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SUMMARY WITH CRITICAL APPRAISAL

Primary Care Initiated Gender-Affirming Therapy for Gender Dysphoria: A Review of Evidence Based Guidelines

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Abbreviations

WPATH	the World Professional Association for Transgender Health

Context and Policy Issues

"Transgender" is an umbrella term used to describe individuals with gender diversity. Transgender people include those whose gender identity or expression differs from that assigned at birth.[1] Gender dysphoria refers to the discomfort or distress caused by the discrepancy between a person's gender identity (their psychological sense of themselves as men or women) and the sex assigned at birth and the associated primary or secondary sexual characteristics and/or expected social gender role.[2] Changes to social role and presentation are typically observed in transgender people. Individuals with gender dysphoria may identify as men and women, or as gender variant, transgender, transsexual, transvestite, non-gender, pangender, polygender, gender queer, androgyne, neutrois or many other terms. The current population estimates of transgender and gender nonconforming people range from 0.17 to 1,333 per 100,000 worldwide.[3] In British Columbia, the number of transgender people was estimated to be over 23,157 (based on a prevalence of 0.5%) in 2014.[4] However, the proportion of this population is likely underestimated.[5] The pressures associated with unmanaged dysphoria and/or the social stigma that can accompany gender diagnosis and transition may result in clinically significant levels of distress that would require medical assistance, in particular, specialist experience of the field.[2]

Historically, medical care for transgender people has been provided in highly specialized gender centers, where mental health professionals, endocrinologists or other specialists carried out appropriate assessment and subsequent treatment if necessary. These treatments can include a combination of medical (cross-sex hormone therapy), surgical (genital reassignment surgery and non-genital surgical procedures), mental health and other related treatments and services (e.g. speech and voice therapy).[2,6,7] However, delayed treatment initiation and barriers to access are common, because the specialists are usually located in major centers. According to a project in Ontario, approximately 70% of transgender people live outside the Greater Toronto Area, although urban centers are often sought out by those who wish to access healthcare.[8]

Since the last decade, there has been increasing recognition that people with gender dysphoria may be well-served in primary care settings and, with additional training, family physicians and nurse practitioners may provide some gender-affirming services.[2,7] The role of primary care providers may include performing initial examinations, working with referring psychiatrists (to make sure there is support available between referral and appointment if needed). Also in the longer term, in a primary care setting, physicians can be responsible for the life-long monitoring of their patient's wellbeing, which involves conducting simple monitoring tests, examinations and medication reviews as recommended by the specialists.[2] In addition to transgender-specific care, transgender people also require ongoing primary and preventive care, such as the need for cervical screening in transmen and breast cancer screening in transwomen.[6] In this way, transgender-specific healthcare needs are assumed to be addressed in a timely and effective manner in the context of primary care.[8] Survey results from a group of 11 adult transgender patients in Ontario echoed that most transgender people expected care to be delivered by family physicians when it is possible.[9] In another interview with 13 physicians from Ontario, the doctors identified barriers when providing healthcare services to transgender patients, such as

challenges accessing resources, a lack of knowledge, ethical considerations regarding medical transitioning treatments, or the process of diagnosing gender identity disorder.[10]

The objective of this report is to review and critically appraise the evidence-based clinical practice guidelines regarding primary care-initiated gender-affirming therapy for adults with gender dysphoria.

Research Question

What are the evidence-based guidelines regarding primary care initiated gender-affirming therapy in adults with gender dysphoria?

Key Findings

One evidence-baseline clinical practice guideline was identified that provides guidance for the health of transsexual, transgender and gender-nonconforming people. The guideline suggests that with appropriate training, hormone therapy can be managed by a variety of healthcare providers, including primary care providers such as primary physician or nursing practitioner. However, the recommendations did not specify whether this treatment can be initiated by primary care providers. The quality of this guideline was limited due to insufficient reporting on searching for evidence and formulating the recommendations. This guideline did not report the strength of recommendations or the quality of the evidence.

