Dear Editor and the Reviewers,

Thank you very much for your comments and advice in response to our manuscript. We appreciate the insight that you provided and strived to make the appropriate corrections for our manuscript.

Reviewer 1: Thank you for your time and reviewing our manuscript. We have addressed your comments and concerns and made the appropriate corrections as follows.

- Reviewer #1: wonder if it would help the reader to understand the text more easily if a clear distinction was made between sex and gender? The former referring biology and the objective realm- the latter being psychosocially constructed and belonging to the subjective realm. The former then becomes the domain of 'hard science' the latter of 'soft science'.
    - A distinction was made between sex and gender at the beginning of our introduction. Thank you for calling this out for us. (page 4 and line 93-96)

- I know there is a general cultural tendency to refer to 'gender affirming treatment' but in my opinion this is a value laden term and not scientifically neutral. If hormonal and surgical treatment for trans people is 'gender affirming' does this make psychotherapy that aims to help a person overcome hatred of their body somehow 'non-affirmative' or even 'gender conversion therapy'? If so, that stigmatises such therapy and increases the risk of trans people receiving unnecessary medical treatment with potentially damaging consequences- including, it seems, increased cancer risk. Such terminology is therefore not in the true interests of trans people; even though some trans people who have already transitioned- and may therefore have a vested interest in justifying medical transition- may advocate its use.
    - In response to your comment on gender affirming treatment, we agree that the mainstay of gender affirming care is psychotherapy, and medical/surgical intervention is an additional/optional pathway if clinically indicated. Mental health evaluations help patients overcome gender dysphoria. Medical and surgical steps are optional, and based on the initial step of the mental health provider to deem the patient medically appropriate for surgery and that surgery or hormone therapy is necessary / helpful for their mental health.

- The author refers to WPATH as the world authority on standards of care for trans people. Arguably the inclusion of 'eunuch gender identity', the links to the 'eunuch archives' the removal of age limits for 'gender affirming' medical treatments for young people etc etc. in its latest SoC8 disqualifies WPATH from such a distinction. WPATH is clearly a lobby group rather than a safe and scientifically reliable organisation- at least in its current form. In my opinion the author could refer to differences of opinion regarding WPATH's reliability rather than accept it as an authority.

    - We adjusted our definition of the WPATH based on their website and mission statement to reflect more of a lobby group than an authority. (page 4 and line 83-86)

- On (I think p1) the author refers to ‘increased social determinants of health’ that may put a trans person at risk. What are those determinants? On perhaps p2 the author talks about gender dysphoria leading a person to ‘consciously or unconsciously unassociated with their remaining organs’. I think I know what the author means, and he/she is making an important point about screening difficulties, but this is not good English.
    - We elaborated on these social determinants of health that may put a trans person at risk or reduced care. (page 4 and line 87-92)
    - We reformatted our PRISMA tables to include on what grounds studies were excluded from consideration. (pages 6, 12, 13, 29, 34, 39, 43,)
- This article needs a full and proper proof read. In several of the tables there were points I did not understand and would have liked more information about. It was not always clear, for instance, on what grounds studies were excluded from consideration.
    - Our article underwent a full and proper proofread by multiple members of our team.

Reviewer 2:Thank you for your time and reviewing our manuscript. We have addressed your comments and concerns and made the appropriate corrections as follows.

- Reviewer #2: Thank you to the authors and the editors for the opportunity to review this manuscript. The authors conducted a systematic review of existing literature relating to transgender cancer screening and management in response to a dearth of such literature. The 70 articles found in PUBMED comprise the results of the study. While standardized cancer screening recommendations are lacking for transgender individuals, this study reviewed case studies and cancer detection and management among transgender individuals across a broad spectrum of gender-affirming care experiences. Interestingly, while in some cases hormonal therapy or certain gender-affirming procedures increased risk of cancer or interfered with cancer treatment, in other cases it did not or was inconclusive. The importance of this study lies in its scoping review of existing literature and ability to distill these findings and their limitations into recommendations for proper cancer screening and management for transgender patients. In particular, the article responds to a lack in studies specifically commenting on how to take gender affirming surgery into account with screening recommendations. I appreciated being able to see case studies of trans patients who had been diagnosed with cancer and received cancer treatment as there is such a dearth of knowledge about these experiences and best practices for managing them. I appreciate the inclusion of the importance of considering elements of psychological health to treatment options for transgender patients. Overall, I think this study points to a need for improved screening measures and further studies of trans experiences of cancer screening and management. The limitations are pretty plainly laid out in a small number of case studies. I would also name that as language is changing, it appears there is limited data on nonbinary people’s experiences with cancer screening and treatment and this should be further explored

    - We have included statements throughout the manuscript on nonbinary patients to make our discussion more thorough and inclusive.
    - We added to the discussion overarching themes in cancer screening and management, however kept individual discussions in each organ section and referred to them as such.
- I think with a strengthened conclusions section, this article can provide clearer recommendations on screening as well as a call for more thorough documentation of trans experiences with cancer detection and treatment and for improved provider education to better support transgender patients.
    - We revisited our conclusion to strengthen it and provide a call for a more thorough documentation of trans experiences with cancer detection and treatment.

