Impact of post-colposcopy management on women's long-term worries: results from the UK population-based TOMBOLA trial

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ABSTRACT

Background Effective cervical screening reduces cancer incidence and mortality. However, these benefits may be accompanied by some harms, potentially including, adverse psychological impacts. Studies suggest women may have concerns about various specific issues, such as cervical cancer.

Aim To compare worries about cervical cancer, future fertility, having sex, and general health between women managed by alternative policies at colposcopy.

Design Multicentre individually-randomised controlled trial, nested within the National Health Service Cervical Screening Programmes.

Setting UK.

Methods 1515 women, aged 20–59 years, with low-grade cytology who attended colposcopy during February 2001–October 2002, were randomised to immediate loop excision or punch biopsies with recall for treatment if cervical intraepithelial neoplasia (CIN)2/3 was confirmed. Women completed questionnaires at recruitment and after 12, 18, 24 and 30 months. Outcomes were prevalence of worries at each time-point (point prevalence) and at any time-point during follow-up (12–30 months; cumulative prevalence). Primary analysis was by intention-to-treat (ITT); secondary per-protocol analysis compared groups according to management received among women with an abnormal transformation zone.

Results Cumulative prevalence of worries was: cervical cancer 40%; having sex 26%, future fertility 24%, and general health 60%. In ITT analyses, there were no statistically significant differences between management arms in cumulative or point prevalence of any of the worries. In per-protocol analyses, between-group differences were significant only for future fertility; cumulative prevalence was highest in women who underwent punch biopsies and treatment.

Conclusions There is no difference in the prevalence of specific worries in women randomised to alternative post-colposcopy management policies.

Clinical trial registration ISRCTN:34841617.

Key message points

- In a randomised controlled trial, we investigated context-specific worries over 30 months between women following alternative management policies at colposcopy.
- During follow-up, the percentages of specific worries in women were: cervical cancer, 40%; having sex, 26%; future fertility, 24%; general health, 60%.
- The prevalence of worries reported by women randomised to immediate loop excision and punch biopsies with selective recall for treatment did not differ.

INTRODUCTION

Cancer screening involves balancing benefits, harms and affordability.[1] Population-level benefits include reduced cancer incidence and/or mortality, and individual-level benefits include cancers avoided or detected earlier. However, these benefits are rarely achieved without some harm and considerable cost. For example, over-diagnosis and over-treatment are increasingly recognised as

important consequences of screening[2 3] because of their potential adverse effects, which include unnecessary health service expenditure and risk of physical and/or psychological after-effects.

There is potential for over-treatment in cervical screening, particularly regarding follow-up of women who have an abnormal primary screening test (either cervical cytology or human papillomavirus (HPV)). Internationally, one of the main follow-up options is referral for a colposcopy examination, which may be followed by immediate loop excision (LLETZ—large loop excision of the transformation zone; or LEEP—loop electrosurgical excision procedure) or targeted punch biopsies with recall for treatment of cervical intraepithelial neoplasia (CIN). Immediate loop excision removes the whole transformation zone and any lesions at a single appointment.[4] However, it may result in over-treatment, and puts women without CIN at risk of physical after-effects (eg, bleeding, infection) and possibly preterm labour.[5–8] A policy of biopsies and selective recall limits treatment to women with histologically-confirmed disease, but these women must return for a second clinic visit. Moreover, some disease may go undiagnosed.

Over-treatment could, potentially, increase the population-level psychological burden associated with screening. However, the psychological impact of alternative post-colposcopy management strategies has received little attention. Two small non-randomised studies and one large population-based randomised controlled trial (RCT), nested within the UK National Health Service Cervical Screening Programmes and known as Trial of Management of Borderline and Other Low-grade Abnormal smears (TOMBOLA), have been reported.[9–12] The RCT found no difference in clinically significant anxiety or depression between women managed by a policy of punch biopsies and selected recall for treatment, and those managed by immediate loop excision.[12] Evidence suggests women who have abnormal cervical screening tests experience a range of very specific concerns (eg, about cervical cancer, their sex lives, and future fertility).[13–17] However, these concerns may not be well captured by generalised measures of psychological wellbeing (such as anxiety) and it is possible that, while different management policies may not differ in their impact on anxiety, for example, they could differ in their impact on specific concerns.

Using data from the TOMBOLA trial, we compared prevalence of context-specific worries over 30 months in women undergoing colposcopy and managed by policies of immediate loop excision, or punch biopsies and selective recall for treatment.

METHODS

Study population

The study was nested within the colposcopy arm of the multicentre TOMBOLA trial.[18 19] Eligible women were aged 20–59 years and had a routine screening cytology test during October 1999–October 2002 which showed mild dyskaryosis or borderline nuclear abnormalities (BNA)—broadly equivalent to low-grade squamous intraepithelial lesions (LSIL) and atypical squamous cells of undetermined significance (ASCUS), respectively. They could have up to one additional BNA result in the previous 3 years. Consenting women were randomised to cytological surveillance (repeat cytology tests in primary care) or a hospital-based colposcopy examination. Those allocated to colposcopy were sent a clinic appointment and a brief information leaflet describing the procedure and a second randomisation; this leaflet did not mention cancer, sex, or fertility.

