Pelvic pain in transgender people using testosterone therapy: A national survey

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Abstract

Objective: This descriptive study aimed to assess the prevalence and characteristics of pelvic pain and explore predictive factors for pelvic pain in transgender (trans) individuals using testosterone therapy. Design: Cross-sectional survey. Setting: Online. Sample: Trans people presumed female at birth, using testosterone for gender-affirmation, living in Australia, and aged > 16 years. Methods: Logistic regression was applied to estimate the effect size of the possible factors contributing to pain after starting testosterone. Main Outcome Measures: Prevalence and characteristics of pelvic pain following initiation of testosterone therapy, type and length of testosterone therapy, menstruation history, and relevant sexual health, gynaecological and mental health experiences. Results: Among 486 participants (median age 27 years), 351 (72.4%) reported experiencing pelvic pain following initiation of testosterone therapy, described most commonly as in the suprapubic region and as "cramping". Median duration of testosterone therapy was 32 months. Persistent menstruation, current or previous history of post-traumatic stress disorder, and experiences of pain with orgasm were associated with higher odds of pelvic pain after testosterone therapy. No associations were observed with genital dryness, intrauterine device use, previous pregnancy, penetrative sexual activities, touching external genitalia, or known diagnoses of endometriosis, vulvodynia, vaginismus, depression, anxiety, or obesity. Conclusions: Pelvic pain is common in trans people following initiation of testosterone therapy. Given the association with persistent menstruation and orgasm, as well as the known androgen-sensitivity of the pelvic floor musculature, further research into pelvic floor muscle dysfunction as a contributor is warranted.

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ABSTRACT

Objective: This descriptive study aimed to assess the prevalence and characteristics of pelvic pain and explore predictive factors for pelvic pain in transgender (trans) individuals using testosterone therapy.

Design: Cross-sectional survey.

Setting: Online.

Sample: Trans people presumed female at birth, using testosterone for gender-affirmation, living in Australia, and aged $>$ 16 years.

Methods: Logistic regression was applied to estimate the effect size of the possible factors contributing to pain after starting testosterone.

Main Outcome Measures: Prevalence and characteristics of pelvic pain following initiation of testosterone therapy, type and length of testosterone therapy, menstruation history, and relevant sexual health, gynaecological and mental health experiences.

Results: Among 486 participants (median age 27 years), 351 (72.4%) reported experiencing pelvic pain following initiation of testosterone therapy, described most commonly as in the suprapubic region and as "cramping". Median duration of testosterone therapy was 32 months. Persistent menstruation, current or previous history of post-traumatic stress disorder, and experiences of pain with orgasm were associated with higher odds of pelvic pain after testosterone therapy. No associations were observed with genital dryness, intrauterine device use, previous pregnancy, penetrative sexual activities, touching external genitalia, or known diagnoses of endometriosis, vulvodynia, vaginismus, depression, anxiety, or obesity.

Conclusions: Pelvic pain is common in trans people following initiation of testosterone therapy. Given the association with persistent menstruation and orgasm, as well as the known androgen-sensitivity of the pelvic floor musculature, further research into pelvic floor muscle dysfunction as a contributor is warranted.

Tweetable Abstract: Pelvic pain is common in transgender people using testosterone

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Keywords (MeSH): Transgender persons; pelvic pain; testosterone; androgens; menstruation disturbances; sexual activity; sexual function

INTRODUCTION

Pelvic pain in transgender and gender diverse (herein referred to as trans) people presumed female at birth, who are using testosterone as gender-affirming hormone therapy (GAHT) is poorly understood.[1] Understanding adverse effects of testosterone therapy is important given that trans people comprise an estimated 0.5 – 4.5% of the adult population,[2-4] and there is an increasing demand for gender-affirming healthcare globally.[5-7]

Testosterone GAHT which may be given at standard doses or low doses for people who desire 'partial masculinisation', is very effective at inducing physical changes including significant genital and reproductive system effects, an increase in body and facial hair, deepening of the voice, increase in muscle mass, and a

decrease in fat mass.[8] Menstrual cessation, one of the most desired aspects of testosterone GAHT, typically occurs within the first six months of therapy, as well as clitoral enlargement, vulvovaginal atrophy and increase in libido.[9, 10] Endometrial changes can be varied regardless of menstrual cessation with either proliferative (in 40%) or atrophic endometrium (in 50%).[11] No significant histopathological changes appear to occur in the ovaries.[12]

