

Colposcopists' experiences of HPV Test of Cure for the follow up of cervical intra-epithelial neoplasia

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Condensation

Colposcopists are generally supportive of the HPV Test of Cure procedure however concerns remain regarding HPV positive cases and risk of false negative HPV results.

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Abstract

Objective: To survey lead colposcopists in England to explore their views on the recently introduced HPV Test of Cure (TOC) following treatment for cervical intra-epithelial neoplasia (CIN) and to determine the extent to which it has impacted their clinical practice and affected their patients.

Methods: An online survey was sent to lead colposcopists across England. Questions were asked focusing on the clinicians' confidence in the ability of TOC to guide follow up in various clinical scenarios and how the implementation of TOC had changed patient management.

Results: There was a 50% (N=88) response rate. 90% of respondents indicated they were happy with the new procedure. In the follow-up questions, 20% indicated they were uncomfortable with the procedure when it was applied to women who were CIN2+ with incomplete excision at the endocervical margin. Open-ended questions elicited positive aspects of TOC including reduced follow-up, increased reassurance for patients and clinicians and a faster return to the call-recall system. Negative observations included concerns around HPV positive cases, possible false negatives and anxiety in those women who were originally subject to the pre-TOC guidelines and were now returned to call-recall "earlier" than originally indicated to them. 11% of respondents also indicated they work around the new guidelines to some extent.

Conclusion: Although clinicians are on the whole positive towards the introduction of TOC , concerns were raised which centre primarily around those patients with CIN2+ combined with positive endocervical margins, issues related to HPV positive cases and the possibility of a false negative HPV result. The possibility of patient anxiety due to return to routine screening earlier than originally expected was also identified as a concern.

Keywords: Test of Cure, HPV, NHSCSP, cervical screening

Introduction

In 2011 the NHS Cervical Screening Programme (NHSCSP) announced the introduction of human papillomavirus (HPV) testing for the purposes of triage and test of cure (TOC). This was based on evidence from six Sentinel pilot sites. Roll out across England commenced from April 2012. Under the old guidelines, once a woman had undergone treatment for cervical intra-epithelial neoplasia (CIN) or cervical glandular intra-epithelial neoplasia (CGIN), she was followed up for at least ten years with cervical screening at 6 months, 1 year and thereafter annually, for 9 years assuming no abnormal results occurred. After ten years she was returned to routine recall. Under the new guidelines, 6 months after a woman has undergone treatment for CIN the HPV TOC protocol uses high risk HPV (HR-HPV) testing to evaluate whether those women require referral for further assessment or whether they can be discharged and recalled for screening in 3 years⁽¹⁾. For CGIN two HPV TOCs were introduced in May 2014– one at 6 months and another at 18 months after treatment.

The introduction of TOC has dramatically changed the follow up of CIN with the intention of stratifying women's risk and reducing the number of screening tests performed in the follow up cohort. One consequence of the change however, is a greater reliance on colposcopic examination in order to exclude high-grade CIN. This creates a difficulty since colposcopy is known to miss high-grade disease⁽²⁾ and in colposcopy following treatment the rate of cervical stenosis and unsatisfactory colposcopy increases⁽³⁾. New technologies, are being developed that may have the potential to increase the accuracy of colposcopy in the future. However, these techniques are either not approved for use in the NHS Cervical Screening Programme or are not mandated as part of the Programme and therefore have not been universally adopted by the NHS.

Cases are emerging of high grade cervical lesions in women who have previously tested negative for HR-HPV. Liverani et al for example, found that of 134 CIN 2+ cases, 19 (14.2%) had tested HR-HPV negative⁽⁴⁾, while Cotton et al reported 22% of women with CIN 2+ as being HPV negative⁽⁵⁾. HPV negative cancers have also been reported in the literature. One European study reported that HPV testing provides 60-70% greater protection against cervical cancer compared to cytology⁽⁶⁾. Whilst this may well be true, Liverani observed that in that research, “only 11 out of 19 cervical cancers detected over 2.5 years after enrolment, were HPV positive at baseline”⁽⁷⁾ (p.85). Amongst those deemed by the authors to be

prevalent by virtue of being diagnosed in the first 2.5 years of the study, 16% were HPV negative at baseline.