Procedures and follow-up

At colposcopy, consenting women were further randomised, using a central telephone service, to immediate treatment by loop excision, or punch biopsies with recall for treatment if CIN2/3 was found. This randomisation was stratified by trial centre, age group, cytology grade, and high-risk HPV status at recruitment. Colposcopists were not blinded to the randomisation. Women who had an adequate colposcopy, and whose transformation zone was considered abnormal, received the assigned intervention. Women with a normal transformation zone were discharged to primary care follow-up by a cytology test after 12 months.

In the immediate loop arm, the whole transformation zone, including the abnormality, was removed. In the other arm, up to four targeted punch biopsies were taken from the most abnormal areas. Women with CIN2/3 on histology were recalled for treatment, usually by loop. Women with no CIN or CIN1 did not receive any further treatment at that time. Follow-up after biopsies or loop was by 6-monthly cytology tests in primary care. Results of these tests determined subsequent actions (next recommended cytology test date or colposcopy referral). If women were referred for colposcopy during follow-up, they attended local NHS clinics and were managed following local protocols. Approximately 3 years post-recruitment, which broadly represented the interval between screening rounds in the NHS screening programmes, women were invited for an exit colposcopy.

Ethical approval was obtained from local research ethics committees and participants provided written informed consent.

Psychological assessments

Women in this analysis were recruited to TOMBOLA from February 2001 onwards (when the psychosocial questionnaires were introduced), had an adequate colposcopy, and consented to the second randomisation (see online supplementary Figure S1; n=1515). The trial protocol specified that the psychological outcomes would include anxiety and depression and

context-specific worries.[18] This paper reports only these context-specific worries; the results relating to generalised anxiety and depression (assessed in a subgroup of 989 of the 1515 women included in this analysis) have been reported elsewhere.[12]

Psychological assessments were completed at the recruitment clinic (T0: baseline assessment) and by post at 12 (T1), 18 (T2), 24 (T3) and 30 (T4) months post-recruitment. The timing was designed to be between follow-up visits to avoid potential 'spikes' of distress associated with these. Outcome information came from the post-colposcopy assessments (ie, T1–T4). The outcome measures were worries about (1) cervical cancer, (2) fertility, (3) having sex, and (4) general health. These were assessed by the Process Outcome Specific Measure (POSM), an instrument developed from focus groups among women who had undergone a low-grade cytology test and follow-up.[20] The instrument as a whole has acceptable repeatability and internal consistency and discriminant validity against the Hospital Anxiety and Depression Scale (HADS).[21] The four relevant questions related to how the respondent had felt in a defined period (table 1). Responses options were 6-level Likert scales ranging from 'strongly disagree' to 'strongly agree'.

The baseline assessment (T0) included questions on socio-demographics and lifestyle, the Multidimensional Health Locus of Control Scale (MHLCS),[22] and the HADS.

Statistical analysis

Questionnaire response rates were computed for each time-point with the denominator comprising the number of women randomised. Socio-demographic characteristics of responders and non-responders were compared at each time-point.

Primary analyses were by intention-to-treat (ITT). Each outcome was analysed separately. Women's responses were reduced to a binary variable: agree/disagree. The point prevalence of 'agreement' was calculated at T0 (baseline) and T1–T4. This was done for all women (ie, combining trial arms) to describe temporal trends in the outcomes, and by arm to compare the psychological impact of the policies. Using data from T1 to T4, the cumulative prevalence of agreement was computed (ie, the percentage of women who agreed with the relevant statement at one or more follow-up time-points). Odds ratios for immediate loop versus biopsies and recall were computed by logistic regression. A model was built for cumulative prevalence and applied to the individual time-points. Risk estimates were adjusted for minimisation variables[23] and significant confounders based on T0 data. Confounders were included in models if they were significant ($p<0.05$) on likelihood ratio tests (LRT). Final models had adequate fit.[24]

For future fertility, the primary analysis included all women. A supplementary analysis was restricted to women who indicated at specific time-points (T1–T4) that they were planning to have a child in the future.

A secondary per-protocol analysis was based on management received, and restricted to women who had an abnormal transformation zone. Women were grouped as follows: punch biopsies only; immediate loop only; and punch biopsies and treatment. The between-group cumulative and point prevalence of each worry was compared using χ^2 tests.

Table 1 Statement stems for the four outcome measures

Type of worry	Statement stem*
Cervical cancer	In the last month, I have been worried that I may have cervical cancer
Sex	In the last month, I have been worried about having sex
Future fertility	In the last month, I have been worried about my ability to have children in the future
General health	In the last month, I have been worried about my general health

*This stem was used at 12, 18, 24 and 30 months post-recruitment (T1–T4); in the baseline questionnaire (T0), each stem started with 'Since getting my smear result'.

