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Editorial

Why a special issue on anal cancer and what is in it?

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Abstract. This editorial describes the contents of this special issue of *Sexual Health* devoted to anal cancer. The aim of the issue is to provide readers with information to assist them in making decisions about what to do about detecting anal cancer early in men who have sex with men with HIV. Should they be advocating screening? It discusses the epidemiology of HPV infection, anal intraepithelial neoplasia, and anal cancer in MSM, heterosexual men and women; anal cancer screening and treatment of anal cancer. And most importantly, what should be done about vaccinating boys with the HPV vaccine.

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Welcome to this special issue on anal cancer, which we commissioned because of the considerable uncertainty – and at times frank disagreement – about how to deal with the important public health issue of anal cancer in men who have sex with men (MSM). Some practitioners are advocating population-based screening of MSM, regardless of their HIV status. Others are not convinced that screening is appropriate but most of us remain quite unsure about what to do. Yet while we deliberate, rates of anal cancer appear to be increasing among MSM with HIV to levels similar to those of bowel cancer in the general population. We hope this special issue will assist you in deciding where you stand about this important public health issue.

The magnitude of the problem is, perhaps, one of the most important points. Grulich *et al*. describe the epidemiology of anal cancer, highlighting its relatively low rate in the general population but considerably higher rate in MSM, particularly in those with HIV where it approaches ~100 per 100 000.[1,2] Despite only a relatively small proportion of the population being MSM, the high rate among MSM is clearly apparent at a population level. Poynten *et al*. describe a much higher incidence of anal cancer in postcodes where gay men more commonly live compared with postcodes where they do not commonly live.[3] And this problem will not go away, with rates of anal cancer rising in both men and women in all countries where time trends have been described.[4]

Pandey describes the anal anatomy, an understanding of which is important for interpreting examination and investigation findings, the pathogenesis of conditions such as internal haemorrhoids and the spread of metastatic anal cancer.[5]

Heywood and Smith review published data on anal sexual practices and highlight the paucity of data that are available at a population level.[6] They make the important point that in many populations, perhaps twice as many heterosexuals engage in anal intercourse as homosexual men, particularly in some countries in Latin America, where heterosexual anal sex is more common.[6] They highlight the paucity of data on the frequency of anal sex and other activities such as digital stimulation, which could potentially transmit the human papillomavirus (HPV).[6]

Machaleck *et al*. take on the task of describing the epidemiology of anal HPV infection in MSM.[7] They highlight the very high prevalence (93%) of HPV infection in MSM with HIV and the high prevalence in HIV-negative MSM (64%).[7] They provide some potential reasons for the apparent absence of a declining age-specific prevalence for anal HPV infection in MSM, when this decline is so clearly apparent in cervical HPV infection.[7] They discuss the paucity of data on the incidence of HPV infection, which highlights how poor our understanding is of the natural history of anal HPV.[7]

Nyitray describes the available data on anal HPV in heterosexual men and women.[8] He describes a surprisingly high prevalence of anal HPV infection among women and lifelong heterosexual men, and also highlights the high concordance between genital and anal sites.[8] Nyitray also poses a series of questions about potential nonsexual and

nonpenetrative methods of transmission that need answering before we can understand the epidemiology of HPV in these groups.[8]

Coutlee *et al*. addresses anal intraepithelial neoplasia (AIN).[9] Like anal HPV infection, AIN is common not only in MSM with and without HIV, but also in heterosexual men with HIV and even in women without HIV.[9] They describe the studies published so far on the prevalence, incidence and risk factors for AIN, and highlight recent biomarkers that may assist in understanding who will and will not progress from infection to high-grade disease and cancer.[9] Joining other authors in this special issue, they highlight the need for a much better understanding of the epidemiology of AIN.[9]

