UK NATIONAL SCREENING COMMITTEE

Screening for Anal Cancer

6 June 2013

Aim

1. To agree the UK National Screening Committee's (UK NSC) formal policy position on screening for anal cancer.

Background

2. A review of screening for anal cancer in adults (aged 18 years old plus) against the UK NSC criteria was carried out in October 2012 by Allice Hocking, Adam Fisher and Lorna Bell from SERIO, Plymouth University.

3. The review's principal aim was to focus on screening studies of the general population rather than high risk groups alone. This focus was adopted to ensure any potential changes in policy or practice as a result of the review are not specific to one particular group in society, and relevant to the general population. As other pre-existing conditions may be present in groups with a higher risk, this area would need to be looked at separate to that of the general population.

4. When the UK NSC looked at this issue last the committee agreed that it did not meet the criteria. However the committee did agree that it was an important issue and the cancer screening programmes (CSP) set up an evaluation of the utility of human papillomavirus (HPV) testing and LBC sampling for the clinical management of patients at high risk of anal cancer. The groups are MSM, HIV+ men and women, women who have anally receptive sex, men and women who have had a solid organ transplant. CSP is working closely with GUM and the Lesbian and Gay Foundation. The project is taking place at the Central Manchester trust.

Consultation

5. A public consultation on the screening review took place between 14th January 2013 to 13th April 2013. Four responses were received to the consultation which are available at Annex A.

Conclusion

6. It is not appropriate to implement a national screening programme for anal cancer because:

- Rates of anal cancer have increased in recent decades, particularly amongst those identified as being at a higher risk, but it remains a rare form of cancer across the general population with only 916 registrations of new cases in 2010. It is more common amongst women and increases with age. Other groups with higher levels of risk include, women with a history of genital dysplasia, men who have sex with men, HIV-positive men and women, and finally people

with immunosuppression such as post-transplant patients. Although anal cancer is generally accepted to have a natural history similar to that of cervical cancer, understanding of it is still underdeveloped.

- Screening methods for anal cancer include anal-rectal cytology and high-resolution anoscopy. Variable sensitivity and specificity rates have been reported in the research to date. There is no research on the acceptability of these tests to the general public although the literature does not suggest that they are not considered safe. The research to date indicates that the benefits of screening to survival rates are not yet fully understood. Much is still unknown about this cancer and the development of it.
- HPV is a known cause of anal cancer, with research showing that the HPV vaccine (currently offered to females to prevent cervical cancer) offers protection against the high risk types of HPV. The HPV vaccine provides an important primary prevention tool against anal cancer, with the vaccination of females offering vaccine conferred benefits to males. There is some discussion in the literature of extending the vaccination programme to males but the Joint Committee on Vaccination and Immunisation (JCVI) has not advised extending routine HPV immunisation to males. This is based on assessment of the cost effectiveness. JCVI keeps its advice and recommendations under review. The committee has asked PHE to produce a study of the impact and cost effectiveness of strategies for selective HPV immunisation of MSM.
- There is still much that is unclear and it is difficult to assess how a general population screening programme would provide a cost effective approach and benefit.

Recommendation

7. The UK NSC is asked to agree the policy position on screening for anal cancer as follows:-

A national anal cancer screening programme is not recommended.

8. The UK NSC is asked to agree that the policy should be reviewed in three years' time unless there is significant new peer reviewed evidence in the meantime.

Annex A

Consultation Responses

NHS Cancer Screening Programmes

Here are my comments on the draft anal review:

Paras 30 and 31. This is all about the conventional Pap smear. This is no longer used in the UK where we are all using liquid based cytology. So either this should be mentioned after describing the evidence, or, in my opinion better, if there is no evidence relevant to LBC then this should simply be stated. One advantage of LBC over the smear is that LBC filters off impurities, with obvious advantages for anal sampling.

Para 33. Survival is irrelevant for cancer screening because of lead time bias. Rather they should look at incidence and mortality. This error is repeated in para 67.

