-changer for cervical screening, it does not appeal to all women. This study showed that offering a choice of non-speculum clinician sampling or self-sampling substantially increased cervical screening uptake in older lapsed attendees across all ethnicities, an approach which could be easily implemented into existing practice in primary care.

Trial registration

International Standard Randomised Controlled Trial Number (ISRCTN): 16007231. National Institute for Health Research Clinical Research Network (NIHR CRN) Central Portfolio Management System (CPMS) ID: 38979

Introduction

High cervical cancer mortality rates in older women have been observed in several countries. (1-3). In the UK, women aged 65 and over account for around half of cervical cancer deaths(4) and 20% of new cases.(5) Most of these arise in women inadequately screened when aged 50-64 years,(6) ages at which screening coverage declines.(7) The number of cervical cancers in women aged over 65 years is expected to rise as life expectancy increases.(8) The negative impact of the COVID-19 pandemic on screening could further compound the issue.(9, 10) The speculum examination is a well-known barrier to cervical screening and can become particularly uncomfortable for older women due to vaginal atrophy, increasing body mass index and musculoskeletal problems.(11, 12) Studies show that older women find cervical screening/insertion of the speculum more painful with age and the menopause.(13, 14)

An obvious solution is to offer HPV (human papillomavirus) testing on self-collected samples.(15) Self-sampling enables women to collect their own sample for cervical screening without a speculum using a vaginal swab or brush. A drawback is the consistent finding that women worry about not self-sampling correctly.(16-19) Offering a clinician-taken sample for HPV testing without a speculum (i.e. "non-speculum HPV testing") is another option. Women would have the reassurance of a clinician-taken sample without the discomfort of speculum insertion. This approach could be particularly appealing to older lapsed attendees who have found screening increasingly uncomfortable with age but lack confidence in self-sampling. Women who have never attended screening by age 50 are more entrenched in their decision to not attend (12) and therefore less likely to respond to such interventions, regardless of what test is offered.

Previously we found that non-speculum clinician sampling was an appealing option for older women, particularly for those who may have been put off screening by the speculum examination.(11) The aims of the present study were to assess the increase in screening uptake associated with offering lapsed attenders aged 50-64 years the option of non-speculum clinician-collected sampling or self-sampling, and the feasibility and acceptability of non-speculum clinician sampling. In addition, we were interested in exploring differences in uptake by ethnic background.

Methods

Eighteen general practices in east London (UK) were invited to take part in this pragmatic, randomized controlled trial (ISRCTN16007231). Of these, 10 participated, all from the boroughs of Tower Hamlets or City and Hackney. Both boroughs have an ethnically diverse population with 55% and 45% from non-white backgrounds, respectively.(20) In England, women aged 50-64 years are sent 5-yearly screening invitations with reminder letters at 18 weeks. Individual GP practices may also provide additional reminders via telephone, text message or letter. Women book their own appointments which are conducted in GP primary care.

Eligible women were identified using the GP electronic patient record system EMIS Web (Egton Medical Information Systems Ltd, 2010) between August 2018 and November 2018. These comprised women were aged 50-64 years on the search date, who were at least 12 months overdue but attended at least once in the previous 15 years. Randomisation was conducted prior to consent using Zelen's design(21) to allow unbiased assessment of the intervention.

In total, 809 women were randomised 1:1 to either the intervention or control arm within each practice. Randomisation was performed separately by each GP practice (on the same day as the EMIS search); to ensure equal numbers from each GP practice were assigned to each study arm (details in Supplement 1). Invitation letters were sent to women randomised to intervention on the same day as randomisation (or next working day). Follow up data were obtained until November 2019.

Intervention arm women were sent a mailout (see Supplement 2) including an invitation letter, a study information leaflet, an HPV information sheet, and a self-sampling kit postal order form with a prepaid return envelope. The invitation letter offered women the option of (i) booking an appointment at their GP practice for a clinician taken sample without using a speculum (a non-speculum sample) or (ii) ordering a self-sampling kit (using the postal order form or telephone). Difficulty in booking appointments is a known screening barrier,(22) therefore GP practices were asked to provide additional routes to make it easier for women to book screening appointments; (see Supplement 1). Women randomised to the control arm

received usual care, i.e. sent invitation letters for cervical screening every 5 years until age 64 and remain eligible for screening in-between invitations if they are overdue.