There are four papers that address issues relating to cytological sampling, processing and sensitivity.[10–13] Darragh *et al*. provide a review of the sampling, processing and reporting of anal cytology.[12] Roberts and Ekman make a compelling argument for a two-tier system of grading for anal cytological and histological reporting, in addition to discussing biomarkers.[10] Roberts and Thurloe describe the performance of anal cytology and cervical cytology, highlighting the considerable number of factors that need to be considered when and if the two are compared.[11] They argue that the comparison between cervical and anal cytology is actually not the issue and that work should focus just on the question of whether a screening program based on anal cytology could reduce the 'incidence of and mortality from,' squamous cell carcinoma of the anus, irrespective of how it compares with cervical cytology.[11] Hillman *et al*. describe the findings of an Australian study demonstrating a low sensitivity of anal cytology.[13] In this study, anal cytology detected HGAIN in only 2 of 21 who had biopsy-proven HGAIN.[13]

Palefsky, one of the pioneers of high-resolution anoscopy (HRA), describes the development, rationale, and current use of the technique.[14] A detailed and practical description of the technique is provided together with high-quality figures of conditions often encountered. Palefsky makes the point that HRA is a 'challenging' technique with a long learning curve even for those experienced in cervical colposcopy.[14]

Fox describes the developing area of treatment options for AIN.[15] Many different treatments have been evaluated in many different study designs, making assessment of what works best difficult.[15] Side-effects and complications of the different treatments are easier to quantify than efficacy and appear to be greater with more aggressive treatments.[15] Despite there being few randomised studies and many different study designs, Fox provides a helpful summary of the current state of knowledge to assist clinicians.[15]

An extensive review of anal cancer treatment is provided by Szmulowicz and Wu.[16] They highlight its relatively late presentation, often despite persistent symptoms, and encourage a high index of suspicion among clinicians.[16] They describe the different approaches to treatment including, in highly selected cases, local excision with and without radiation or chemotherapy.[16] They highlight the absence of reports on the effect of treatment on sexual function, which is also relevant to the more destructive treatments for AIN.[16]

The complex issue of the cost-effectiveness of screening for anal cancer is dealt with in a systematic review by Howard.[17] She describes how cost-effectiveness estimates are calculated.[17] Some studies suggest that anal cancer screening is cost-effective but others suggest that it is not. The inconsistency between studies is related to the paucity of data on which the models are based and, like several other papers in this issue, highlight the urgent need for a better understanding of the key issues such as the epidemiology and natural history of AIN.[17]

The potential adverse psychosocial impact of anal cancer screening is discussed by Landstra *et al*.[18] The review did not find that anal cancer screening significantly affected general mental health but screening does generate some increased worry about anal cancer in those screened.[18] The paper has some suggested approaches to minimise this and makes some recommendations for measuring the impact of anal cancer screening.[18]

One topic that is not covered in this special issue is the use of prophylactic HPV vaccines in men and, specifically, their role in preventing anal cancer in MSM.[19] The efficacy of the HPV vaccines in preventing AIN in MSM is high, with a per protocol efficacy of 78% in a recent study.[19] The data from the surveillance of genital warts suggest that even if heterosexual men do not receive the vaccine, they are likely to receive significant protection against exposure to oncogenic HPV types through the herd immunity associated with vaccinating women.[20,21] In contrast, MSM receive no benefit from vaccinating women.[21] If MSM are to benefit from HPV vaccines, then vaccination programs need to either involve all men or selectively target MSM.

There are, however, two major problems with using selective vaccination of only MSM. First, MSM are generally only willing to identify as MSM to health care providers after they have had considerable sexual exposure and may therefore already be infected with the oncogenic HPV types.[22] Second, there are both programmatic and pragmatic issues with achieving substantial vaccine coverage and disease control through any targeted (as opposed to universal) vaccination program.[23] We would advocate a universal vaccination program in all boys before sexual activity, as was currently recommended by an Australian Government Pharmaceutical Benefits Advisory Committee.[24] This would afford the same protection to homosexual men as is afforded to women, but would also ensure that all men are protected from other cancers (e.g. oropharyngeal cancer) related to the oncogenic HPV virus.[25]

Finally, Grulich *et al*. provide their views on the way forward for anal cancer prevention in high-risk groups, based on the reviews in this issue and other recently published data.[26]

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