Pelvic pain in people presumed female is extremely common in the general population with 17 – 81% reporting dysmenorrhoea, 8 – 22% reporting dyspareunia and 2 – 24% reporting noncyclical pain.[13] Chronic pelvic pain persisting beyond six months, affects 1 in 7.[14] Causes are multifactorial and rarely reflect a single pathological process.[15]There is a considerable economic burden on people experiencing chronic pelvic pain and on healthcare systems worldwide.[16]Diagnosis and management can be challenging and requires an individualised approach.[17]

As clinicians (gynaecologists, endocrinologists, physiotherapists), we have seen increasing numbers of trans individuals on testosterone seeking assistance to relieve symptoms of pelvic pain. However, at the time of conception of this study, no studies had been published on the topic of pelvic pain in trans individuals using testosterone GAHT. From our clinical perspective, we hypothesised that pelvic pain in trans people using testosterone is predominantly lower abdominal, and similar to menopause, that atrophic vaginitis and vaginal intercourse would contribute to pelvic pain.[18] Further, we hypothesised that pre-existing endometriosis, vulvodynia, or vaginismus would be risk factors. Given the limited research on the prevalence and/or the characteristics of pelvic pain experienced by individuals using testosterone GAHT this was an exploratory study aiming to identify the prevalence of pelvic pain in trans people using testosterone GAHT and to explore potential factors associated with experiencing pelvic pain after commencing testosterone GAHT.

METHODS

We conducted an online cross-sectional survey of trans individuals using testosterone GAHT utilising a non-probability snowball sampling approach. The survey was open between 28th August 2020 to 31st December 2020 to Australian residents over the age of 16 years who identified as part of the trans community and were using testosterone for gender affirmation. The survey was designed collaboratively by our core team of researchers (SZ, AWFQ, TC, KE) who are members of the Australian trans community, and clinicians specialised in trans healthcare.

Survey data were collected and managed using REDCap electronic data capture tools hosted at The University of Melbourne. The study received ethical and governance approval by the Austin Health Human Research Ethics Committee (Reference Number HREC/57155/Austin-2019), ACON Research Ethics Review Committee (Reference Number 2020/03) and the Thorne Harbour Health Community Research Endorsement Panel (Reference Number THH/CREP 20-006).

Written informed consent was not obtained, however the survey preamble outlined that completing the survey implied consent. Inclusion criteria were assessed via three screening questions: a) currently living in Australia; b) identification as trans ("is your gender different to what was presumed for you at birth?"); and c) aged 16 years or older. Participants in this study were recruited from a larger longitudinal Australian trans health study known as *TRANSform* . Participants in*TRANSform* were recruited using a non-probability snowball sampling approach with recruitment calls posted on social media (Facebook and Instagram) and via over 100 trans and gender diverse community support groups and organisations in Australia.

A total of 670 participants who indicated that they were using testosterone therapy for gender affirmation were emailed an individualised link to a survey titled "Pain experiences in trans men and trans masculine people using testosterone survey". A small participation incentive (AUD$5 gift card) was provided for completion.

Survey questions are outlined in detail in the Appendix. In brief, demographic data and testosterone formulation, dosage and duration of use were obtained. Participants were asked to provide self-reported testosterone concentrations. Participants were asked to describe characteristics and location of pelvic pain and rate sever-

ity as well as compare the presence of pelvic pain prior to and after commencing testosterone therapy for gender affirmation.

Potential associated factors were explored including persistent menstruation; presence of genital dryness; history of hysterectomy or oophorectomy; presence of pain with sexual activities; use of intrauterine device; known diagnoses of depression, anxiety, PTSD, endometriosis, vulvodynia (pain in the area around the vulva, not necessarily with touch), or vaginismus (involuntary tightening of the muscles around the vagina, not necessarily with penetration). The number of pregnancies (including miscarriages and terminations) and number of live births was also determined.

Participant characteristics are reported as frequency (percentage) for categorical variables, and median (standard deviation), or median (interquartile range) as appropriate for not normally distributed data, are included. Logistic regression was used to estimate the effects of the possible factors contributing to pain on the odds of experiencing pain after starting testosterone. The factors considered in the regression were selected prior to performing the analysis based on potential risk factors for pelvic pain from expert opinion (given the lack of published research in this field). Results are reported as odds ratios with corresponding 95% confidence intervals (CI). This is a complete case analysis with an alpha level of 5% ($P<0.05$) considered statistically significant. Statistical analyses were performed using R version 4.0.2 (R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

Of the 670 trans people presumed female at birth and using testosterone GAHT who were invited to complete the survey, a total of 506 responded to the survey. After removing duplicates and incomplete responses, 486 valid responses remained.