Methods

Literature Search Methods

A limited literature search was conducted by an information specialist on key resources including Medline and PsycINFO via OVID, the Cochrane Library, the University of York Centre for Reviews and Dissemination (CRD) databases, the websites of Canadian and major international health technology agencies, as well as a focused internet search. The search strategy was comprised of both controlled vocabulary, such as the National Library of Medicine's MeSH (Medical Subject Headings), and keywords. The main search concepts were gender and primary care. Search filters were applied to limit retrieval to health technology assessments, systematic reviews, meta-analyses, or network meta-analyses, and guidelines; where possible, retrieval was limited to the human population. The search was also limited to English language documents published between January 1, 2010 and March 23, 2020.

Selection Criteria and Methods

One reviewer screened citations and selected studies. In the first level of screening, titles and abstracts were reviewed and potentially relevant articles were retrieved and assessed for inclusion. The final selection of full-text articles was based on the inclusion criteria presented in Table 1.

Table 1: Selection Criteria

Population	Adults with gender dysphoria
Intervention	Gender-affirming therapy (e.g., hormone replacement therapy) initiated by a primary care practitioner (e.g., physician, nurse practitioner)

Comparator	Not applicable
Outcomes	Recommendations regarding the initiation of gender-affirming therapy in the primary care setting
Study Designs	Evidence-baseline clinical practice guidelines

Exclusion Criteria

Articles were excluded if they did not meet the selection criteria outlined in Table 1, they were duplicate publications, or were published prior to 2010. Guidelines with unclear methodology were also excluded.

Critical Appraisal of Individual Studies

The included guidelines were assessed with the Appraisal of Guidelines for Research and Evaluation (AGREE) II instrument.[11] Summary scores were not calculated for the included studies; rather, the strengths and limitations of each included guideline were described narratively.

Summary of Evidence

Quantity of Research Available

A total of 110 citations were identified in the literature search. Following screening of titles and abstracts, 103 citations were excluded and seven potentially relevant reports from the electronic search were retrieved for full-text review. Four potentially relevant publications were retrieved from the grey literature search for full-text review. Of these potentially relevant articles, 10 publications were excluded for various reasons, and one evidence-based guideline met the inclusion criteria and was included in this report. Appendix 1 presents the PRISMA[12] flowchart of the study selection. An additional publication that did not meet the inclusion criteria, but may be of potential interest, is provided in Appendix 5.

Summary of Study Characteristics

One relevant evidence-based guideline was identified and included in this report.[13] Additional details regarding the characteristics of this publication are provided in Appendix 2.

Study Design

The evidence-based guideline was developed by the World Professional Association for Transgender Health (WPATH) and was published in 2012.[13] WPATH is an international multidisciplinary professional association that publishes standards for the care of transgender and gender-variant persons. The purpose of this guideline was to provide guidance for health professionals to assist transsexual, transgender, and gender nonconforming people with safe and effective pathways to achieving lasting personal comfort, in order to maximize their overall health, psychological well-being and self-fulfillment. The current version (version 7) was an update of previous versions of the WPATH guidelines for the transgender population. During the development of this guideline, a Writing Group in charge of preparing the first draft of guidance was established within WPATH, as well as an International Advisory Group of transsexual, transgender and gender nonconforming individuals to provide input on its revision. The quality of the

evidence that informed the guidelines, and the strength of the recommendations, were not reported.

Country of Origin

The WPATH is an international multidisciplinary professional association. The authors indicated that the guideline is intended for worldwide use. Because most of the clinical experience and knowledge in this field came from a North American and Western European perspective, in applying these guidelines to other cultural contexts, health professionals should be sensitive to the differences and adapt the guidance according to local realities.

Patient Population

The target population of the WPATH guideline is transsexual, transgender and gender-nonconforming people. The WPATH guideline is intended to be used by healthcare professionals who plan and provide treatment for the target population across clinical settings, including the primary care setting,

Interventions and Comparators

The WPATH guideline includes recommendations regarding the assessment of, and gender-affirming therapy for, gender dysphoria. The interventions considered for management of gender dysphoria were primary care, gynecologic and urologic care, reproductive options, voice and communication therapy, mental health services (such as assessment, counseling or psychotherapy), and hormonal and surgical treatments.

Outcomes

The intended outcome of the WPATH Guideline is alleviation of gender dysphoria. Specifically, surgical outcomes (e.g. patient well-being, cosmesis or sexual function), psychosocial functioning and global functioning, patient satisfaction, health-related quality of life, mortality and psychiatric morbidity were considered by the guideline panel when developing the recommendations.

