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#### Cervical cancer prevention in transgender men: a review

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Running head: Cervical cancer in transgender men

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## Abstract

There is increased awareness of transgender physical and mental health widely and in academic research. A significant proportion of transgender men will retain their cervix with an increased risk of cervical cancer. In this review of cervical cancer screening among transgender men, we try to estimate how many transgender men still have a cervix, understand to identify challenges and barriers to cervical screening and propose possible solutions. Organised cervical screening programmes need to consider the needs of this population, in particular the provison of HPV self-sampling.

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## Keywords

Cervix, cancer, screening, transgender, transmen.

## Tweetable Abstract

Transgender men need access to cervical screening

## Background

As transgender people face increasing acceptance in society, transgender physical and mental health is receiving growing interest in academic research. Both WHO and the American Psychiatric Association recently removed transgender identity from the list of psychiatric disorders<sup>1</sup>. There remains many uncertainties and challenges to be resolved for the appropriate care and management of transgender people in the health care system.

Gender-affirming care maybe easier to access as the recognition of patient's rights, informed consent and self-determination start to dismantle barriers such as gate-keeping and marginalisation and indeed ignorance. Transgender people should now be able to dictate their own transition path based on their personal needs and preferences<sup>2</sup>. Some may choose to have gender-affirming hormone therapy and access sequential surgical procedures as well as change their legal status and documents. Others may choose to go through some or none of these.

The transgender population offer a diversity of health needs, linked either to their gender identity, to their assigned gender at birth or both. This can be a complex challenge to healthcare systems when it comes to programs based on sex-specific health needs, such as cervical, breast or prostate cancer screening.

In this paper on cervical screening among transgender men (TM, "individuals who were assigned the female gender at birth, but identify as male or along a transmasculine spectrum"<sup>3</sup>), we will try to estimate the risk of cervical cancer in this population, understand how it affects them, try to identify problems and propose tentative solutions.

Legal transition refers to the administrative change of the name and/or the legal gender. Medical transition can encompass androgen therapy and/or one or several surgical procedures. The most common surgical procedures among TM patients are, in descending order, bilateral mastectomy, hysterectomy (with or without removal of the ovaries) and genital reassignment surgery<sup>4,5</sup>

# Prevalence of transgenderism

Depending on the chosen definition, estimates on prevalence can vary substantially. Researchers have been using different proxies such as the number of people identifying with another gender than the one assigned at birth, attending a gender clinic, starting gender-affirming hormone therapy, requesting or having for surgery or legally changing one's gender<sup>6</sup>. A recent review of prevalence estimated that self-identified transgender and gender non-conforming individuals represented 100 to 2,000 per 100,000 of the global population (0.1% to 2%), and that 1 to 30 per 100,000 individuals would receive gender-affirming care<sup>7</sup>.

The ratio of transgender women (TW) to transgender men is generally above 1, but has varied widely over time and it is now getting closer to 1<sup>2</sup>. In Goodman's review<sup>7</sup>, estimates for TM ranged from 200 to 7,300 per 100,000 for individuals self-identifying as transgender ; from 0.7 to 420 per 100,000 for those who received a diagnosis of *Gender Identity Disorder* or similar, and from 0.25 to 12 per 100,000 for those who actually received transgender-affirming care. The Netherlands was one of the few countries which provided prevalence estimates for these three definitions and the Dutch prevalence was intermediate between the highest and the lowest of the values above.

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The gap between people self-identifying as transgender and those accessing gender-affirming care can be explained by several factors. First, not all transgender people want to undergo gender-affirming treatment or, indeed, have the resources to do so. Secondly, the data included in the review were collected between 1960 and 2015, and access to gender-affirming care has considerably changed over this periond<sup>2</sup>. Thirdly , while self-identification can be assessed in nation-wide surveys, access to care was measured in clinic-based studies; a selected part of the population<sup>7</sup>. And lastly, even for trans people who are willing to access gender-affirming services, the diagnostic criteria of the DSM-V and the ICD-10 require that the gender dysphoria has to be persistent for a certain period – generally 2 years – before being allowed to access gender-affirming care<sup>8</sup>. These all contribute to a considerable proportion of TM retaining their cervix.

#### How many transgender men have a cervix?

In the 2015 U.S Transgender Survey (USTS), 71% of TM (n=7,950) ever received androgen therapy and 14% had hysterectomy<sup>5</sup>. Similarly, in the biggest Dutch clinic for gender-affirming care, 72.9% of adult TM (n=1,624) had started androgen therapy and 83.8% of those who were on testosterone for more than 1.5 years had undergone oophorectomy<sup>2</sup>.