Characteristics of participants

Detailed characteristics are outlined in Table 1. The median age of the 486 respondents was 27 years (23, 34). Twenty respondents were aged between 50 – 67 years (presumed postmenopausal). Twenty (4.1%) of the respondents identified as Aboriginal or Torres Strait Islander, 7 (1.44%) reported having a variation of sex characteristics (intersex) and a further 45 (9.26%) indicated they didn't know if they had a variation of sex characteristics.

The median duration of testosterone GAHT of participants was 32 months (14.0, 60.5) with intramuscular testosterone undecanoate injections the most used formulation. Self-reported total testosterone concentrations from participants most recent blood tests (N=144) ranged from 0.9 nmol/L to 56 nmol/L, with a median of 16.2 nmol/L (11.9, 22.0).

Characteristics of pain in people experiencing pain after commencing testosterone therapy

A total of 351 (72.2%) of the study sample experienced pelvic pain after starting testosterone therapy. Of those 351 respondents, 316 (90%) reported pelvic pain 'sometimes' and 35 (10%) reported pelvic pain 'always or almost always'. Of the 20 respondents aged over 50 years and presumed postmenopausal, 9 (45%) reported pelvic pain 'sometimes' and 2 (10%) reported pelvic pain 'always or almost always'.

A majority (N=345, 98.3%) reported some form of pelvic pain prior to starting testosterone therapy. This included 190 (65.5%) who 'always or almost always' and 89 (30.7%) who 'sometimes' experienced pain around menstruation, 48 (14.3%) who 'always or almost always' and 102 (30.5%) who 'sometimes' experienced pain around ovulation, and 31 (9.3%) who 'always or almost always' and 140 (41.9%) who 'sometimes' experienced pain between menstrual periods.

The most common description of pain was cramping (described by 72.6%), followed by aching (58.1%), stabbing (39.9%) and sharp (33.9%). The pain was most commonly located in the hypogastric region (described by 87.2% of respondents) (Figure 1). The median score for pain severity after commencement of testosterone GAHT on a scale from 0 to 10 (most severe pain) was 6.2 (4.0, 7.7). This was similar to the median score of 6.7 (5.5, 7.8) reported for pain severity around menstruation prior to commencement

of testosterone GAHT. Consistent with this, the median score in response to the question "How does the pelvic pain you experience using testosterone compare to the pelvic pain you experienced prior to starting testosterone?" (0 = much less severe, 5 = about the same to 10 = much more severe), was 4.3 (2.2, 6.8).

Associated factors

Multivariable regression demonstrated that there was a higher odds of reporting pelvic pain after starting testosterone in people also experiencing persistent menstruation, or who had a current or previous diagnosis of PTSD (Table 2). Pelvic pain was also positively associated with pain with orgasm. A total of 11.3% (N=39) reported that pelvic pain 'always or almost always' resulted in them stopping sexual activity or made them consider alternative ways/methods of being sexually active, and 39.2% (N=135) reported this was 'sometimes' the case.

Treatments for pelvic pain in people using testosterone

The most reported treatments used for relieving pelvic pain included analgesic medication 'pain killers' (56.7%, N=199), with non-steroidal anti-inflammatory drugs (NSAID) (Ibuprofen, Diclofenac and Aspirin) and paracetamol reported most as being helpful (Table 3). Few individuals had hysterectomy (N=26), or oophorectomy (N=21) and inferences are limited.

DISCUSSION

Main Findings

Pelvic pain after initiation of testosterone therapy appears to be a common occurrence, reported by 72.2% of trans people responding to this online survey. Cramping pain in the suprapubic (hypogastric) regions were the most common descriptors. Factors associated with increased odds of reporting pain with testosterone were persistent menstruation (OR 4.46 (1.33, 14.97)), pain with orgasm (OR 32.72 (10.65, 100.52)), and current or previous diagnoses of PTSD (OR 2.50 (1.07, 5.85)). NSAIDs were most commonly used to relieve pain. Of the small number of participants (n=26) who had undergone hysterectomy, 72% reported reduction in pain.