Summary of Critical Appraisal

In the published WPATH guidelines, the overall objective, the scope and rationale of the guidelines were specifically described.[13] The involvement of the relevant professional groups in the guideline development process was not specified. Brief details of the guideline development process were provided. The guideline was stipulated to have been based on the best available science and expert professional consensus; however, information with respect to the search strategy and the methods of study selection were not reported, therefore it was not clear whether a systematic literature search strategy was employed to identify relevant evidence. The initial recommendations were drafted and discussed within a Writing Group of WPATH, and also circulated among the other groups in WPATH, such as the International Advisory Group to receive their feedback. Consensus on the recommendations was reached via internal (within a Writing Group of WPATH) and external (among other groups of WPATH) discussions. After revisions, the final guidance document was presented to the WPATH Board of Directors for approval. The guideline did not provide the methods for grading the evidence; thus, the quality of evidence was unknown. In addition, guideline recommendations were not graded (e.g., as “strong” or “weak”). Specific recommendations were not easily identifiable. Funding sources in support of the guideline development were reported. There were no concerns about editorial independence. This guideline was developed by an international multidisciplinary

professional association, and during the recommendation development, the authors indicated that most of the clinical experience and knowledge in transgender health come from a North American and Western European perspective, therefore the guideline may be generalizable to the Canadian context, in Canadian patients with gender dysphoria.

Additional details regarding the strengths and limitations of the guideline are provided in Appendix 3.

Summary of Findings

The WPATH guideline makes recommendations regarding hormone therapy in the target population. It indicates that with appropriate training, "feminizing/masculinizing hormone therapy can be managed by a variety of providers, including the primary care providers such as nurse practitioners, physician assistants and primary care physicians (p. 41)".[13] Given the multidisciplinary needs in the target population seeking hormone therapy, WPATH strongly encourages the increased training and involvement of primary care providers in the area of feminizing/masculinizing hormone therapy. In addition, WPATH acknowledges the important role of primary care providers in preventive care, indicating that "every transsexual, transgender and gender-nonconforming person should partner with a primary care provider for overall health care needs (p. 65),"[13] besides hormone providers and surgeons. However, the guideline did not specify whether the management of gender dysphoria can or cannot be initiated by primary care providers. The strength of these recommendations, and the quality of the supporting evidence, were not reported.

Limitations

One relevant evidence-based clinical practice guideline was identified for this review.[13] In the WPATH guideline, the strength of the recommendations was not graded, nor the quality of the evidence. It was unknown whether the evidence was collected using a systematic review approach, and the recommendation development process was not described in sufficient detail. Due to the high amount of uncertainty associated with the methodology of this guideline, the quality of the recommendations may be compromised.

The evidence that informed guideline was also limited by a lack of prospective data in the included studies. The guideline authors pointed out that due to the controversial nature of sex reassignment surgery, almost all of the studies in this area have been retrospective.

Conclusions and Implications for Decision or Policy Making

One evidence-baseline clinical practice guideline published in 2012 was identified that provides guidance for the health of transsexual, transgender and gender-nonconforming people.[13] The guideline suggests that with appropriate training, hormone therapy in patients with gender dysphoria can be managed by a variety of healthcare providers, including primary care providers. However, the recommendations did not specify whether this treatment can be initiated by primary care providers.

The quality of this guideline was limited due to a lack of sufficient details provided for the methods used in searching for evidence and formulating the recommendations. In addition, this guideline did not report the strength of recommendations or the quality of the evidence. There is uncertainty associated with this low-quality guideline and its recommendations should be interpreted with caution.