It appears that a substantial proportion of TM have a cervix, even though 57% of TM in the USTS indicated that they wanted to have a hysterectomy ultimately. Permanent sterilisation (defined as the definitive loss of the reproductive function) used to be listed as a mandatory step to change one's legal gender, and as a recent Lancet's editorial highlighted, it is still the case in many places such as Japan or some US states<sup>1</sup>. Growing acceptance of transgender people in society is leading to less restrictive laws<sup>5</sup>. In 2012, Sweden became the first country to abolish the requirement for hysterectomy/oophorectomy for legal change of gender followed by 26 other countries in Europe<sup>9</sup>.

While some experts argue for hysterectomy/oophorectomy, and point to the additional preventive advantage that transmen after surgical removal may not develop cervical cancer and have a much reduced risk of ovarian cancer, others including healthcare professionals (HCPs) point to the individual's autonomy suggesting that regular screening according to the guidelines for cisgender women (whose gender identity matches the sex that they were assigned at birth) may be sufficiently safe <sup>10,11,12</sup>.

This will lead to two things. First, as legal and medical arguments for hysterectomy weaken, we can expect a growing population of transgender men who retain their cervix and so, their need for cervical screening. Second, while some TMs with a cervix will remain registered legally as women, an increasing proportion will be registered as men. In Belgium, for example, 40% (n=605) of all legal gender changes among TM occurred in the year following removal of sterilization from the legal list of requirements<sup>13</sup>. In the context of a population-based preventive programme, those TMs could be missed from call-recall as the process to identify the target population uses data on current legal gender status.

## Are transgender men with a cervix exposed to HPV and cervical cancer?

Persistent infection with high-risk types of HPV is a true prerequisite for cervical intra-epithelial neoplasia (CIN). With regular screening, and the treatment of high-grade CIN, the development of invasive cancer can be avoided<sup>14</sup>. We found only one study estimating HPV prevalence in TM (mean age 27.5y, SD 5.7), showing 16% of high-risk HPV positivity in self-collected vaginal swabs, a prevalence which is comparable to cisgender women<sup>15</sup>. TMs could even be at greater risk of HPV infection than cisgender women: there is some evidence that TM individuals engage in sexual activity with partners across the gender spectrum, have multiple concurrent partners, engage in condomless receptive vaginal and/or anal sex with cisgender men and have higher rates of STI diagnoses, despite low rates of screening<sup>16</sup>. According to the USTS<sup>5</sup> self-reported HIV prevalence was 0.3% among TM compared with <0.1% for the general US population<sup>17</sup>. No data exist on the risk of cervical cancer in TM, but an increased risk compared with the general population could be anticipated given the higher rates of STIs.

The prevalence of HPV and uptake of cervical cancer screening among TM could be assessed from screening and cancer registries if transgender status is collected. Retrieving data from such epidemiological studies would be possible with appropriate ethical, information governance and research approvals and provide a useful insight for service providers.

According to a WHO-report TM who retain their female genitalia often miss out on cervical screening and other sexual health services, as they may not seek out or may not be included in the target lists for screening invitations based on the gender recorded in population registries. As a result, they are at increased risk of gynaecological cancers<sup>18</sup>. Indeed, even with a similar HPV

prevalence, TMs are particularly at risk of cervical cancer due to a lower uptake of screening<sup>3,19</sup> compared with cisgender women. In the USTS, 27% of TM who still had their cervix had a Pap test in the last year against 43% of the adult cisgender female population in the US<sup>5</sup>. In another US-study<sup>3</sup>, 64.3% of TM were up to date with screening recommendation against 73.5% of cisgender women. Additionally, TM have more inadequate Pap test results due to cytomorphological changes (atrophy) associated with androgen therapy<sup>20,21</sup>. The androgenic effect on genital tract, with tissue epithelial atrophy and tissue shrinkage, results in speculum insertion and cervical screening test collection being more uncomfortable and indeed painful.

What are the barriers that transgender men face in assessing cervical cancer screening? Systemic barriers stemming from the health care system can apply to general access to care for transgender people, while other barriers are specific to access to cervical cancer prevention for TM. The intrapersonal barriers are tied to TM individuals' knowledge, behavior and practice, while the structural barriers are from external causes. Table 1 shows the different barriers TMs are faced with. Still TMs are often faced with discrimination and stigmatization by HCP's, leading to a delay in treatment<sup>16</sup>. Moreover, in many countries there is a lack of insurance coverage for gender-affirming surgical procedures. Specifically, on cervical cancer screening, barriers include the lack of TM-targeted education material and the absence of specific guidelines<sup>16,23</sup>. Important intrapersonal barriers include a high prevalence of past sexual and/or emotional trauma, the distress associated with genital examination and the general distrust of healthcare delivery systems<sup>3,16,19,24</sup>.

Table 1. Structural, intrapersonal, systemic and specific barriers to cervical cancer screening for TM.