Consistent with our hypothesis and the only other published study describing pelvic pain in trans people using testosterone GAHT, is the prevalence of approximately 70% and the description as cramping, most commonly in the hypogastrium or suprapubic region, followed by right and left iliac regions.[1]

Whilst our exploratory study cannot determine causation or mechanisms of pain, the increased likelihood of reporting pain in people with persistent menstruation and orgasm may possibly suggest increased pelvic floor muscle dysfunction.[19] It is known that levator ani, the collective group of pelvic floor muscles consisting of the deeper layer of pubococcygeus, the iliococcygeus, and the puborectalis, as well as superficial perineal muscles such as the bulbospongiosus, are enriched with androgen receptors and exquisitely androgen-sensitive in male humans, and in male rodents.[20] Androgen-receptor knock out mice, and men who have androgen deprivation therapy for prostate cancer have a marked reduction in the size of the levator ani muscle.[21, 22] Androgens have been shown in female humans and rats to have anabolic effects on pelvic floor muscles.[23-25] As such, it is plausible that with testosterone GAHT may affect the pelvic floor and perineal muscle, and therefore may contribute to the experience of pain.

Whilst pain from endometriosis has been described to worsen with orgasm and penetrative sexual activity,[26] inconsistent with our hypothesis, our analysis did not show an association between having a diagnosis of endometriosis, diagnosis of vaginismus, vulvodynia or genital dryness and pelvic pain.

Participants who reported persistent menstruation had a significantly higher odds (OR 4.46) of reporting pain after starting testosterone. Individuals who do have persistent vaginal bleeding would generally be continuing to have typical rises and falls in estradiol and progesterone concentrations over the course of a menstrual cycle. Pelvic pain in people with persistent menstruation may arise from factors such as dysmenorrhoea from myometrial contractions, the release of inflammatory mediators that cause endometrial shedding, or pelvic floor muscle dysfunction. Menstruation with fluctuations in estradiol and testosterone levels have

been demonstrated to affect pelvic floor muscle activity with significantly higher levels of muscle tone in the luteal phase relative to the follicular and ovulatory phases.[27]

Sexual dysfunction among trans people has been reported to be very common, likely compounded by increased sexual desire after commencing testosterone therapy.[28] However there is little published research.[29] Those who had pain with orgasm had a significantly elevated odds (OR 32.72) of reporting pelvic pain after starting testosterone GAHT. Pain with orgasm or dysorgasmia, is one of the least understood and poorly studied areas in sexual medicine, involving a complex interplay of psychological, neural, vascular, and endocrine factors. It has been hypothesised that dysorgasmia may be the result of bladder neck contractions, uterine neuro-inflammation, uterine contractions and/or pelvic floor musculature dystonia.[30, 31] As such, treatment for sexual pain would be best tailored to the individual with a multidisciplinary approach involving gynaecology, physical therapy, pain management, sexual therapy, and mental health professionals who specialize in chronic pain.[32] Further research is needed on aetiologies and evaluating multimodal approaches.

There is a known clear association between chronic pain and PTSD in people of all genders, explained by both genetic and environmental factors.[33, 34] We observed that people who had a current or previous diagnosis of PTSD had a 150% higher odds (OR 2.50 (1.07, 5.85)) of reporting pelvic pain after starting testosterone GAHT. Research has previously shown that in cisgender women with chronic pelvic pain, that there is an increased prevalence of abuse experiences, high number of major life events and diagnosis of PTSD (but not depression).[35, 36] It is not possible to disentangle whether experiencing severe pelvic pain causes PTSD or trauma-related factors that contributed to PTSD also impact upon pelvic pain. One study in 107 cisgender women suggests that temporally, PTSD appears to precede the diagnosis of chronic pelvic pain supporting a partial role for PTSD or its trauma-related trigger in the pathophysiology of chronic pelvic pain.[37]

Notably previous studies in people presumed to be female have suggested an independent association between chronic pelvic pain and anxiety, depression and mixed anxiety and depressive disorder.[38] This was not observed in our analyses which potentially may be related to the high prevalence of depression and anxiety among trans people overall.[39]