- I've included more specific comments broken into section below: I also suggest using "gender affirming surgery" rather than "transition" or "transition related surgery." In the cases where such language needs to be retained because it reflects the language used in other studies, I suggest providing that caveat.
    - We rephrased any transition related surgery to gender affirming surgery where appropriate. (page 11 line 258; page 14 line 363; page 15 line 373; page 14 line 362-365; page 15 line 373; page 19 line 468; page 20 line 469-471, 480; page 36 line 829)

- Another language/ framing point I would suggest keeping in mind are instances where the onus seems to be placed on trans patients for lack of follow-up. Ex on page 26 "This risk may weight even more heavily on the TGGD patients as they may not be as adherent to follow-up protocols or as willing to seek medical attention, ultimately leading to delayed recognition and diagnosis.32" This kind of framing implies that this is the fault of trans patients rather than a failure of the medical system to be a place that is inclusive of and safe for trans patients. I suggest rewording such instances to be clear that it is not about transgender patients' negligence but rather barriers to care, including a well-founded fear of medical mistreatment.
    - We made a point to remove the onus placed on trans patients for lack of follow up by rephrasing and adding context to our discussions throughout the paper.

- Structure: In terms of structure, it was unclear to me if "barriers to care" section was already going into the results or if that was an extension of the introduction, however the introduction also included information I would have classified as belonging to a methods section. Instead, methods seem to be sprinkled throughout the article which was a bit confusing to encounter. I suggest creating consistency in formatting of headings and sub-headings. I also wasn't sure if there should be a separate discussion section as some element of discussion seems to be weaved throughout.
    - We revisited the formatting of headings and subheadings to create more consistency throughout the paper. (page 5 lines 109-115; page 7 lines 164-195; page 14 line 362; page 15 line 377; page 18 line 435; page 19 line 468; page 21 line 483; page 22 line 520;

- Introduction: I suggest providing the caveat in the first sentence that this may be a severe underestimate of the actual number of trans people in the US as there is no census data to back this number and other estimates include. This suggests numbers maybe be higher in younger
  population: https://www.glaad.org/files/aa/2017_GLAAD_Accelerating_Acceptance.pdf
  First paragraph where it says "no cancer screening recommendations specific to the population" I recommend specifying which population.
    - For our introduction, we provided a statement about the underestimate of actual number of trans patients in the US. (page 4 and lines 77-78)

- Barriers to care: This section could benefit from references backing up statements about discomfort with care on the part of both providers and trans patients. I also recommend explicitly naming that a lack of trans inclusive screening protocols may be driving lower levels of screening (ex. ACS recommends mammogram for "women" so if a provider is following this, they wouldn't screen a trans man or nonbinary person for whom this screening is actually relevant). On page 7 instead of "culturally sensitive language" I suggest saying "gender-inclusive language." Breast: This section begins with a statement about breast cancer impact on "women", but presumably means cisgender women. I suggest creating that distinction for trans inclusivity as I imagine transgender women were not included in this data.
    - We kept barriers to care in the introduction as a way to set up the tone of the paper. We revisited barriers in the conclusion to strengthen this message. (page 7 and line164-210)
    - Four barriers to care, we added references, explicitly called out lack of trans inclusive screening protocols, and rephrased gender inclusive language. (page 7 and lines 172-195)

- Management: This opens with talking about breast augmentation procedures. In addition to suggestion that "transgender females" be replaced by "transgender women" I also suggest considering inclusive of nonbinary individuals where relevant. For example, nonbinary people may also undergo breast augmentation procedures. Later in this paragraph the phrase "female to male transition" is used to refer to top surgery however these are not synonymous and "female to male transition" is considered outdated by many.
    - We clarified some of the confusing wording throughout the manuscript. We also maintain consistency on how this population was referred to throughout the paper by using transgender women and transgender men in place of previous terms. (Page 4 line 91; page 7 line 174; page 7 line 176; page 8 line 191-192; page 9 line 219; page 10 line 244; page 25 line 586,591, 595; page 27 line 625; page 30 line 678,684,686,688,691; page 31 line 701, 703, 707, 715,; page 32 line 729, 733; page 33 line 739; page 35 line 824; page 36 line 831,835,846; page 40 line 936, 941,943, 949, 952, 954; page 41 line 965; page 44 line 1058)

- Gender affirming care is often used to replace "transition" as transition can include a broad scope of things, sometimes physical, sometimes not. I would instead recommend

phrasing this sentence with something along the lines of "Chest masculinization, often referred to as 'top surgery' is used by some people to achieve a more masculine appearing chest." Note that top surgery can also refer to chest feminization procedures. I suggest that instead of including the two sentences about nonbinary people at the end of the paragraph, including them throughout.
    - For the management section, we replace transition with gender affirming care. We also changed top surgery to chest masculinization and chest feminization. We included discussions of nonbinary patients throughout.