RESULTS

Participants' characteristics

A total of 1515 women were included—754 randomised to immediate loop and 761 to biopsies and recall (see online supplementary Figure S1). Almost three-quarters (73%) were recruited with BNA cytology (see online supplementary table S1). The minimisation variables, and socio-demographic, lifestyle and psychosocial variables assessed at recruitment (T0), were balanced between arms. Worries about cervical cancer, having sex, future fertility and general health at recruitment were also balanced (table 2). Seven hundred and eighty-four women (52%) had an abnormal transformation zone at colposcopy (immediate loop, 343; biopsies and recall, 441) and were included in the secondary per-protocol analysis.

Response rates

At recruitment, 98% of women completed the psychosocial questionnaire (see online supplementary figure S1). Response rates were 73%, 67%, 64%, and 60% at 12, 18, 24, and 30 months, respectively, and did not differ between arms. At every time-point, the response rate was higher among women who were: older; recruited with BNA cytology; white; married/co-habiting; parous; not currently using oral contraceptives; or ex-smokers.

Cervical cancer worries

At recruitment, 68% of women were worried about having cervical cancer (figure 1). By 12 months, this had declined to 28% and fell at each subsequent time-point (18 months, 23%; 24 months, 20%; 30 months, 18%). The cumulative prevalence of cancer worries

Table 2 Primary analysis by intention-to-treat: prevalence of worries at recruitment and during follow-up, overall and by management arm, with OR*, 95% CI and p values from likelihood ratio tests

		Follow-up				
Type of worry	**Recruitment T0**	**12 months T1**	**18 months T2**	**24 months T3**	**30 months T4**	**Cumulative T1–T4**
Cervical cancer						
Overall prevalence	67.7	27.8	22.8	20.3	17.8	40.4
By arm						
Immediate loop excision	67.8	27.0	22.2	18.8	16.3	38.6
Punch biopsies & selective recall	67.6	28.6	23.3	21.7	19.4	42.2
OR†, 95% CI	–	0.93 (0.69 to 1.25)	0.92 (0.69 to 1.28)	0.79 (0.56 to 1.13)	0.78 (0.53 to 1.13)	0.86 (0.67 to 1.10)
p Value	–	0.634	0.632	0.199	0.190	0.232
Sex						
Overall prevalence	27.9	14.1	12.7	11.6	11.7	25.7
By arm						
Immediate loop excision	29.7	12.6	11.4	11.4	11.4	23.8
Punch biopsies & selective recall	26.1	15.7	14.0	11.8	11.9	27.6
OR‡, 95% CI	–	0.78 (0.54 to 1.14)	0.81 (0.54 to 1.21)	0.96 (0.62 to 1.49)	0.84 (0.53 to 1.31)	0.81 (0.61 to 1.07)
p Value	–	0.199	0.302	0.859	0.437	0.402
Future fertility						
Primary analysis—all women						
Overall prevalence	24.4	16.9	14.7	12.5	12.0	24.3
By arm						
Immediate loop excision	25.4	17.0	13.3	13.3	12.3	24.1
Punch biopsies & selective recall	23.5	16.9	16.0	11.8	11.7	
OR§, 95% CI	–	0.93 (0.62 to 1.39)	0.70 (0.46 to 1.07)	1.11 (0.69 to 1.79)	0.86 (0.52 to 1.42)	0.88 (0.63 to 1.25)
p Value	–	0.717	0.098	0.670	0.553	0.486
Secondary analysis—restricted to women planning to have a child in the future						
Overall prevalence	62.7	45.3	42.0	37.9	39.0	57.1
By arm						
Immediate loop excision	62.2	43.5	38.2	38.8	38.1	55.6
Punch biopsies & selective recall	63.3	47.4	45.7	37.0	40.0	58.6
OR¶, 95% CI	–	0.85 (0.55 to 1.33)	0.68 (0.43 to 1.08)	1.09 (0.65 to 1.86)	0.83 (0.47 to 1.45)	0.92 (0.62 to 1.35)
p Value	–	0.488	0.100	0.737	0.503	0.663
General health						
Overall prevalence	68.9	36.1	36.8	36.5	35.0	59.9
By arm						
Immediate loop excision	68.5	37.6	38.5	37.4	36.0	61.0
Punch biopsies & selective recall	69.3	34.5	35.0	35.7	33.9	58.8
OR**, 95% CI	–	1.17 (0.90 to 1.53)	1.17 (0.88 to 1.54)	0.99 (0.74 to 1.32)	1.02 (0.76 to 1.37)	1.06 (0.83 to 1.36)
p Value	–	0.249	0.279	0.956	0.885	0.644

*OR for immediate loop excision versus punch biopsy and selective recall.
†Adjusted for minimisation variables, plus anxiety, MHLCS powerful others, worries about cancer at T0, feeling about self.
‡Adjusted for minimisation variables, plus anxiety, MHLCS powerful others, worries about sex at T0, ethnic group.
§Adjusted for minimisation variables (with age grouped as 20–29, 30–39, 40–59), plus anxiety, worries about fertility at T0, reproductive history.
¶Adjusted for minimisation variables, plus anxiety, worries about fertility at T0, reproductive history.
**Adjusted for minimisation variables, plus anxiety, depression, ethnic group, worries about general health at T0, and support received.
MHLCS, Multidimensional Health Locus of Control Scale.