Non-speculum samples were taken at the GP practice by the usual cervical screening sample-takers. Sample-takers were provided with written and pictorial instructions for collecting the sample (Supplement 3).

Women who ordered self-sampling kits had a kit posted to their home address. Self-sampling kits included a flocked swab (FLOQSwab 552C™, Copan Italia, Brescia, Italy), a laboratory request consent form, a freepost envelope pre-addressed to the testing laboratory, written and pictorial instructions detailing how to collect a self-sample, a study information leaflet, an HPV information sheet, and a questionnaire (see Supplement 4).

Study samples (non-speculum and self-samples) were tested for the presence of HPV DNA. Conventional screening samples were tested as per the national programme at the time (liquid-based cytology). HPV test results were posted to women, copied to their GP practice. HPV positive results letters advised women to book a conventional (speculum) follow up test. Women were managed according to the result of the conventional test under the national cervical screening programme.

A questionnaire (see Supplement 5) was included in non-speculum and self-sampling kits for women to complete after sample-taking, eliciting information about women's experience of the test (using four-point Likert scales), previous barriers to screening and future screening preferences.

All samples were analysed within seven days of receipt by the Cytology Department at Barts Health NHS Trust, London, UK. HPV testing was performed using Cobas® 4800 HPV Test (Roche Diagnostics GmBH). For details on the laboratory analyses, see Supplement 1.

Statistical analysis

Electronic GP records provided data on each woman's age, ethnicity, cervical screening attendance, cervical screening results and time since the last recorded screen. The laboratory provided data on study sample HPV results, cytology and colposcopy data.

Statistical analyses were pre-specified in the protocol and described in the statistical analysis plan; additional analyses are noted as such. The primary outcome was the proportion of

women with any form of cervical screening within 4 months by study arm. The study was powered to detect a difference in screening uptake of 6% in controls versus 13% in the intervention arm at 4 months: a sample size of 367 per arm would give 90% power with a two-sided alpha of 0.05. We assumed that uptake in the control arm would be 4%-8%, and a sample of 800 participants would give between 75% and 93% power under a range of scenarios. Secondary analyses considered (i) screening within 12 months; (ii) differences in uptake by age, ethnicity and time since the last screen; and (iii) perceptions of the sampling approaches. Evaluating uptake within 12 months enabled us to assess whether any increased uptake seen at 4 months was maintained, rather than being a "nudge" effect prompting women who would have attended anyway, to be screened earlier.

The proportion in each study arm who had any form of screening was reported stratified by age at randomization, ethnic background and time since last screen ("late" (6-9.99 years), "very late" (10-14.99 years)). Chi-squared tests (or Fisher's exact tests, if there were <5 women expected in any cell) were performed to assess differences in the type of screening test selected by stratification variables in the intervention arm. Logistic regression analyses investigated potential interactions between study arm and each of (i) age, (ii) ethnicity and (iii) time since the last screen, with the outcome of screening uptake (not pre-specified in the protocol). A Kaplan-Meier plot was produced, showing the time of screening for the control arm versus the intervention arm (i) conventional (speculum) screening, (ii) conventional (speculum) screening or self-sampling and (iii) any form of screening.

For questionnaire data, differences between attitude items toward non-speculum sampling and self-sampling were dichotomised and explored using Chi-square tests (or Fisher's exact tests if appropriate).

Results

A total of 809 women were randomised in the study (intervention n=404, control n=405). Of these, 16 were found to be ineligible due to inaccurate GP screening records. A further nine were excluded as we had no information on their screening attendance during the trial period (they were not in the GP record system at final data collection having presumably left the GP practice). Therefore, 393 eligible women were in the intervention arm and 391 in the control arm. Table 1 shows demographic characteristics and Figure 1 shows the study flowchart.

Forty-three percent were from non-White backgrounds. The number of women from each GP practice ranged from 21-172. A summary of the characteristics of the participating GP practices is provided in Supplement 6.

Uptake 4 months after randomisation was significantly higher in the intervention arm: 20.4% (N=80/393) vs 4.9% (N=19/391, absolute difference=15.5%, 95% CI: 11.0%-20.0%, p<0.001). This difference was maintained at 12 months; 30.5% (N=120/393) vs 13.6% (N=53/391), respectively (absolute difference=17.0%, 95% CI: 11.3%-22.7%, p<0.001).