Clinical implications

Treatment of pelvic pain can be challenging in the general population.[17] A multidisciplinary biopsychosocial approach which addresses contribution of various factors to the individual is needed.[40] This may include medical therapies, pelvic floor physical therapy, addressing sexual function, hypersensitivity to pain and psychological factors such as PTSD.[40] Respondents to this survey had reported various self-management strategies. Over the counter pain-relieving medications in the form of paracetamol, NSAIDs and heat were the most frequent strategies reported to manage pelvic pain. In a Cochrane review of management of dysmenorrhea, NSAIDs and heat were recommended as first line treatment to alleviate pain symptoms produced by the release of prostaglandins from the endometrial lining. It is recommended that these strategies are initiated 48 hours prior to onset of menses. Irregular bleeding and amenorrhea may explain the ineffectiveness of these strategies in this population; with limited warning of the onset of breakthrough bleeding episodes.[41]

Many trans people seek hysterectomy and/or oophorectomy as part of gender-affirmation, or due to pelvic pain or ongoing or abnormal bleeding. Of the individuals in this study who had a hysterectomy, pelvic pain was the most common indicator for surgery (64%), followed by gender dysphoria (48%). A total of 72% (N=18) reported relief of pelvic pain symptoms after hysterectomy. Whilst the overall number of respondents undergoing a hysterectomy and/or oophorectomy was too small for meaningful statistical analyses, surgery would indeed cure persistent menstruation which was much more likely in people reporting pain after commencing testosterone therapy. Moreover, cisgender women have also reported resolution or decrease in pelvic pain following hysterectomy.[42] It must be noted that five individuals (20%) in this study reported no change in their pelvic pain and two (8%) reported an increase in pelvic pain following hysterectomy. Further research is warranted.

Whilst further studies need to evaluate the possibility of high pelvic floor muscle tone as a causative factor for pelvic pain in trans people after starting testosterone for gender affirmation, a recent systematic review of

pelvic floor physical therapy to release myofascial trigger points found positive beneficial effects, particularly in people with chronic pelvic pain and dyspareunia.[43] Given the lack of current treatments available to alleviate often debilitating pelvic pain in trans people on testosterone therapy, pelvic floor physical therapy may be a low-risk, treatment strategy to trial in addition to simple analgesics.[40]

Strengths and Limitations

This study has multiple limitations. As this was an online survey recruited through non-probability snowball sampling, this may have encouraged a greater proportion of responders who were younger individuals and may not be representative of the broader trans community. Of the 670 people participating in the larger *TRANSform* study who indicated they were using testosterone therapy and were invited to participate in this testosterone and pain study, 486 responded, corresponding to a response rate of 72.5%. There may well have been responder bias, with individuals experiencing pain syndromes more likely to respond and overrepresenting the proportion of individuals on testosterone experiencing pelvic pain. Further, as participants were asked to recall experiences from prior to commencing testosterone, there is the possibility of recall bias. Medical conditions and testosterone levels were self-reported, and we were unable to confirm diagnoses or blood test results. We also acknowledge that questions regarding penetrative sexual activities did not specify vaginal or anal penetration. Standardised questionnaires for sexual dysfunction were not included, and these are not validated for trans and gender diverse populations. The impact of testosterone therapy on sexual function warrants further investigation.

Despite the limitations, this survey is the largest study to date exploring pelvic pain in trans people using testosterone therapy and is hypothesis generating for future studies examining the pathophysiology of, or the effectiveness of interventions on pelvic pain.

CONCLUSION

Pelvic pain occurring after commencing testosterone GAHT is frequently reported by trans people. The increased likelihood of reporting pain in people with persistent menstruation, and orgasm, as well as the known androgen-sensitivity of the pelvic floor musculature warrant further research on pelvic floor muscle dysfunction as a contributor.[19] Until further evidence is available, a tailored multidisciplinary trauma-informed approach addressing the needs of the individual with pelvic pain should be provided, which may encompass pain management, sexual function, addressing persistent menstruation and mental health.

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DISCLOSURE OF INTERESTS

The authors report no conflicts of interest.

AUTHOR CONTRIBUTIONS

SZ: Conceptualization, Data Curation, Formal analysis, Methodology, Project administration, Writing - original draft, Writing - review & editing. **LB:** Conceptualization, Methodology, Writing - original draft, Writing - review & editing. **AFQW:**Conceptualization, Formal analysis, Methodology, Writing - review & editing. **SYL:** Formal analysis, Writing - review & editing.**TC:** Conceptualization, Methodology, Writing - review & editing. **LMA:** Conceptualization, Methodology, Writing - review & editing. **KE:** Conceptualization, Methodology, Writing - review & editing. **CVE:** Conceptualization, Methodology, Writing - review & editing. **SRG:** Conceptualization, Methodology, Writing - review & editing. **JDZ:** Conceptualization,

Methodology, Supervision, Writing - review & editing. **ASC** : Conceptualization, Methodology, Project administration, Funding Acquisition, Supervision, Writing - original draft, Writing - review & editing.