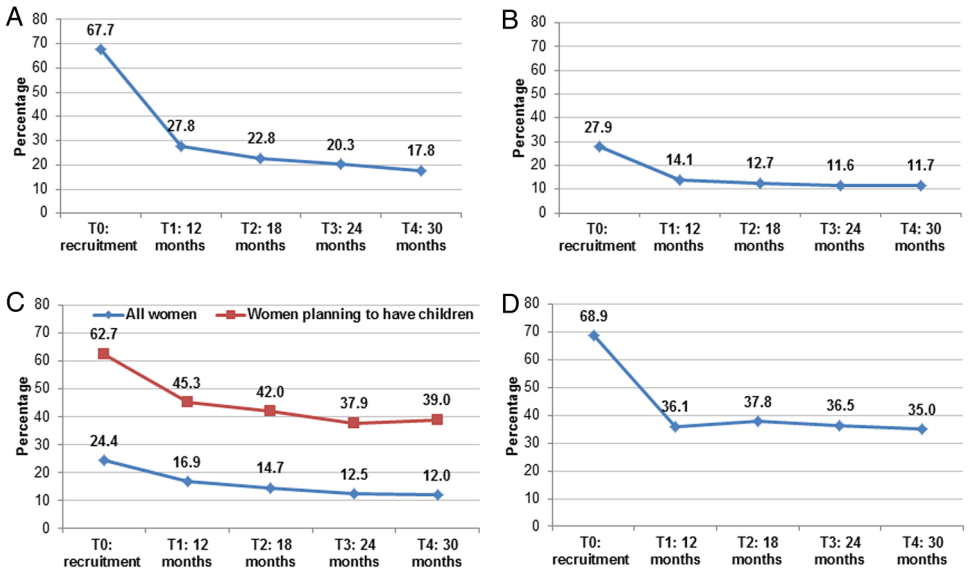

Figure 1 Overall prevalence of worries at recruitment and each time-point during follow-up. (A) Percentage of women worried about having cervical cancer. (B) Percentage of women worried about having sex. (C) Percentage of women worried about their ability to have children. (D) Percentage of women worried about their general health.

during follow-up (ie, at one or more of T1–T4) was 40%. In ITT analysis, the cumulative prevalence of cancer worries was slightly lower in the immediate loop arm than the biopsies and recall arm (39% vs 42%), but the multivariate odds ratio did not differ significantly from unity (OR 0.86, 95% CI 0.67 to 1.10; LRT p=0.232) (table 2). There were no differences between arms in point prevalence, or risk, of cancer worries at any follow-up time-point (T1/T2/T3/T4).

In per-protocol analysis, cumulative prevalence of cancer worries was highest in women who underwent biopsies and treatment (55%), slightly lower in those who had biopsies only (49%), and lowest in those who had immediate loop only (43%); these differences were not statistically significant (p=0.120) (table 3). There were no significant between-group differences in cancer worries at any follow-up time-point (see online supplementary table S2).

Sex worries

At recruitment, 28% were worried about having sex, falling to 12–14% during follow-up (figure 1). The cumulative prevalence was 26%. In ITT analysis, there were no significant differences between arms in cumulative prevalence (table 2), or point prevalence.

In per-protocol analysis, cumulative prevalence of worries about sex was highest in women who had biopsies and treatment, and slightly lower in other groups, but these differences were not statistically significant (table 3). No significant between-group differences were found at any individual time-point (see online supplementary table S2).

Future fertility worries

One-quarter of all women were worried about future fertility at recruitment, 17% at 12 months, and 12% at 30 months (figure 1). The cumulative prevalence was 24%. By ITT, there were no significant differences in cumulative or point prevalence between arms (table 2). When the analysis was restricted to women who were planning to have a child in the future, 45% were worried about future fertility at 12 months and 39% at 30 months (figure 2). In ITT analysis, neither cumulative nor point prevalence differed significantly between arms.

In per-protocol analysis of all women, cumulative prevalence of future fertility worries varied significantly between groups (biopsies and treatment, 48%; immediate loop only, 33%; biopsies only, 26%; p=0.001) (table 3). Significant between-group differences were also seen at 12 and 18 months. When the analysis was restricted to women planning to have a child in the future, significant between-group differences were found only at 12 months (see online supplementary table S2).

General health worries

At recruitment, 69% of women were worried about their general health. This fell to 36% at 12 months and did not change thereafter (figure 1). Cumulative prevalence of general health worries was 60%. This did not differ significantly between arms; nor did point prevalence (table 2).

In per-protocol analysis, cumulative prevalence of general health worries was highest in women who had biopsies and treatment and slightly lower in other groups (p=0.057) (table 3). There were no significant between-group differences at any time-point.