Conventional screening uptake within 12 months was very similar in the two arms, intervention 12.7% (N=50/393) and control 13.6% (N=53/391). Of those screened in the intervention arm, 22.5% (N=27/120) had a non-speculum clinician sample, 35.8% (N=43/120) had a self-sample, and 41.7% (N=50/120) had a conventional (speculum) sample.

For the intervention arm, women who were 'late' were more likely to be screened within 4 months than women who were 'very late' (i.e. 1-4.99 years v 5-10 years overdue, respectively) (23.9% vs 12.4%, p=0.016) (Table 2). This remained true at 12 months (36.0% vs 18.2%, p<0.001). No statistically significant differences in uptake by age or ethnicity were observed in the intervention arm (Table 2). However, a trend for decreasing uptake with increasing age was observed in the control arm but not the intervention arm.

Selection of screening test differed by ethnicity in the intervention arm (p<0.001). Within 12 months, half the screened women from White backgrounds self-sampled (50.7%, N=38/75), whereas the majority of women from Asian (53.3%, N=8/15), Black (71.4%, N=15/21) and Mixed/other/unknown backgrounds (66.7%, N=6/9) attended conventional (speculum) screening (Table 3). Differences by age (p=0.066 (4 months) and p=0.164 (12 months)) and time since the last screen (p=0.185 (4 months) and p=0.241 (12 months)) were not statistically significant, though an increasing proportion of screened women had a conventional (speculum) sample with increasing age.

Figure 2 shows the Kaplan-Meier plot for screening attendance up to 12 months. The pattern of screening uptake for conventional screening (clinician-sampled speculum) was very similar for both study arms. Self-sampling was most common in the first month. All non-speculum clinician samples were collected within 5 months.

Of the 393 women in the intervention arm, 63 (16.0%) ordered a self-sampling kit, and of these 43 (68.2%) returned a sample. Information on the number of women who booked versus attended a non-speculum clinician appointment was not available.

The vast majority (94.3%, 66/70) of women who returned a study sample tested HPV negative. Four women tested HPV positive: two non-speculum clinician samples, and two self-samples; all attended appropriate follow-up. The two non-speculum screen positives had abnormal cytology (one mild dyskaryosis, one moderate dyskaryosis); both attended colposcopy and had normal histology on biopsy. Both self-sample screen positives had negative cytology.

The questionnaire response rate was 85.7% (60/70) and was lower for non-speculum clinician sampling (67% (18/27) versus self-sampling 97.7% (42/43)). Both approaches scored similarly in measures of acceptability and confidence in doing the test properly (Table 4). By contrast, a higher proportion of self-samplers were "not at all" or "not very" confident in the test accuracy (64% vs. 24% in the non-speculum group, p=0.009). More women who had the non-speculum test experienced embarrassment (27.8% vs. 4.8% in the self-sample group; p=0.021) and believed it was important to have a clinician take the sample (88.9% (16/18) vs 26.2% (11/42), respectively p<0.001). A high proportion in both groups (72.2% (13/18) non-speculum, 88.1% (37/42) self-sampling) "agreed" or "strongly agreed" that it was important to have a choice of tests. Future screening preferences aligned with the sampling option chosen. Small numbers limited our ability to assess previous barriers to screening. Nevertheless, both groups endorsed similar barriers, though a higher proportion of self-samplers endorsed embarrassment and practical barriers to screening.

Discussion

Summary

Offering non-speculum and self-sampling significantly increased screening uptake amongst older lapsed attender women. The fact that uplift remained at 12 months suggests that these women would not have otherwise attended. Encouragingly, increased uptake was observed across all ethnic backgrounds, age groups and screening histories. Our findings provide further evidence that offering women a choice is important and will be conducive to higher screening uptake. Although more women opted for self-sampling than non-speculum

clinician-taken sampling, the fact that a substantial proportion chose the latter suggests that it appeals to the older lapsed attender population and could increase uptake beyond offering self-sampling alone.