References

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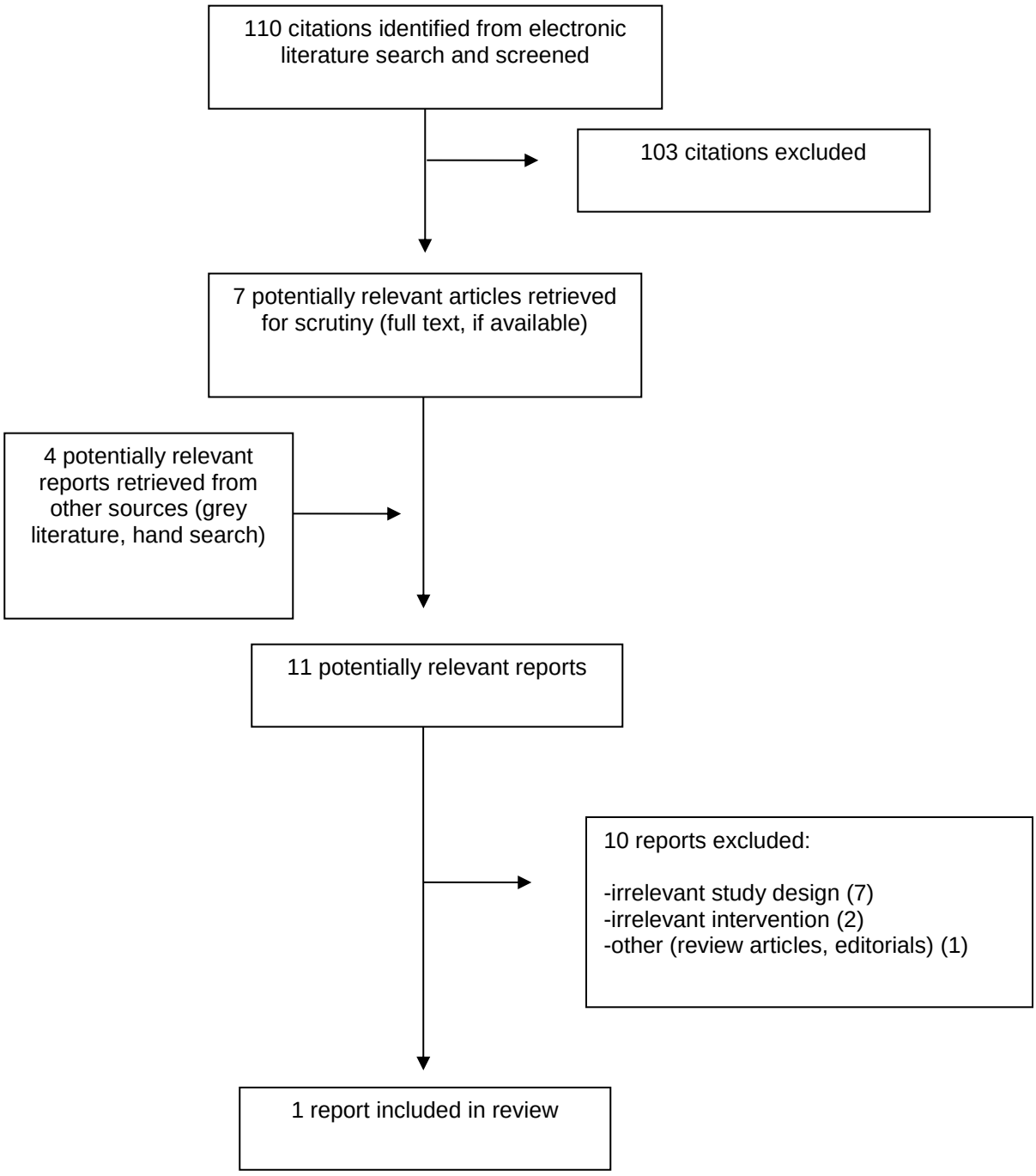
Appendix 1: Selection of Included Studies



Appendix 2: Characteristics of Included Publications

Table 2: Characteristics of Included Guideline

Intended Users, Target Population	Intervention and Practice Considered	Major Outcomes Considered	Evidence Collection, Selection, and Synthesis	Evidence Quality Assessment	Recommendations Development and Evaluation	Guideline Validation
WPATH Guideline (version 7), 2012[13]						
Intended users: Healthcare providers Target population: transsexual, transgender and gender-nonconforming people	Assessment and gender-affirming therapy for gender dysphoria	Surgical outcomes, psychosocial functioning, global functioning, patient satisfaction, HRQoL, mortality and psychiatric morbidity	The guideline authors indicated that the guideline was "based on the best available science and expert professional consensus (p. 110)"; however, no information was provided for the search strategy and the methods of study selection.	Not performed	The initial recommendations were drafted and discussed within a Writing Group of WPATH, and also circulated among the other groups in WPATH, such as the International Advisory Group to receive their feedback. Consensus on the recommendations was reached via internal (within a Writing Group of WPATH) and external (among other groups of WPATH) discussions. Strength of recommendations were not evaluated.	After revisions, the final guidance document was presented to the WPATH Board of Directors for approval. The guideline was submitted to journal and underwent regular peer review process. There is no plan available for future updates for the guideline.