DISCUSSION

Long-term post-colposcopy worries

In this study of context-specific worries reported by women undergoing colposcopy and related

Table 3 Secondary per-protocol analysis: cumulative prevalence of worries during follow-up, by management received*

Type of worry	Cumulative prevalence n	%
Cervical cancer		
Colposcopy & punch biopsies only	134	49.1
Colposcopy & immediate loop excision only	121	43.1
Colposcopy, punch biopsies & treatment	47	54.7
	χ^2 (2df)=4.24; p=0.120	
Sex		
Colposcopy & punch biopsies only	88	32.4
Colposcopy & immediate loop excision only	81	28.9
Colposcopy, punch biopsies & treatment	33	38.4
	χ^2 (2df)=2.82; p=0.245	
Future fertility—all women		
Colposcopy & punch biopsies only	70	25.8
Colposcopy & immediate loop excision only	93	33.2
Colposcopy, punch biopsies & treatment	41	47.7
	χ^2 (2df)=14.63; p=0.001	
Future fertility—restricted to women planning to have a child in the future		
Colposcopy & punch biopsies only	70	60.3
Colposcopy & immediate loop excision only	93	62.4
Colposcopy, punch biopsies & treatment	41	69.5
	χ^2 (2df)=1.44; p=0.487	
General health		
Colposcopy & punch biopsies only	155	56.6
Colposcopy & immediate loop excision only	180	64.5
Colposcopy, punch biopsies & treatment	59	68.6
	χ^2 (2df)=5.72; p=0.057	

*Includes women whose transformation zone at colposcopy was abnormal and who, because of this, underwent additional management procedures.

interventions, the proportion who reported worries at one or more time-points during 30 months' follow-up was high (general health, 60%; cervical cancer, 40%; having sex, 26%; future fertility, 24%). Given how many women undergo colposcopy annually (whether following abnormal cytology and/or a positive HPV test), this implies that the population-level psychological burden of context-specific worries is considerable. In terms of possible explanations, rather than 'resolving' an abnormal screening test, a colposcopy is the start of a series of follow-up 'events' (which may include further tests or examinations in primary care or hospital clinics, biopsies or treatment over an extended time). For example, in TOMBOLA, women with a normal colposcopy were recommended to have annual cytology tests and other women 6-monthly tests; women only returned to routine recall after three negative tests. Being under ongoing follow-up at a colposcopy clinic has recently been shown to be an important driver of long-term distress.[25] In some settings, HPV testing has recently been introduced in follow-up of women treated for CIN.[26–28] Under these protocols, HPV-negative women are returned to routine recall, thereby removing them from extended follow-up. Whether this approach will alleviate women's worries remains uncertain. In recent qualitative work among women who had an HPV test as part of their follow-up, most were overwhelmingly concerned about their initial cytology result and/or its treatment, and the HPV test did not mediate these concerns.[29]

Alternative management policies

While immediate loop offers advantages to the health services because women can be investigated and treated in a single appointment, it may result in considerable over-treatment, at least among women with low-grade cytology.[5 19 30] It is possible that this potential overtreatment could result in a greater population-level psychological burden because women may associate treatment with there being 'something wrong' with their cervix, irrespective of whether or not they actually had CIN. Indeed, some women view any treatment as undesirable.[9] Alternatively, this policy could result in a lower psychological burden since it involves a single appointment and attending a colposcopy clinic is associated with considerable anticipatory distress.[31] In fact, our ITT analysis found no significant differences between management policies for any worries, either over the entire follow-up period or at any individual time-point, in line with our findings for clinically significant anxiety and depression.[12] Our findings are consistent with a small (n=100) non-randomised study from Sweden which reported no significant differences in state anxiety or sexual functioning at 6 and 24 months between women who did, and did not, have loop following punch biopsies.[10 11] In contrast, another study reported lower anxiety in women who had immediate loop than in those managed by biopsy and selective recall; however, that study was also small (n=272), was not randomised, and administered a generalised measure of the psychological burden 1 week post-colposcopy when women managed by punch biopsy were still awaiting results.[9]

Because eligible women had low-grade cytology, half had a normal colposcopy and no further investigation or treatment at that time. The per-protocol analysis was conducted in recognition of this. Cumulative prevalence of every worry was highest in the group who underwent biopsies and treatment (although between-group differences were mostly not statistically significant). In terms of potential explanations, some women express a desire not to return to a colposcopy clinic,[9] so a second treatment-related visit may generate distress and worries. In addition, returning for treatment extends the length of time a woman waits for a more 'definitive' outcome and this wait may induce worries. Moreover, women in the biopsy and treatment group had CIN2/3, and this diagnosis has been associated with increased anxiety post-colposcopy.[32] Finally, women undergoing biopsies and

treatment have more physical after-effects than other women, and physical and psychological after-effects appear related.[6 33]

Specific worries

In TOMBOLA, most women were recruited following a single low-grade cytology test and their risk of cancer would have been very low.[34] The findings that more than one-quarter were worried about having cervical cancer at 12 months and one-fifth at 30 months are, therefore, of particular concern. This observation is not limited to our setting; among 100 women in Sweden who were followed post-colposcopy, fear of cancer was reported by 26% at 6 months and 30% at 24 months.[11] The most likely explanation is that women commonly (but erroneously) think that cervical cytology is a test for cancer[12 17 35] In TOMBOLA, during follow-up, women would have had several interactions with healthcare professionals both in hospital and in primary care facilities. The fact that so many remained worried about cancer suggests there may be some deficiency in services, information or support.