Strengths & limitations

As far as we are aware, offering HPV testing on non-speculum clinician-taken samples for cervical screening has not been tried before, therefore novelty is a key study strength. Uptake of the non-speculum sampling approach was reasonable, demonstrating feasibility in a real-world setting. The study also benefited from an ethnically diverse sample which enabled us to examine uptake by ethnicity. This randomised controlled trial was successfully conducted in a deprived and ethnically diverse setting with known capacity issues. There were limited appointments available and long waiting times on telephone booking lines. The study recruited well despite these challenges suggesting it was well -designed and -conducted.(23)

The main study limitation was the use of GP records to determine participant eligibility and time to conventional screen. GP records are not linked to the English national screening database, therefore records of attendance can be inaccurate. However, the impact of this on primary endpoint analysis is addressed via randomisation. Potentially, non-speculum clinician sampling uptake was underestimated due to difficulty getting appointments. Similarly, conventional screening uptake in the intervention arm may have been overestimated at practices that provided additional booking systems for the study. The fact that the study documents were only provided in English may have also led to lower uptake of intervention screening tests given the ethnic diversity of the study population.

Comparison with existing literature

The increased participation of 17% (absolute increase) in our study is larger than that observed in previous UK self-sampling trials: 12% in women aged 50-65 years(24) and 6%-7% for ages 25-65 years.(24, 25) Our observed uptake is also higher than the 10% increased participation associated with self-sampling reported in a rapid review of cancer interventions(26) and a study of opportunistically offering self-sampling to non-attendees in primary care (9%).(27) The STRATEGIC trial found no increase in uptake compared to the control arm when young women aged 25 who had not been screened within 6 months of their first screening invitation were offered the choice of a timed appointment, nurse

navigator or requesting a self-sample kit.(28) Potentially, the comparatively high uptake is due to the focus on lapsed attenders (i.e. the exclusion of never-attenders). An alternative explanation is that having both a clinician-taken and self-collected non-speculum sample option enhances uptake synergistically. The observed increase in participation is also substantially larger than that seen in studies using other interventions, such as education(29) or text message reminders.(30)

Low acceptability of self-sampling and a preference for clinician-taken sampling amongst Asian women has been reported previously.(31) High proportions of women from Indian and Afro-Caribbean backgrounds have reported concern about not carrying out the self-sampling test properly.(32)

Implications for research or practice

Barriers to screening attendance amongst older women include increased discomfort with the speculum, concerns about body image, musculoskeletal problems with ageing or perceptions of low risk(33) due to sexual inactivity or long-term monogamy. Offering the choice of self-sampling and non-speculum clinician sampling appears to overcome these barriers and substantially increase uptake. Evidence of the clinical need for non-speculum screening approaches in older women is exemplified by the fact that 3% (7/215) of women aged 50-64 years could not have their routine screening sample taken due to pain (unpublished data). Having the option to take a non-speculum clinician sample in scenarios where obtaining a speculum sample is difficult would remove the need for further appointments and avoid a potential lapse in screening attendance. This is a benefit that would impact all women of screening age, as difficulty obtaining speculum samples is not limited to older women. Similarly, although never attenders were excluded from the present study, potentially non-speculum clinician sampling has the potential to appeal to those who have been avoiding screening because of the speculum.

The benefit of attending screening (protection offered) increases with longer time since last screen.(34) Although uptake in our study was lower amongst women who were “very late” versus those who were “late”, the observed 9.5% uptake within 12 months in “very late” women is sufficiently large to confer substantial benefit.

Non-speculum clinician sampling appealed most to women who prefer a clinician to take their sample and are less constrained by practical barriers to getting screened. Conversely, women who find screening embarrassing and have difficulties in getting/making an appointment may prefer self-sampling. A further advantage of non-speculum clinician sampling is that the screener-woman interaction is maintained, which can be a useful platform for enquiry about gynaecological issues and cervical screening.

It appears increasingly likely that offering a choice of test will be important to ensure high uptake.(26) Non-speculum clinician sampling could be a valuable supplement to self-sampling and warrants further research in larger studies. The rollout of HPV primary testing in many developed countries, including England, makes the introduction of these alternative approaches increasingly feasible. Validation of test performance for this novel approach using paired sampling studies will be important, as will an understanding of the resource and workload implications.

Additional information

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Ethics approval and consent to participate

Ethics approval for the study was granted by the London - Stanmore Research Ethics Committee (18/LO/1175), IRAS ID: 242943. All women who returned a study (non-speculum) sample provided written informed consent.

This study was performed in accordance with the Declaration of Helsinki.

Competing interests

AL declares nonfinancial support from Copan Italia and Roche outside the submitted work.

All other authors declare no conflict of interest.