- Male to female transition: In addition to previous comments on language, the sentence "Patients that did not undergo surgery or hormone therapy were excluded as they otherwise align with cis-gender males," in the first paragraph I would suggest rewording or removing as it reads currently as invalidating of transgender people who have not sought physical change/ medical forms of gender-affirming care. I would suggest instead saying something that is not aligning trans femmes with cisgender men and instead framing as follows, "Patients that did not undergo surgery or hormone therapy were excluded as we were largely interested in understanding how these factors influenced breast cancer detection and management."
    - For the breast section, we fixed phrasing to state Cisgendered women to avoid confusion. (page 18 line 446)

- Hormonal therapy only: On page 16 in response to the statement, "This further highlights the necessity to determine what the real impact of gender affirming hormone therapy in on cancer and whether it is reasonable to allow patients to continue therapy despite cancer diagnosis and treatment," I would like to suggest deleting the second half of this sentence and instead focusing on suggesting further research be done to find ways to mitigate risk of continuation of gender-affirming care. The second half of this sentence is implying that it would be okay for providers to infringe upon patient's bodily autonomy when it comes to hormone use when, for example, it would be the patient's decision to decide whether or not they want to undergo certain forms of care. I think this is a slippery slope when HRT is already often framed as non-essential.
    - For the male to female transition section, we adjusted language based on previous comments. We removed a statement on excluding patients who only underwent hormone therapy from our analysis and rephrased this to emphasize our interest in understanding how these factors influence breast cancer detection and management. We also rephrased a sentence on the impact of gender affirming hormone therapy continuation based on your comments. (page 17 and line 411-412)

- Female to male transition: Same comment as above about the sentence: "Patients that did not undergo surgery or hormone therapy were excluded as they otherwise align with cis-gender females."
    - For the female to male transition section, we removed a similar sentence about excluding patients with hormone therapy only. (page 20 lines 474-476)

- Cervical cancer screening: Please cite this: “TGGD patients often undergo hysterectomies partially with the goal of not requiring to endure regular gynecological screening visits that may worsen their gender dysphoria.”
    - For the cervical cancer screening, we added citations of worsening gender dysphoria with regular gynecologic screening (page 31 lines 711-713)

- Ovaries- Screening: Pg 34- recommendations for TGGD individuals described as same as cisgender women—I suggest clarifying that this is talking about TGGD individuals with ovaries, as I imagine not all TGGD individuals should have the same screenings. Prevention and management: I appreciated the extensive summary of recommendations for TGGD around screening as it related to gender-affirming care.
    - For the ovaries section, we clarified phrasing about transgender individuals with ovaries in relation to screening. (page 35 and line 804-805)

- Prostate: Page 38, please cite “While Estrogen has a short-term risk of thrombosis, the long-term risk of estrogen use is unclear.” Comments on “Currently, screening guidelines for the TGGD population are the same as cis men.” Same as above, specify that rather than TGGD population what is meant is TGGD people with prostates. On pg. 40 “and patients’ fear of discrimination can delay cancer diagnosis and treatment” I have the same comment as above. I suggest more clearly delineating the medical barriers that exist to accessing care moving away from onus on TGGD patients.
    - For prevention and management section,we fixed specific phrasing in the prostate section for transgender patients and prostate screening. We also clarified the medical barriers that exist to remove the onus from transgender patients Not receiving appropriate screening frequency (page 42 lines 981-990)

- Conclusion: I would love to see the conclusion built out a bit more with a clear delineation of what screening recommendations could be distilled from the literature review and what remains inconclusive. I also want to push back on the authors statement that “TGGD patients should receive care at institutions capable of providing a multi-disciplinary approach with internists, reproductive endocrinologists, psychotherapists, and respective oncologic teams.” While I agree that, in many cases, this would be the best approach, I also believe that there should be more stress on the necessity of provider education around trans-specific needs so that trans patients are not isolated in their care options. I would love to see more specificity and summary of what was discussed in the results in the conclusion section. In particular, a large focus was on screening and detection but the conclusion provides recommendations focused on the phase after diagnosis

  In the conclusion section, we elaborated on our discussion about screening recommendations and pointed towards specific organ sectionsfor more in depth discussions. We also removed a statement on receiving multidisciplinary care to focus more on provider education about transpacific needs. We also provided overarching themes related to screening andmanagement but pointed towards organ sections for more detailed discussions of specifics. (page 45 and line 1077-1092)

Once again, we really appreciate the time and consideration you've given towards improving our manuscript. We hope that our corrections have been made satisfactory, however invite further conversation as you see fit. Thank you again! We look forward to hearing back from you soon.

Sincerely,

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