DETAILS OF ETHICS APPROVAL

The study received ethical and governance approval by the Austin Health Human Research Ethics Committee (Reference Number HREC/57155/Austin-2019), ACON Research Ethics Review Committee (Reference Number 2020/03) and the Thorne Harbour Health Community Research Endorsement Panel (Reference Number THH/CREP 20-006).

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TABLES AND FIGURES

Table 1. Characteristics of the study sample

Characteristic	N	%
Age (N=479)		
16 – 25	192	40.3
26 – 35	190	39.7
36 – 45	62	12.9
46 – 55	25	5.2
56 – 65	9	1.9
66 – 75	1	0.2
Limited Gender Category (N=486)		
Man/Trans man	373	76.8
Non-binary	113	23.3

Characteristic	N	%
Testosterone Formulation (N=486)*		
Testosterone undecanoate (Reandron)	358	73.7
Testosterone enanthate (Primoteston depot)	38	7.8
Testosterone esters (Sustanon 250)	10	2.1
Testosterone 1% gel (Testogel)	62	12.8
Testosterone 2% gel (Testavan)	10	2.1
Testosterone 5% cream (Androforte 5)	11	2.3
Testosterone 2% cream (Androforte 2)	1	0.2
Other	3	0.6
Self-Reported Testosterone Dosage (N=486)		
Full dose	430	87.7
Half dose	33	6.8
Quarter dose	9	1.9
Other (e.g., change in dosage)	14	3.7
Self-reported Testosterone Blood Concentrations nmol/L (N=144)		
0.0 – 4.9	5	3.5
5.0 – 9.9	18	12.5
10.0 – 14.9	38	26.4
15.0 – 19.9	35	24.3
20.0 – 24.9	23	16.0
25.0 – 29.9	14	9.7
30.00+	11	7.6
Consistency of testosterone use (N=485)		
Consistent use since starting	426	87.8
Regularly stop and start use	10	2.1
Other (e.g., change in dosage or formulation)	46	9.5
Unsure/Prefer not to say	3	0.6

*Multiple responses allowed for this question so total responses do not sum to 100%

Table 2. Factors associated with pain after starting testosterone therapy.

Factors	**Pelvic pain since commencing testosterone (N=351) N (%)**	**No pelvic pain since commencing testosterone (N=122) N (%)**	**Odds ratio (95% CI)***	**P-value***
Persistent menstruation Yes No Unsure/Prefer not to say	53 (16%) 266 (80%) 13 (4%)	12 (11%) 94 (86%) 3 (3%)	4.46 (1.33, 14.97)	**0.015**
Genital dryness Sometimes/Always Never Unsure/Prefer not to say	192 (55%) 140 (40%) 19 (5%)	50 (41%) 65 (54%) 6 (5%)	1.82 (0.89, 3.74)	0.103

Factors	Pelvic pain since commencing testosterone (N=351) N (%)	No pelvic pain since commencing testosterone (N=122) N (%)	Odds ratio (95% CI)*	P-value*
Intrauterine device in situ Yes No Unsure/Prefer not to say	38 (11%) 312 (89%) 1 (0.3%)	9 (7%) 112 (93%) 0	1.74 (0.37, 8.11)	0.480
Duration of testosterone therapy (months) Median (IQR)	34 (17, 61)	24 (10, 57)	1.00 (1.00, 1.01)	0.524
Diagnosis of endometriosis Yes No Unsure/Prefer not to say	39 (11%) 302 (86%) 9 (3%)	3 (3%) 117 (97%) 1 (0.8%)	4.41 (0.41, 47.54)	0.221
Diagnosis of vulvodynia or vaginismus Yes No	67 (19%) 284 (81%)	8 (7%) 114 (93%)	1.95 (0.66, 5.78)	0.230
Previous pregnancy None One or more Unsure/Prefer not to say	311 (89%) 39 (11%) 1 (0.3%)	109 (90%) 12 (10%) 0 (0.0)	1.17 (0.31, 4.45)	0.821
Current or previous PTSD Current/previous Never Unsure/Prefer not to say	122 (35%) 194 (56%) 32 (9%)	17 (14%) 92 (76%) 12 (10%)	2.50 (1.07, 5.85)	**0.035**
Current or previous depression Current/previous Never Unsure/Prefer not to say	292 (83%) 50 (14%) 9 (3%)	82 (67%) 34 (28%) 6 (5%)	2.62 (0.86, 7.98)	0.091
Current or previous anxiety Current/previous Never Unsure/Prefer not to say	280 (80%) 59 (17%) 11 (3%)	78 (65%) 35 (29%) 7 (6%)	0.97 (0.32, 2.95)	0.961
Obesity Body mass index <30 kg/m^2 Body mass index [?]30 kg/m^2	232 (67%) 116 (33%)	96 (80%) 24 (20%)	1.38 (0.62, 3.07)	0.425
Pain with orgasm Sometimes/Always Never Unsure/Prefer not to say	208 (59.3) 125 (36.1) 13 (3.8)	10 (8.6) 99 (85.3) 7 (6.0)	32.72 (10.65, 100.52)	**<0.0001**