# Recommendations for screening programs and healthcare professionals

Training of HCPs is essential to improve transgender access to health care in general as well as cervical screening and HPV vaccination. Training HCPA needs to include care of transgender patients<sup>22</sup>. Intervention research shows that training on LGBT+ (Lesbian, Gay, Bisexual and Transgender, "with the "+" indicating inclusion of all sexual and gender minority identities")

topics as short as half-day for fifth-year undergraduate students improved their confidence to clinically assess a transgender patient from 35% to 84%<sup>25</sup>. Cytologists need to be aware of the particular features of dysplasia in atrophic cervical cells, in order to avoid over- and underdiagnosis<sup>21</sup>.

If atrophy is clearly present vaginal application of estriol or estradiol (cream, gel or tablets) during one or two months before taking the pap-smear should be considered. Due to vaginal atrophy, and possibility of no previous penetrative sex, the speculum exam should be performed by an appropriately trained or experienced HCP's and with the smallest possible speculum or replaced by a HPV test.

Self- or provider-collected HPV NAAT (nucleic acid amplification testing) can be a solution in this population by reducing physical and psychological discomfort and fear associated with this medical procedure<sup>19</sup>. Accuracy of HPV testing on self- vs provider-collected HPV testing is similar for detection of CIN in cisgender women when using clinically-validated PCR-based HPV DNA assay<sup>26,27</sup>. However, Reisner et al. found that HPV testing in self-collected vaginal specimens was less sensitive than in provider-collected cervical specimens (71.4%) among TM<sup>15</sup>. Ninety percent of TM participants expressed a preference for self- over provider-collection. Some had concerns and suggested developing new tools to facilitate self-sampling technique and empower them to use these and so support a subset of the population who would otherwise not undergo screening <sup>15</sup>. In the general female population, the offer of self-sampling devices is more effective than invitation or reminder letters to reach non-screened women<sup>27</sup>.

Organized cervical screening programs should not overlook transgender men. A specific opt-in procedure should be foreseen to allow inclusion in the target population for cervical cancer screening for TM with a cervix. This includes TM who have not undergone hysterectomy as well as TM who have undergone supracervical hysterectomy<sup>21</sup>. TM who have undergone total hysterectomy should not be included unless history of previous high-grade CIN<sup>18</sup>. In those countries where cervical cancer screening for women in targeted age-groups is free of charge this should also be the case for TMs.

While studies in ciswomen show that routine HPV-vaccination in public health programmes for those above the age of 25 are not recommended, it would be appropriate to offer vaccination to

TM below the age of 25. As in cisgender woman, HPV-vaccination above the age of 25 is debatable<sup>28</sup>.

Health surveillance system should routinely collect transgender status information<sup>4</sup>. A paper by Gatos suggests a "two-question" approach, asking current gender identity and gender assigned at birth, separately. Specific guidelines need to be developed based on informed arguments<sup>23</sup> as data on gender is sensitive and issues around data security and access complex and challenging. Other gender-related health conditions such as breast, neo-vagina and prostate cancer screening in transgender women also need to be addressed. Future research should focus on documenting the risks of high risk HPV and CIN in TM.

# Conclusion

A significant proportion of TM retain their cervix and are at risk of cervical cancer due to an equal or possibly higher risk of acquiring HPV as well as personal and structural barriers to access cervical screening, this resulting in a lower uptake. Organised cancer screening programs have to include the needs of this population in general, including the benefits of HPV NAAT testing on self-samples in particular. Up to the age of 25, TM could be offered HPV vaccination if not already vaccinated. As in cisgender woman, HPV-vaccination above the age of 25 is debatable. Future research on HPV and cervical cancer should include transgender individuals as unique populations.

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None. Completed disclosure of interest forms are available to view online as supporting information.

Contribution to authorship

SW and MA made substantial contributions to conception and design, drafted the manuscript and approved the final version

SMG, MC and MK made substantial contributions to conception and design, revised the manuscript critically for important intellectual content and approved the final version

Details of ethical approval

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Table 1

Systemic	Specific

Lack of provider knowledge	Female-only waiting rooms
Identification of target population in organized	Woman-centered and heteronormative patient
programs if based on legal/registered gender	education materials
identity	Language from providers during the screening
Lack of insurance coverage for procedures affecting	exam <sup>16</sup>
anatomy not typically associated with an individual's	Absence of specific guidelines <sup>23</sup>
legally recognized gender	
Stigma and discrimination by healthcare providers	
and insurance providers, leading to postponement	
of care <sup>16</sup>	
Overall lack of HPV and cancer research that	
includes transgender men and women as unique	
and disaggregated populations <sup>22</sup>	
Distrust of healthcare delivery systems due to a	Discomfort or distress caused by genital
history of maltreatment	examination <sup>3,16,19,24</sup>
High prevalence of past sexual or emotional	Lack of knowledge that the cervix may be retained
trauma <sup>16</sup>	after some approaches to hysterectomy <sup>16</sup>

Intraperson

Structural