British Association for Sexual Health and HIV (BASHH)

Although it is explicitly stated that the scope of this review is anal cancer screening in the general population it bases the review on an HTA review on the cost effectiveness of anal cancer screening in the HIV positive population (1)

In declaring that the scope does not cover recommendations for high risk groups BASHH does not consider that the review takes adequate account of the relative risk of anal cancer in people living with HIV. In a recent study (2) the incidence rate of anal cancer in HIV positive men who have sex with men was 131 per 100 000 person years (py) and 30 per 100 000 py and 46 per 100 000 (py) in HIV positive women and heterosexual men respectively. The demographically adjusted rate ratio for HIV positive MSM was approximately 80. Rates have increased significantly since the introduction of effective antiretroviral therapy in 1996. This burden of disease is not reflected in paragraph 16.

While direct evidence of the risk of progression from high grade anal intraepithelial neoplasia (HGAIN) to anal cancer is not known a recent systematic review estimated the rate of progression to be 1 in 377 in HIV positive individuals (3). The prevalence of HGAIN in HIV positive MSM is approximately 30%.

Criterion 3: BASHH believes there should be a stronger recommendation for HPV vaccination of MSM up to age 26. Under the current policy only girls are vaccinated and while it is expected heterosexual males will benefit due to herd immunity it is thought unlikely MSM will do so. Furthermore there is now substantial evidence of the efficacy, safety and cost-effectiveness of HPV vaccination to prevent warts, HPV persistence and HGAIN in young MSM even after commencement of sexual activity (4-7).

The review does not make it clear that the screening methods discussed (anal cytology and high resolution anoscopy) are not designed to detect anal cancer. Their purpose is to detect HGAIN.

The review contains no reference to the treatment of HGAIN the identification of which is the primary purpose of screening. Treatment modalities for HGAIN include imiquimod, infra-red coagulation, electro-cautery, laser, and surgery. Several of these treatments have been subject to randomised controlled trials (8-10) albeit with clinical endpoints of recurrent HGAIN rather than anal cancer. While benefit from reduced incidence of anal cancer might be expected confirmation of this is required from larger, long term studies.

Overall BASHH agrees that there is insufficient evidence to support anal cancer screening in the general population. However we consider the disproportionate and increasing burden of anal cancer in people living with HIV is justification for specific examination of the case for this group. BASHH also considers there is a strong case to extend HPV vaccination to MSM 26 years old or younger which will reduce the risk of anal cancer in the future.

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3. Machalek D, Poynten M, Jin F et al. Anal human papillomavirus infection and associated neoplastic lesions in men who have sex with men: a systematic review and meta-analysis. Lancet Oncol 2012;13:487-500
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Response to Screening for Anal Cancer (UK NSC) 2012

It is ten years since the NSC last addressed this issue and it is unfortunate to see that there really has been very limited progress in the field. The ability to detect anal cytological dysplasia and anal intraepithelial neoplasia has been confirmed by a number of studies reporting reasonable sensitivity and specificity in different populations at risk. In the last decade a number of moderate size cohort studies have reported on the successful treatment of AIN with ablative and immunomodulatory therapies, although all report a high relapse rate with time. Despite this no studies have evaluated the progression of anal dysplasia to malignancy (perhaps this will never be undertaken in view of the experience in cervical dysplasia at the National Women's Hospital, Auckland, New Zealand, 1965-74).

The lack of knowledge of the natural history of AIN even in the highest risk group (HIV+ve MSM), along with the poor evidence surrounding the value of interventions, makes cost effectiveness modelling extremely difficult and I would venture unreliable. As noted in the 2008 BHIVA, BASHH and FFPRHC guidelines, the role of anal screening is not yet proven [1] [2 3]. Whilst some centres have instituted screening pilots [4 5], the cost effectiveness analyses have produced both positive and negative results [6-11].

The important research implications suggested in this review are almost the same as those suggested a decade ago and I am concerned that many NHS units have instituted anal cancer screening on a routine basis outside of research trials despite this lack of evidence. Some of the suggested research areas have been already addressed in some studies (such as the power of screening tests &the acceptability of the method). The potential benefits of screening to survival rates and the impact of HPV vaccination on anal cancer incidence would seem to be essential areas of research that should be encouraged by the NSC. Meanwhile the commissioners may wish to consider whether the current screening practices in some organisations are justified.

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Royal College of Physicians

Please take this email as confirmation that the Royal College of Physicians wishes to endorse the views already submitted by Professor Bower on behalf of the Association of Cancer Physicians. I would be grateful if you could confirm receipt.