Factors	Pelvic pain since commencing testosterone (N=351) N (%)	No pelvic pain since commencing testosterone (N=122) N (%)	Odds ratio (95% CI)*	P-value*
Pain with touching of external genitalia Sometimes/Always Never Unsure/Prefer not to say	127 (36.2) 212 (61.6) 5 (1.5)	23 (19.8) 93 (80.2) 0 (0.0)	0.84 (0.32, 2.16)	0.715
Pain with penetrative sexual activities Sometime/Always Never Unsure/Prefer not to say Don't do penetrative activities	230 (66.5) 60 (17.3) 9 (2.6) 47 (13.6)	50 (43.1) 29 (25.0) 2 (1.7) 35 (30.2)	1.18 (0.58, 2.40)	0.640

'Unsure/Prefer not to say' was treated as missing and excluded from analysis; *Odds ratio (95% CI) and P-values from logistic regression mutually adjusted for all factors presented in table.

Table 3. Treatments for pelvic pain in people using testosterone

Characteristic	N	%
Types of treatment reported as helpful (N=351)*		
Pain killers	199	56.7
Heat	160	45.6
Testosterone therapy	77	21.9
Other (e.g. massage, progesterone implant, IUD)	63	17.9
Cannabis	40	11.4
Exercise	39	11.1
Unsure/Prefer not to say	22	6.3
Estrogen containing vaginal cream or pessary	16	4.6
Progesterone tablet	9	2.6
Danazol tablets	0	0.0
GnRH agonists	0	0.0
Types of painkillers reported as helpful (N=351)*		
Non-steroidal anti-inflammatory drugs (Ibuprofen, Diclofenac and Aspirin)	163	46.4
Paracetamol	108	30.8
Combination of paracetamol and Ibuprofen	47	13.4
Morphine	34	9.7
Tramadol	10	2.8
Types of treatment reported as unhelpful (N=351)*		
Pain killers	64	18.2
Exercise	61	17.4
Unsure/Prefer not to say	52	14.8
Heat	48	13.7

Characteristic	N	%
Testosterone therapy	32	9.1
Progesterone tablet	21	6.0
Other (e.g. progesterone implant, IUD)	16	4.6
Estrogen containing vaginal cream or pessary	12	3.4
Cannabis	12	3.4
GnRH agonists	2	0.6
Danazol tablets	1	0.3
Impact of hysterectomy on pain (N=25)		
(0 to 29) Pain is worse since hysterectomy	2	8.0
(30 to 69) Pain is about the same	5	20.0
(70 to 100) Pain is better since hysterectomy	18	72.0
Reasons for hysterectomy (N=25)*		
Pelvic pain	16	64
Gender dysphoria	12	48
Ongoing bleeding	5	20
Other (e.g. Cancer diagnosis, phalloplasty, endometriosis)	11	44
Impact of oophorectomy on pain (N=21)		
(score 0 to 29) Pain is worse since oophorectomy	3	14.3
(score 30 to 69) Pain is about the same	4	19.0
(score 70 to 100) Pain is better since oophorectomy	14	66.7

*Multiple responses allowed for this question so total responses do not sum to 100%

Figure 1. Diagram of abdominal and pelvic regions (N=351)

Figure Legend: Location of pelvic pain selected by number of respondents describing pelvic pain since starting testosterone therapy. Multiple responses allowed for this question so total responses do not sum to 100%.