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Authors' contributors

AL, PS, JW, TH, and TR designed the study concept. AL, PS, JW, TH and JR wrote the study protocol. RL and AL wrote the manuscript. RL wrote the statistical analysis plan and conducted the statistical analysis. PS oversaw the statistical analysis. AL, PS, RL, JW, LM interpreted the data. JR acquired the data. All authors revised and approved the manuscript before submission.

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Table 1: Demographic characteristics of trial participants, by intervention arm

	Intervention		Control	
	N	%	N	%
Total	393	100	391	100
Age				
50-54	127	32.3%	135	34.5%
55-59	155	39.4%	131	33.5%
60-64	111	28.2%	125	32.0%
Ethnic background				
White	229	58.3%	218	55.8%
Black	69	17.6%	67	17.1%
Asian	56	14.2%	67	17.1%
Mixed/other/unknown	39	9.9%	39	10.0%
Time since the last screening test				
Late (6-9.99 years)	272	69.2%	264	67.5%
Very late (10-15 years)	121	30.8%	127	32.5%
GP Practice				
1	16	4.1%	15	3.8%
2	15	3.8%	16	4.1%
3	58	14.8%	54	13.8%
4	50	12.7%	49	12.5%
5	50	12.7%	47	12.0%
6	36	9.2%	39	10.0%
7	8	2.0%	13	3.3%
8	50	12.7%	51	13.0%
9	87	22.1%	85	21.7%
10	23	5.9%	22	5.6%

Table 2: Percentage of women screened within a) 4 months and b) 12 months, by intervention arm, by age, ethnicity, time since last screen and GP practice

	% screened (N screened/N eligible)			
	within 4 months		within 12 months	
	Intervention	Control	Intervention	Control
TOTAL	20.4% (80/393)	4.9% (19/391)	30.5% (120/393)	13.6% (53/391)
Age				
50-54	19.7% (25/127)	5.9% (8/135)	29.1% (37/127)	16.3% (22/135)
55-59	21.3% (33/155)	5.3% (7/131)	32.9% (51/155)	12.2% (16/131)
60-64	19.8% (22/111)	3.2% (4/125)	28.8% (32/111)	12.0% (15/125)
Ethnic background				
White	23.1% (53/229)	2.8% (6/218)	32.3% (74/229)	11.0% (24/218)
Black	20.3% (14/69)	4.5% (3/67)	29.0% (20/69)	17.9% (12/67)
Asian	16.1% (9/56)	11.9% (8/67)	26.8% (15/56)	19.4% (13/67)
Mixed/other/unknown	10.3% (4/39)	5.1% (2/39)	23.1% (9/39)	10.3% (4/39)
Time since the last screening test				
Late (6-9.99 years)	23.9% (65/272)	6.1% (16/264)	36.0% (98/272)	15.9% (42/264)
Very Late (10-15 years)	12.4% (15/121)	2.4% (3/127)	18.2% (22/121)	8.7% (11/127)
GP practice				
Practice 1	6.3% (1/16)	0.0% (0/15)	25.0% (4/16)	20.0% (3/15)
Practice 2	33.3% (5/15)	6.3% (1/16)	40.0% (6/15)	12.5% (2/16)
Practice 3	19.0% (11/58)	1.9% (1/54)	24.1% (14/58)	7.4% (4/54)
Practice 4	16.0% (8/50)	4.1% (2/49)	28.0% (14/50)	8.2% (4/49)
Practice 5	26.0% (13/50)	8.5% (4/47)	30.0% (15/50)	12.8% (6/47)
Practice 6	5.6% (2/36)	10.3% (4/39)	22.2% (8/36)	17.9% (7/39)
Practice 7	0.0% (0/8)	0.0% (0/13)	12.5% (1/8)	15.4% (2/13)
Practice 8	22.0% (11/50)	2.0% (1/51)	30.0% (15/50)	7.8% (4/51)
Practice 9	29.9% (26/87)	5.9% (5/85)	44.8% (39/87)	21.2% (18/85)
Practice 10	13.0% (3/23)	4.5% (1/22)	17.4% (4/23)	13.6% (3/22)

Table 3: Screening test selected among women who were screened within a) 4 months and b) 12 months, by age, ethnic background and time since last screening test