With the precise timeline of HPV infection still imperfectly understood⁽⁸⁾ and the changes to the NHSCSP over the past 4 years introducing a considerable role for HPV testing in the screening programme, it would be timely to evaluate the experience of the colposcopists working under the new guidelines. The current study was conducted to investigate the impact the introduction of the TOC protocol has had on colposcopists and their views on patient management.

Materials and Method

An electronic survey was conducted of all 191 lead colposcopists across England following consultation with the British Society for Colposcopy and Cervical Pathology (BSCCP). An email was sent with a link to an online 11 item self-report survey. The only demographic data collected was the region in which they worked and when their unit implemented TOC.

Respondents were then asked to rate how comfortable they were with the TOC protocol in different clinical scenarios on a 5 point Likert scale (1-completely uncomfortable, 5-completely comfortable). Further items, were open-ended questions, and asked respondents to give their views on TOC and to comment on any positive or negative aspects from both the point of view of the clinician, patient and service delivery.

Results

There was a response rate of 50% (N=88)¹. 4% (N=4) adopted the procedure as part of the pilot before April 2012, 40% (N=35) adopted it in 2012, 48% (N=42) adopted it in 2013 and 8% (N=7) adopted it in 2014.

When asked how comfortable they were with the guidelines, the vast majority (90%, N=79) indicated with a score of 4 or 5 that they were comfortable. Only 2% (N=2) indicated that they were not comfortable with a score of 1 or 2. 3% (N=3) declined to answer the question and 4% (N=4) gave a neutral 3 response.

¹ Although the survey was successfully (ie no out of office/bounce back messages received) sent to 176 of the 191 email addresses, we are aware that some of these will not be current due to the unavailability of revised up to date email lists. In addition some clinicians may have been unable to respond due to local IT security measures – one clinician contacted the first author to indicate that s/he was unable to access the survey for this reason. Therefore the response rate of 50% is likely to be an underestimate.

Question 4 probed the responses to question three by asking the same question broken down by patient classification. The responses are shown in Table 1.

Respondents were asked what they felt the positive and negative aspects of TOC were. These were open ended questions and responses were grouped into categories. Positive aspects of the procedure were identified as follows: less follow-up including attendant reduction in non-compliance and reduced patient anxiety associated with repeat medical tests (44%, N=37), reassurance for patient and/or clinician (30%, N=25), faster return to call-recall system (29%, N=24), evidence-based practice (10%, N=8) and reduced workload/cost saving (7%, N=6). There were comments by 10 respondents (N=12) that did not fall into these categories. One respondent stated that “Encourages better cooperation between community (smearing) and Hospital (colposcopy). Allows a proper community/hospital screening program to be developed, used and audited.” Two comments concerned the nature of the test – one saying it was easier to get a result, whilst the other commented it was useful where the cervix is very scarred. One respondent stated that even when cytology is subsequently abnormal at 3 years it can still be treated. Other comments included that the test provides additional information (N=2), it could be done by a GP (N=1), after seeing a round of these patients, no concerns (N=1) and it identifies the major HPV serotypes implicated in CIN. One commented that “It also prompt referrals for the BNC with HGHPV +ve”.

82% of respondents (N=72) identified negative aspects of TOC. These were categorised as follows: concerns around HPV positive cases, including patient anxiety and concerns about discharging these patients (28%, N=20); concerns about false negative results (11%, N=8); anxiety of women who had been treated under the old guidelines and were returned to 3 yearly recall “early” (11%, N=8); a feeling that more evidence was needed (8%, N=6); concern that something might be missed (7%, N=5); general patient anxiety (7%, N=5); an increase in workload/colposcopist responsibility (7%, N=5); issues around explaining HPV to patients (6%, N=4); confusion in primary care (6%, N=4); concern about the quality of the cervical sample taker/ the screening test missing something (6%, N=4) and the time needed for patients/GPs/colposcopists to adjust to the change (4%, N=3). There were 10 uncategorised comments as follows: “CIN1 not treated and just followed up with smear after 3 years”; “Does not treat HPV”; “having to explain to women why they have a "new" lesion when their next smear is positive... some women are going privately to have another smear test, another HPV test...”; “HPV testing is not comprehensive enough; not all high risk serotypes are tested for”; “If the loop has come back as negative and MDT has downgraded