Given that women underwent investigations and procedures specifically for follow-up of abnormal cervical cytology, it was surprising that prevalence of worries about general health at recruitment (69%) and during follow-up (60%) was so high. We asked about general health because focus group research found that women who'd had abnormal cytology and follow-up were concerned about this. The high prevalence of these worries may, in part, be due to women with a high level of general health concerns choosing to participate in cervical screening and/or our trial which was investigating optimal management of low-grade cytology results. More generally, further research is needed to understand how an abnormal screening result and its follow-up translates into more general heath worries. As regards future fertility, in the Swedish study 31% of women aged 23–50 years reported fears about future fertility at 6 months and 20% at 24 months.[11] Our percentages were slightly lower but we included women aged 50–59 years who would not have had such concerns. Our finding that one-quarter of women had worries about having sex during follow-up complements growing evidence that colposcopy and related procedures may impact adversely on women's sexual functioning.[10 14 36–38]

Strengths and limitations

TOMBOLA is one of the few longitudinal studies of psychological after-effects of colposcopy and the only randomised comparison of the psychological burden of alternative post-colposcopy management policies. Further strengths include the large size and population basis, and consideration—in this paper—of specific concerns raised by women with abnormal cervical cytology. The 52% participation rate compares favourably with population-based epidemiological studies.[39] Questionnaire response rates fell over time and it is impossible to know whether respondents' and non-respondents' psychological outcomes differed. While the questionnaire was informed by the findings of focus groups and had acceptable psychometric properties,[20] the outcome measures were single items and this is a limitation. It is possible that sending women a questionnaire asking about how they were feeling may have prompted some to report worries that they would not otherwise have been concerned about, but this is a limitation of all similar questionnaire-based studies. We distributed a brief standard information leaflet before colposcopy, but know nothing about other information provided to women (or that which they sought themselves) at the appointment or during follow-up. Women are likely to differ substantially in information seeking and receipt, but the randomisation should have provided balance between the arms in this regard. Neither the information leaflet, nor the letter which informed women in the immediate loop excision arm of their histology results, mentioned overtreatment so the worries reported here by these women should not reflect concerns associated with having received a procedure that may not have been necessary. Although there are some concerns about the impact of loop excision on pregnancy outcomes, these largely emerged in the scientific literature after TOMBOLA follow-up was completed (the last psychosocial questionnaire were dispatched in spring 2005), meaning that the results reported here for worries about future fertility should be unaffected. Almost all treated women had loop excision so the results do not necessarily generalise to other treatments (eg, ablation). Finally, while we describe patterns over time in each worry for all women in each arm, it is likely that these conceal different temporal trajectories in different groups of women (eg, for some women worries may decline over time while for others they may remain stable or rise); future research would be of value to describe these patterns and determine which women follow each trajectory.

Implications

We have previously shown that, in the UK context (with well-organised, population-based screening), in women referred to colposcopy with low-grade cytology, the policies of immediate loop excision and punch biopsies and selective treatment are equivalent in both clinical effectiveness (ability to detect CIN2/3 over 3 years) and cost effectiveness.[19 40] Where they differ is in relation to the potential for over-treatment, which is greater with immediate loop. Despite this difference, the ITT findings reported here, together with our previous work on clinically significant anxiety and depression,[12] indicate that the long-term psychological burden of the two policies does not differ.

CONCLUSION

The over-treatment associated with a policy of immediate loop excision at colposcopy does not translate into a differential prevalence of context-specific worries compared with a policy of punch biopsies and recall for treatment. Irrespective of how women are managed, the worries reported by women undergoing colposcopy and related interventions are multidimensional and may persist longer-term. Strategies to alleviate this psychosocial burden are needed to reduce the harms associated with cervical screening.

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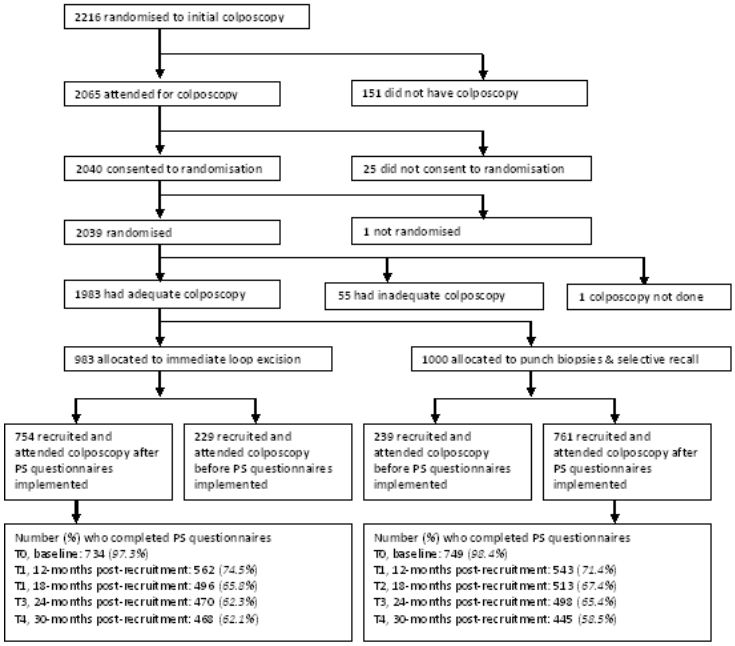
Supplementary Figure 1. Numbers of women randomised and included in the psychosocial (PS) comparison



Supplementary Table 1. Baseline characteristics of women included in analysis, by trial arm: numbers and percentages (unless otherwise stated).