APPENDIX

Testosterone use was explored through the questions "What date (approximately) did you start testosterone therapy?" and "What type of testosterone are you currently using?" with fixed-response options that included all commonly available forms of testosterone (injections, gels/creams, implants). Participants were also asked "How have you been using testosterone?", with the multi-choice options of consistent, intermittent or 'other' use, and "What dose of testosterone are you on?" with fixed-response options of full, half, quarter or 'other' dose. Testosterone blood levels were ascertained with the question "What were your testosterone levels on your most recent blood test? [nmol/L]".

Experiences of pelvic pain before using testosterone were assessed with fixed-response options (always or almost always, sometimes, never) to "Did you ever experience pelvic pain prior to starting testosterone therapy?". Those participants who indicated they experienced menstruation before starting testosterone, were also asked fixed response options (always, almost always, sometimes and never) to "Did you experience pain around the time of bleeding/periods? (i.e. in the couple days before or during bleeding/periods)", "Did you experience pelvic pain between bleeding/periods?" and "Did you experience pelvic pain at or around the time of ovulation?". Participants were also asked to rate their pain with on a scale of 0 to 10 with 10 = most severe pain.

Experiences of pelvic pain since the commencement of testosterone GAHT were assessed with fixed response options (always or almost always, sometimes, never) to "Have you experienced pelvic pain since commencing testosterone therapy?". Those participants who experienced pelvic pain since commencement of testosterone, were then asked to rate the severity of this pain on a scale of 0 to 10, with 10 = most severe pain. Those

who reported pelvic pain both prior to and since commencement of testosterone, were asked "How does the pelvic pain you experience using testosterone compare to the pelvic pain you experienced prior to starting testosterone?" on a scale of 0 = much less severe to 10 = much more severe. Participants were also asked to describe their pain from fixed-response options, and to ascertain the location of the pelvic pain, participants were asked to locate the pain on a diagram of the abdominal and pelvic regions (Figure 1).

The effectiveness of treatment strategies were assessed with fixed-response options to "What treatment or strategies (if any) have eased your pelvic pain?" and "What treatments or strategies have you tried that have not worked?".

The effect of testosterone use on menstruation was assessed by asking those participants who reported experiencing bleeding/periods prior to starting testosterone to provide a Yes or No response to "Have your periods/bleeding stopped since starting testosterone?". Those participants who had experienced cessation in menstruation were asked to provide a fixed-response to "How long did it take your periods/bleeding to stop after starting testosterone?". Participants were also asked if they experienced genital dryness.

Associations between pelvic pain and sexual activity were also explored. Those participants who indicated that they were sexually active (including masturbation) were asked whether they experienced pelvic pain or other pain during a range of sexual activities. This included fixed-response options (always or almost always, sometimes, never) to "Does touching of your external genitalia cause pain?", "Do penetrative sexual activities, provoke pain?" and "Does orgasm cause pain?". The impact of pelvic pain on sexual activity was assessed with fixed-response options (always or almost always, sometimes, never) to "Does the pelvic pain stop you or make you consider alternative ways/methods of being sexually active?".

Diagnosed pelvic conditions were explored to identify potential treatments or factors related to pelvic pain. This included Yes or No responses to "Have you ever had an *intrauterine device (IUD)?"* , and whether they had ever been diagnosed with endometriosis, vulvodynia (pain in the area around the vulva, not necessarily with touch), or vaginismus (involuntary tightening of the muscles around the vagina, not necessarily with penetration). The number of pregnancies (including miscarriages and terminations) and number of live births was also determined.

Participants were asked if they had previously undergone a hysterectomy or oophorectomy. Those who indicated they had a hysterectomy, were asked "What was the reason for the hysterectomy?" with fixed-response options and "How has the hysterectomy affected your pelvic pain?" on a scale of 0 = pain is far worse to 10 = pain is far better. Similarly, those participants who indicated they had an oophorectomy, were asked "How has the oophorectomy affected your pelvic pain?" on a scale of 0 = pain is far worse to 10 = pain is far better.

To assess any associations between pelvic pain and mental health, participants were also asked whether they had a previous or current diagnosis of post-traumatic stress disorder (PTSD), depression, or anxiety. Self-reported height and weight provided an approximation of body mass index (BMI).