the smear later, we cannot discharge the patient on open exeter without doing a TOC”; “not sure about glandulars being included”; “splitting hairs”; “unnecessary colposcopies”; “The treatment is for CIN and not for HPV. Patients are still at risk of recurrence, 3 year recall is too long”; “very difficult in older women, whom 'normal recall' is no further smears if ~60 yrs old or more - this is not appropriate as still at risk for ~10-20 yrs, but won't get any more smears”.

Respondents were asked whether they thought the procedure had affected their patients. 64% (N=56) indicated that it had, 20% (N=18) indicated that it had not, whilst 16% (N=14) were not sure. Those who responded ‘yes’ indicating that they felt it had affected their patients were asked to elaborate further. 44 respondents (79%) made positive comments about the procedure, 22 (39%) made negative comments and 1 (2%) was neutral. Most of the comments repeated the positive and negative aspects of the procedure outlined above, however new observations included the fact that it provided an opportunity to educate women about HPV (N=1), that it increased patient satisfaction (N=1), “we have gone off protocol for a number of older women and picked up an early cancer at 12/12 smear in one” (N=1), “few patients request more frequent smears and some of the GP's/colposcopist provide it privately which is confusing” (N=1).

Respondents were asked whether they thought the procedure had affected their clinical practice. 85% (N=75) indicated that it had while 15% (N=13) indicated that it had not. All respondents were asked to elaborate further and 82% (N=72) chose to do so. 39% (N=28) commented on the reduced follow up and/or reduced workload, 18% (N=13) reiterated that they had more confidence as a result of the new procedure, 8% (N=6) commented that they followed the guidelines or that the guidelines had completely changed, 6% (N=4) indicated it either led to a temporary or permanent increase in workload, 6% (N=4) mentioned the role of primary care – either stating that women were discharged to primary care or that there were concerns about the role of primary care, 3% (N=2) indicated they had concerns about discharging older women, and 3% (N=2) indicated that it was hard to follow patients up and conduct audit under the new protocol. There were also some uncategorised comments as follows: there was reduced follow up in colposcopy previously; it is now easier to discharge older women and those with scarring on the cervix; it is harder to confidently discharge women, especially those who are HPV positive even with negative colposcopy until there is more research data available; less reliance on colposcopy for follow up now; the change in follow up has affected counselling; it's now easier to put stop smoking advice into context;

having to put faith in histology and accept clinical impressions are not always accurate; there is now a reliance on colposcopy that the “cure” has happened even when TOC is positive which is sometimes impossible; patients are being referred back years after treatment who are cytology negative, HPV positive; the new protocol enables proper care planning and for the introduction of new colposcopic techniques and colposcopes to rationalise care.

Additionally, 11% (N=8) of respondents indicated that they worked around the guidelines in some cases as follows: “We had a HG CIN picked up as we brought patient back in 12 months, not 3 years as per recommendation in this age group”; “I am very unlikely to report colposcopy as "normal" when referred with low-grade HR- HPV or failed TOC as do not wish to send to 3 yr recall”; “Increased tendency to biopsy negative cytology and positive hr hpv colposcopies”; “Given the poor specificity of colposcopy in the post treatment cervix I use DYSIS® in all failed TOC with a negative smear. - I think this should be considered in national guidance”; “greater tendency to take biopsies to confirm no CIN”; “Introduction of nurse led test of cure smear clinic. I tried to discharge for community TOC but primary care had some anxiety”; “have changed my advice to discharge more women inform my private patients of change in NHS policy, so offer them the choice of follow up in 3 years or remain under annual review”; “I may use my clinical judgement to decide the indication for an earlier smear”.