HRQoL = health-related quality of life; WPATH = the World Professional Association for Transgender Health.

Appendix 3: Critical Appraisal of Included Publications

Table 3: Strengths and Limitations of Guidelines using AGREE II[11]

Item	WPATH Guideline (version 7), 2012[13]
Domain 1: Scope and Purpose	
1. The overall objective(s) of the guideline is (are) specifically described.	Yes
2. The health question(s) covered by the guideline is (are) specifically described.	Yes
3. The population (patients, public, etc.) to whom the guideline is meant to apply is specifically described.	Yes
Domain 2: Stakeholder Involvement	
4. The guideline development group includes individuals from all relevant professional groups.	Unclear
5. The views and preferences of the target population (patients, public, etc.) have been sought.	Unclear
6. The target users of the guideline are clearly defined.	Yes
Domain 3: Rigour of Development	
7. Systematic methods were used to search for evidence.	Unclear
8. The criteria for selecting the evidence are clearly described.	No
9. The strengths and limitations of the body of evidence are clearly described.	No
10. The methods for formulating the recommendations are clearly described.	Partially
11. The health benefits, side effects, and risks have been considered in formulating the recommendations.	Yes
12. There is an explicit link between the recommendations and the supporting evidence.	No
13. The guideline has been externally reviewed by experts prior to its publication.	Unclear
14. A procedure for updating the guideline is provided.	No
Domain 4: Clarity of Presentation	
15. The recommendations are specific and unambiguous.	Partially
16. The different options for management of the condition or health issue are clearly presented.	Yes
17. Key recommendations are easily identifiable.	Partially
Domain 5: Applicability	
18. The guideline describes facilitators and barriers to its application.	No
19. The guideline provides advice and/or tools on how the recommendations can be put into practice.	No
20. The potential resource implications of applying the recommendations have been considered.	Partially
21. The guideline presents monitoring and/or auditing criteria.	No
Domain 6: Editorial Independence	

Item	WPATH Guideline (version 7), 2012[13]
22. The views of the funding body have not influenced the content of the guideline.	Unclear
23. Competing interests of guideline development group members have been recorded and addressed.	No

AGREE = the Appraisal of Guidelines for Research & Evaluation; WPATH = World Professional Association for Transgender Health.

Appendix 4: Summary of Recommendations in Included Guideline

Table 4: Summary of Recommendations in Included Guideline

Recommendations	Supporting Evidence
WPATH Guideline (version 7), 2012[13]	
"With appropriate training, feminizing/masculinizing hormone therapy can be managed by a variety of providers, including nurse practitioners, physician assistants, and primary care physicians… Given the multidisciplinary needs of transsexual, transgender, and gender-nonconforming people seeking hormone therapy, as well as the difficulties associated with fragmentation of care in general, WPATH strongly encourages the increased training and involvement of primary care providers in the area of feminizing/masculinizing hormone therapy. If hormones are prescribed by a specialist, there should be close communication with the patient's primary care provider. Conversely, an experienced hormone provider or endocrinologist should be involved if the primary care physician has no experience with this type of hormone therapy, or if the patient has a pre-existing metabolic or endocrine disorder that could be affected by endocrine therapy (p. 41)" "While hormone providers and surgeons play important roles in preventive care, every transsexual, transgender, and gender-nonconforming person should partner with a primary care provider for overall health care needs (p. 65)"	Clinical trials providing evidence for developing recommendations were identified; however, no details regarding study design and findings were reported.

WPATH = World Professional Association for Transgender Health.

Appendix 5: Additional References of Potential Interest

Guideline with Unclear Methodology

Gamble RM, Taylor SS, Huggins AD, Ehrenfeld JM. Trans-specific geriatric health assessment (TGHA): an inclusive clinical guideline for the geriatric transgender patient in a primary care setting. *Maturitas.* 2020;132:70-75.