	Within 4 months				Within 12 months			
	% (N) of screened women in the intervention arm with this screening test				% (N) of screened women in the intervention arm with this screening test			
	Non-speculum	Self-sample	Speculum	p-value (Chi-squared*)	Non-speculum	Self-sample	Speculum	p-value (Chi-squared*)
Age								
50-54	28.0% (7)	40.0% (10)	32.0% (8)	0.066	24.3% (9)	27.0% (10)	48.6% (18)	0.164
55-59	18.2% (6)	48.5% (16)	33.3% (11)		15.7% (8)	37.3% (19)	47.1% (24)	
60-64	45.5% (10)	50.0% (11)	4.5% (1)		31.3% (10)	43.8% (14)	25.0% (8)	
Ethnic background								
White	24.5% (13)	62.3% (33)	13.2% (7)	<0.001	21.3% (16)	50.7% (38)	28.0% (21)	<0.001
Black	28.6% (4)	7.1% (1)	64.3% (11)		19.0% (4)	9.5% (2)	71.4% (15)	
Asian	66.7% (6)	0.0% (0)	33.3% (3)		46.7% (7)	0.0% (0)	53.3% (8)	
Mixed/other/ unknown	0.0% (0)	75.0% (3)	25.0% (1)		0.0% (0)	33.3% (3)	66.7% (6)	
Time since the last screening test								

Late (6-9.99 years)	27.7% (18)	43.1% (28)	29.2% (19)	0.185	22.4% (22)	32.7% (32)	44.9% (44)	0.241
Very late (10-15 years)	33.3% (5)	60.0% (9)	6.7% (1)		22.7% (5)	50% (11)	27.3% (6)	
TOTAL	28.8% (23)	46.3% (37)	25.0% (20)		22.5% (27)	35.8% (43)	41.7% (50)	

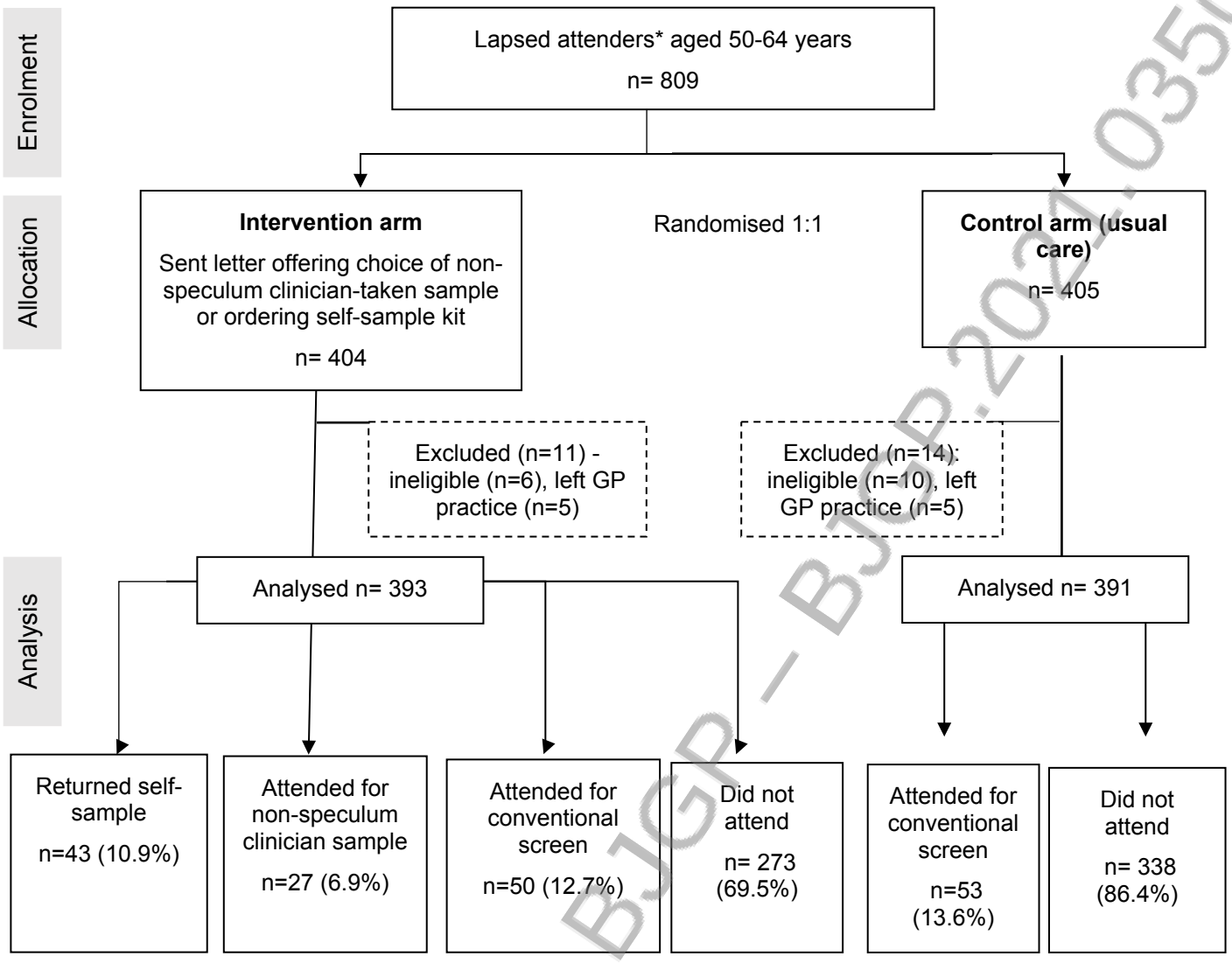
*Fisher's exact test used for ethnic background

