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Editorial

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Should we start screening for anal squamous intra-epithelial lesions in HIV-infected homosexual men?

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In 1968 Wilson and Jungner[1] published 10 criteria that a screening program should meet before it is introduced (Table 1). Several potentially suitable screening tests have since been rejected by public health authorities because they failed to meet at least one of the 10 criteria. One example is screening for prostate cancer by measuring prostate specific antigen (PSA). Not only was there no disease-specific or overall mortality benefit from PSA screening in a recent systematic review[2] but it generated a large amount of unnecessary, costly and harmful treatment.[3]

One of the latest candidate diseases for screening in HIV-infected men who have sex with men (MSM) is anal squamous cell carcinoma, or more precisely, its likely precursor, anal intraepithelial neoplasia (AIN), also known as anal squamous intraepithelial lesions (ASIL). Although they have been revised and adapted by other workers, it is worth considering Wilson and Jungner's original criteria before deciding to screen for ASIL to prevent anal cancer.

Anal cancer is uncommon in the general population with an annual incidence of ~1.5/100 000 but it occurs much more frequently in MSM and even more commonly in MSM with HIV. In the Multicentre AIDS Cohort Study, the incidence of anal cancer was 14/100 000 person-years in MSM, 69/100 000 in HIV-positive MSM and 137/100 000 in HIV-positive MSM in the more recent antiretroviral therapy era.[4] Another cohort study of HIV-positive MSM reported a rate of 75/100 000 person-years.[5] The rate of 14/100 000 in MSM is comparable to rates of cervical cancer before the introduction of cervical screening.[6] Screening for ASIL is hoped to reduce mortality from anal cancer in MSM as it has for cervical cancer.

This issue of *Sexual Health* contains two reports on the acceptability of elements in the screening process for ASIL. They address the sixth of Wilson and Jungner's criteria, namely that the test for the condition should be acceptable to the population.

Botes, Hillman and colleagues report on 291 MSM who collected their own anal smear samples for cytological detection of ASIL.[7] They inserted a moistened polyester swab 3–4 cm and rotated it for at least 1 minute. Eighty-six percent found it very or somewhat acceptable and only one respondent regarded it as 'not acceptable at all'. Mostly minor pain was reported by about a third of the men and bleeding by a sixth. The high acceptability reported here is consistent with that reported for self-collected anal swabs for the diagnosis of sexually transmissible infections, even if the sample-collection for cytology is more vigorous.[8]

The same group also examined the acceptability of the next recommended step in the anal cancer screening algorithm, namely high-resolution anoscopy (HRA) and biopsy.[9] Of 105 MSM who had HRA, 70% responded to a questionnaire and 91% of these men scored HRA as either somewhat or very acceptable. Two-thirds of the men reported bleeding and just over half reported minor pain. While the total number offered HRA is not reported and the authors also comment that they did not ask respondents if they would undergo a repeat examination, these figures are very respectable for an inherently uncomfortable examination. They probably reflect well upon the amount of prior counselling given to participants and some respondents in this study did comment on the value of effective communication.

Anal cancer screening also fulfils several the other criteria for screening: it is an important health problem (criterion one), and it is probably detectable at an early stage (i.e. AIN, criterion three). And criterion nine has been addressed by a modelling exercise in

Table 1. Wilson and Jungner's criteria for establishing a disease screening program[1]

(1) The condition sought should be an important health problem.
(2) There should be an accepted treatment for patients with recognised disease.
(3) Facilities for diagnosis and treatment should be available.
(4) There should be a recognisable latent or early symptomatic stage.
(5) There should be a suitable test or examination.
(6) The test should be acceptable to the population.
(7) The natural history of the condition, including development from latent to declared disease, should be adequately understood.
(8) There should be an agreed policy on whom to treat as patients.
(9) The cost of case-finding (including diagnosis and treatment of patients diagnosed) should be economically balanced in relation to possible expenditure on medical care as a whole.
(10) Case-finding should be a continuing process and not a 'once and for all' project.

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1999 that predicted cytological screening for ASIL would be cost-effective, particularly at higher CD4 counts.[10] However, the modelling results were sensitive to the rate of progression of ASIL to cancer, and to the effect of treatment (which was assumed in this exercise to reduce cancer risk by 75%). That is, cost-effectiveness depends on a significant rate of progression and reasonably effective treatment. A more recent analysis found that screening for ASIL would be unlikely to be cost-effective.[11] However, studies of cost-effectiveness highlight the three significant concerns about screening for ASIL with anal cytology and HRA.

First, anal cancer is much less common than ASIL. Anal cancer has an incidence of between 75 and 137/100 000 person-years in HIV-infected MSM[4,5] so a large clinic caring for 1000 such patients might expect an average of one case annually. In contrast, the prevalence of high-grade ASIL has been reported at anywhere between 22 and 52%[12–14] in the same group. On this basis between one-quarter and one-half of the entire clinic population would be required to undergo some form of treatment.

Second, treatment of ASIL has until recently consisted of ablation or the application of trichloracetic acid, leaving patients with at least some pain and the risk of bleeding, infection, anal stenosis and a high likelihood of recurrence or persistence. Ablative treatments, include CO_2 laser, infrared coagulation (resolution occurred in 64%),[15] and surgical excision followed by office-based treatment of recurrence (86% resolution after three years).[16] Topical trichloroacetic acid appeared to clear 71% of high-grade lesions, and one-third of patients experienced complete resolution.[17]

Two recent treatments that may be better tolerated, but no more effective, include topical imiquimod and 5-fluorouracil. Self-applied imiquimod was recently reported to be moderately effective in a small randomised trial.[18] When combined with an open-label extension period, 61% of treated patients experienced clearance of high-grade ASIL or downgrading to low-grade histology. In a prospective single-arm study of topical 5-fluorouracil, lesions improved in 57% of patients, with recurrence noted in half of those who experienced complete clearance.[19] Hence there is no generally accepted treatment for ASIL (criterion two). But it is clear that many patients will need repeat HRA and the rate at which they return for more will be the real test of the acceptability of this procedure.

The third concern about identifying and treating ASIL is that the natural rate of reversion from high-grade to lower grade histology is unknown but may be high. Treatment studies have generally not included a placebo arm, leading to uncertainty about the relative proportions of patients cured compared with those who experienced natural resolution. The mismatch between the high prevalence of ASIL and the comparatively low incidence of cancer, points to a gap in our understanding of the relationship between these two conditions (criterion seven). A large cohort study of anal cytology in MSM recently began recruiting in Sydney[20] and will eventually answer this critical question.

We believe that screening for ASIL using cytology or HRA should not yet be promoted as standard medical care and should be confined to research that carefully addresses each of the criteria for screening. In this way any eventual screening program can be implemented in the knowledge that it is doing more good than harm.

Conflicts of interest

None declared.

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