Characteristic	Immediate loop excision		Punch biopsies & selective recall		Total	
	n	*%*	*n*	*%*	*n*	*%*
Total	754	100.0	761	100.0	1515	100.0
Clinical, socio-demographic and lifestyle factors						
Age (years)						
20-29	315	41.8	321	41.2	636	42.0
30-39	212	28.1	206	27.1	418	27.6
40-49	159	21.1	168	22.1	327	21.6
50-59	68	9.0	66	8.7	134	8.8
Recruitment cytology test						
Borderline nuclear abnormalities	553	73.3	555	72.9	1108	73.1
Mild dyskaryosis	201	26.7	206	27.1	407	26.9
Trial centre						
A	241	32.0	247	32.5	488	32.2
B	179	23.7	177	23.3	356	23.5
C	334	44.3	337	44.3	671	44.3
Human papillomavirus status[1]						
Not high-risk	407	54.0	404	53.1	811	53.5
High-risk	270	35.8	282	37.1	552	36.4
Not known[2]	77	10.2	75	9.9	152	10.0
Post secondary school education/training						
None	202	26.9	191	25.2	393	26.1
Through work with formal qualification	142	18.9	150	19.8	292	19.4
Qualifications other than degree from college/university	207	27.6	221	29.2	428	28.4
University/college degree	199	26.5	196	25.9	395	26.2
Not stated	4		3		7	
Employment status						
Full-time paid employment	388	51.6	370	48.8	758	50.2
Part-time paid employment	166	22.1	186	24.5	352	23.3
Student	59	7.9	83	10.9	142	9.4
Not in paid employment	139	18.5	120	15.8	259	17.1
Not stated	2		2		4	
Marital status						
Married/living as married	405	64.2	422	55.9	827	55.1
Divorced/separated/widowed	110	14.7	94	12.5	204	13.6
Single	232	31.1	239	31.7	471	31.4
Not stated	7		6		13	

Supplementary Table 1. Cont'd

Ethnicity						
White	722	96.4	725	95.8	1447	96.1
Others	27	3.6	32	4.2	59	3.9
Not stated	5		4		9	
Parity						
Have children	418	55.9	426	56.5	844	56.2
Have been pregnant, but do not have	79	10.6	90	11.9	169	11.3
Never been pregnant	251	33.6	238	31.6	489	32.6
Not stated	6		7		13	
Oral contraceptive use						
Never used	420	56.3	392	51.9	812	54.1
Former user	92	12.3	100	13.2	192	12.8
Current user	234	31.4	263	34.8	497	33.1
Not stated	8		6		14	
Smoking status						
Never smoked	371	49.6	355	47.0	736	48.3
Former smoker	119	15.9	138	18.3	257	17.1
Current smoker	258	34.5	263	34.8	521	34.6
Not stated	6		5		11	
Physical activity						
<1 time/week	301	40.3	294	39.2	595	39.7
1-3 times/week	179	24.0	171	22.8	350	23.4
>3 times/week	267	35.7	286	38.1	553	36.9
Not stated	7		10		17	
HADS anxiety and depression						
Anxiety						
Non-case (<8)	406	57.4	427	58.5	833	58.0
Possible case (8-10)	134	19.0	139	19.0	273	19.0
Probable case (11+)	167	23.6	164	22.5	331	23.0
Not completed	47		31		78	
Depression						
Non-case (<8)	656	92.9	668	91.6	1324	92.3
Possible case (8-10)	35	5.0	48	6.6	83	5.8
Probable case (11+)	15	2.1	13	1.8	28	2.0
Not completed	48		32		80	