Table 4: Perceptions of non-speculum clinician sampling versus self-sampling and previous barriers to screening

	Non-speculum (n=18)	Self-sample (n=42)	p-value (Chi-squared*)
	n (%)	n (%)	
Overall experience of test			
Excellent/good	15 (83.3%)	37 (88.1%)	p=0.735
Fair/Poor	3 (16.7%)	5 (11.9%)	
Discomfort			
None	11 (61.1%)	24 (57.1%)	p=0.775
Mild/Quite a lot/Severe	7 (38.9%)	18 (42.9%)	
Unpleasantness			
Not at all	11 (61.1%)	34 (82.9%)	p=0.07
Mildly/Fairly/Very	7 (38.9%)	7 (17.1%)	
Embarrassment			
Not at all	13 (72.2%)	40 (95.2%)	p=0.021
Mildly/Fairly/Very	5 (27.8%)	2 (4.8%)	
Anxiety			
Not at all	12 (66.7%)	27 (65.9%)	p=0.952
Slightly/Fairly, Very	6 (33.3%)	14 (34.2%)	
Confidence test done properly			
Not at all/not very	1 (5.9%)	2 (4.9%)	p=1.0
Fairly/very	16 (88.9%)	39 (92.9%)	
Confidence in test accuracy			
Not at all/not very	4 (23.5%)	27 (64.3%)	p=0.009
Fairly/very	13 (76.5%)	15 (35.7%)	
Future preference			
Non-speculum	12 (70.1%)	1 (2.4%)	p<0.001
Self-sample	4 (23.5%)	38 (90.5%)	
Speculum	1 (5.9%)	0 (0%)	
No preference	0 (0%)	3 (7.1%)	
Previous barriers to screening			
Forgotten	4 (22.2%)	7 (16.7%)	p=0.719
More important things to worry about	0%	5 (11.9%)	p=0.309
Too busy	2 (11.1%)	9 (21.4%)	p=0.478

Not sexually active	4 (22.2%)	11 (26.2%)	p=1.0
Pain	10 (56.6%)	23 (54.8%)	p=0.955
Same partner long time	0%	3 (7.1%)	p=0.547
Too embarrassed	0%	8 (19.1%)	p=0.091
Frightened	2 (11.1%)	1 (2.4%)	p=0.212
Bad experience	3 (16.7%)	13 (31.0%)	p=0.346
Decided not worth going for screening	1 (5.6%)	5 (11.9%)	p=0.658
Important to have a clinician take the sample			
Not important / somewhat important	2 (11.1%)	31 (73.8%)	p<0.001
Fairly important / very important	16 (88.9%)	11 (26.2%)	

*Fisher's exact test used for all except experience, discomfort, unpleasantness, anxiety



* at least 12 months overdue screening but had attended at least once in the previous 15 years according to GP records