Finally there was an open ended question inviting any further comments. Most of these repeated points identified above. Additional comments included a description of a specific incident, a suggestion that TOC should be test of “clearance” rather than cure, confusion because some patients are in TOC whilst some are not, a suggestion that it should be extended to other areas such as vault smears and an observation that there are lots of centres with too much follow up in colposcopy. Lastly, there were two questions included in the responses in relation to other topics outside the scope of this study.

Comment

At first glance, the responses to question 3 suggest that the vast majority of colposcopists are happy with the new TOC protocol however, further probing reveals some disquiet with the procedure in certain patient groups. Where patients with CIN2+ have incomplete excision on the endocervical margin, 20% of clinicians are not satisfied while another 20% are neither satisfied nor dissatisfied. This contrasts with the 100% of colposcopists who were satisfied with using TOC in patients with complete excision of CIN1 and is likely to reflect the clinical

uncertainty associated with those patients which would previously have been monitored over 10 years. Some of this disquiet may well stem from previous research⁹ that proposed that “careful follow-up is essential for at least 10 years after conservative treatment of CIN” (p978). However this research was published prior to current knowledge about HPV and it could be argued that HPV TOC enables efficient selection for follow-up of those women who remain at risk post-operatively whilst reassuring those who are not¹⁰.

There are considerable advantages to the new protocols as colposcopists identified including patient reassurance, speedy return to the call-recall system and cost savings. The latter is one of the drivers for introducing HPV TOC for cytologically negative women. Recent modelling suggests that there would be a cost saving of £9388 per 1000 women compared to cytology only and that an additional 8.4 CIN3+ cases would be averted⁽¹¹⁾. However, despite 90% of colposcopists indicating their satisfaction with the procedure in question 3, when offered the opportunity to identify any negatives about the procedure, 82% chose to do so including clinicians from the original pilot sites as well those from sites that rolled out the procedure later. The most sizeable area mentioned was patient and clinical concerns about HPV positive results. Other negatives raised were general patient anxiety, or anxiety as a result of from moving from the old guidelines to the new ones, concerns around false negative results and a fear that something might be missed. In the changes to clinical practice follow-up open ended question, some clinicians indicated that they were working around the guidelines to an extent to combat colposcopy negative, HPV positive cases. It is not possible from this study to ascertain if this is on an individual case basis which should involve an MDT discussion, or a routine approach; routinely disregarding the national guidelines has the potential to undermine the TOC protocol and its implementation rationale.

Several respondents suggested that further evidence was needed before they could be fully confident and it may well be that confidence in HPV TOC will increase or conversely may decrease over time as more evidence is accrued. Full evidence on the effectiveness of TOC in routine practice across the NHS Cervical Screening Programme will only become evident with time and therefore it is imperative that there is accurate, prospective data collection, ideally at a population level, in order to ensure the guidelines appropriately reflect the available evidence.

This study provides important evidence about the responses of clinicians to this significant change in national screening guidelines that affected clinical practice. The findings of this

study should be taken into account in the event of future major changes in the Cervical Screening Programme in particular in relation to the training and evidence required for clinical staff to be able to confidently support the changes when rolled out in practice.

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Table 1: How comfortable respondents were with the guidelines by patient classification.

Patient classification	Comfortable (4 or 5)	Neutral (3)	Uncomfortable (1 or 2)
CIN1 complete excision	100% (N=88)	0	0
CIN2+ complete excision	98% (N=86)	1% (N=1)	1% (N=1)
CIN1 incomplete excision at the endocervical margin^{a,b}	85% (N=75)	5% (N=4)	9% (N=8)
CIN2+ incomplete excision at the endocervical margin^b	59% (N=52)	20% (N=18)	20% (N=18)
CIN1 incomplete excision at the ectocervical margin	93% (N=82)	7% (N=6)	0

CIN2+ incomplete excision at the ectocervical margin	83% (N=73)	11% (N=10)	6% (N=5)
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^a1 respondent declined to answer this question

^bWhere numbers do not total 100%, this is due to rounding errors