Supplementary Table 1. Cont'd

Health locus of control [3]						
Chance						
mean (sd)	19.1 (5.23)		18.6 (5.21)		18.8 (5.26)	
Not completed	77		50		127	
Internal						
mean (sd)	26.1 (4.16)		26.1 (4.12)		26.1 (4.18)	
Not completed	56		38		94	
Powerful others						
mean (sd)	16.7 (5.64)		16.8 (6.01)		16.7 (5.83)	
Not completed	65		45		110	
POSM outcomes						
I feel well enough informed about what my smear result means[4]						
Agree	656	90.1	662	89.1	1318	89.6
Disagree	72	9.9	81	10.9	153	10.4
Not completed	26		18		44	
The information received has answered the concerns I have had about my smear result						
Agree	664	92.5	679	94.0	1343	93.3
Disagree	54	7.5	43	6.0	97	6.7
Not completed	36		39		75	
The way I feel about myself has changed[4]						
For the better	61	8.4	74	10.0	135	9.2
No change	476	65.4	473	63.8	949	64.6
For the worse	191	26.2	194	26.2	385	26.2
Not completed	26		20		46	
My sex life has changed[4]						
For the better	14	1.9	15	2.0	29	2.0
No change	551	76.3	573	78.0	1124	77.1
For the worse	54	7.5	56	7.6	110	7.6
Not sexually active	103	14.3	91	12.4	194	13.3
Not completed	32		26		58	
I intend to continue having regular smears						
Agree	721	99.3	739	99.9	1460	99.6
Disagree	5	0.7	1	0.1	6	0.4
Not completed	28		21		49	

Supplementary Table 1. Cont'd

I believe that having regular smears reduces my risk of getting cervical cancer						
Agree	687	96.4	707	97.0	1394	96.7
Disagree	26	3.7	22	3.0	48	3.3
Not completed	41		32		73	
What do you feel your chances of getting cervical cancer are compared to other women?						
Lower than average	67	9.4	59	8.0	126	8.7
Average	527	73.6	548	74.7	1075	74.1
Higher than average	122	17.0	127	17.3	249	17.2
Not completed	38		27		65	
I have generally been satisfied with the support I have had from other people[4]						
Agree	633	89.9	669	92.5	1302	91.2
Disagree	71	10.1	54	7.5	125	8.8
Not completed	50		38		88	

1 Based on polymerase chain reaction analysis with GP5+/6+ consensus primers, followed by enzyme immunoassay for detection of 14 "high-risk" HPV types

2 Includes women whose samples were inadequate for analysis, and women who did not have HPV test

3 Assessed by multi-dimensional health locus of control scale (MHLCS)

4 These statements began with the stem "Since getting my smear result"

Supplementary Table 2. Secondary per-protocol analysis: point prevalence of worries at each time-point during follow-up, by management received[1].

Type of worry	12 months		18 months		24 months		30 months	
	T1		T2		T3		T4	
	n	*%*	*n*	*%*	*n*	*%*	*n*	*%*
Cervical cancer								
Colposcopy & punch biopsies only	81	34.6	60	27.9	59	27.6	40	22.2
Colposcopy & immediate loop excision only	85	35.4	47	21.8	37	19.0	39	20.5
Colposcopy, punch biopsies & treatment	34	45.3	19	27.5	16	26.2	18	30.0
	χ^2 (2df) = 3.01; p=0.222		χ^2 (2df) = 2.39; p=0.302		χ^2 (2df) = 4.38; p=0.112		χ^2 (2df) = 2.36; p=0.307	
Sex								
Colposcopy & punch biopsies only	42	18.0	33	15.6	33	15.7	18	10.5
Colposcopy & immediate loop excision only	40	17.1	29	13.5	26	13.9	24	12.9
Colposcopy, punch biopsies & treatment	21	28.0	16	23.5	6	10.0	13	21.7
	χ^2 (2df) = 4.64; p=0.098		χ^2 (2df) = 3.93; p=0.140		χ^2 (2df) = 1.28; p=0.528		χ^2 (2df) = 4.90; p=0.086	
Future fertility *- all women*								
Colposcopy & punch biopsies only	36	15.5	36	17.2	31	14.8	24	14.0
Colposcopy & immediate loop excision only	58	24.3	42	19.8	37	18.9	35	18.8
Colposcopy, punch biopsies & treatment	32	42.7	21	31.3	11	18.3	15	25.4
	χ^2 (2df) = 24.07; p=0.00		χ^2 (2df) = 6.31; p=0.043		χ^2 (2df) = 1.26; p=0.532		χ^2 (2df) = 4.22; p=0.121	
Future fertility *- restricted to women planning to have a child in the future*								
Colposcopy & punch biopsies only	36	41.4	36	48.6	31	42.5	24	40.0
Colposcopy & immediate loop excision only	58	48.7	42	43.3	37	41.1	35	41.7
Colposcopy, punch biopsies & treatment	32	68.1	21	48.8	11	35.5	15	48.4
	χ^2 (2df) = 8.81; p=0.012		χ^2 (2df) = 0.63; p=0.731		χ^2 (2df) = 0.45; p=0.799		χ^2 (2df) = 0.61; p=0.735	
General health								
Colposcopy & punch biopsies only	84	36.1	79	36.6	75	34.9	66	36.7
Colposcopy & immediate loop excision only	100	41.8	96	44.9	77	39.5	65	34.0
Colposcopy, punch biopsies & treatment	34	45.3	27	39.1	23	37.7	23	38.3
	χ^2 (2df) = 2.74; p=0.254		χ^2 (2df) = 3.12; p=0.210		χ^2 (2df) = 0.94; p=0.626		χ^2 (2df) = 0.49; p=0.784	

1 includes women whose transformation zone at colposcopy was abnormal and who, because of this, underwent additional management procedures