Figure 1. Trial flow diagram

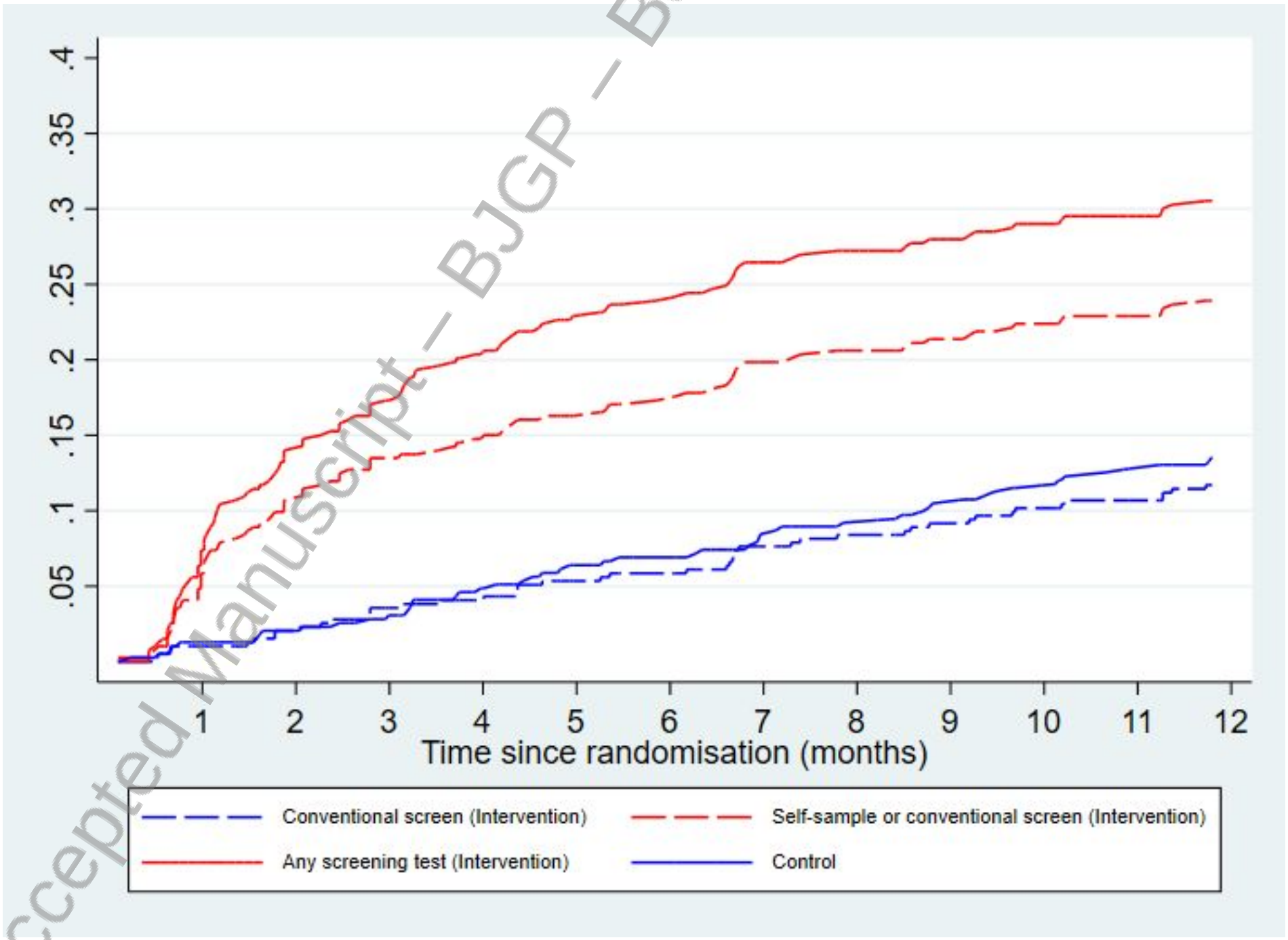


Figure 2. Kaplan Meier plot showing time to screen for intervention and control groups for the various sampling approaches. The distance between “Conventional screen (intervention)” (dashed blue line) and “Any screening test (Intervention) (solid red line) is the additional uplift in screening from non-speculum clinician sampling and self-sampling. The difference between the “Self-sample or conventional screen (intervention)” (red dashed line) and “Any screening test (intervention)” (red solid line) represents the number of women with a non-speculum clinician taken sample. All screening in the control arm is conventional (speculum) screening as this is the only screening method currently available in the England national screening programme.