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FOCUSED REVISION

Practice resource-focused revision: Standardized pedigree nomenclature update centered on sex and gender inclusivity: A practice resource of the National Society of Genetic Counselors

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Abstract

This focused revision builds on the expert opinions from the original publications of 'Recommendations for human standardized pedigree nomenclature' published in 1995 and updated in 2008. Our review of medical publications since 2008 did not identify any fundamental systematic alternative pedigree nomenclature. These findings attest to the relevance of most of the nomenclature with the critical exception of the nomenclature used to denote sex assigned at birth and gender. While we are not recommending the creation of any new pedigree symbols, a major focus of this publication is clarification of the use of symbols and language in the description of the distinction between sex and gender, with a view to ensuring safe and inclusive practice for people who are gender-diverse or transgender. In addition, we recommend modifications to the way that carrier status is depicted. Our goal is to respect individual differences and identities while maintaining biologically, clinically, and genetically meaningful information.

KEYWORDS
family history, gender inclusivity, genetic counseling, pedigree, pedigree nomenclature

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2 | PURPOSE

In 2015, the NSGC Practice Guidelines Committee (PGC) adopted Institute of Medicine (IOM) standards for development of evidence-based clinical practice guidelines. NSGC guidelines published prior to 2015 do not meet IOM criteria to remain classified as a Clinical

Practice Guideline. Based on recommendations from expert reviewers, the PGC has concluded that the original Guidelines document, published in 2008 (Bennett et al., 2008) is still relevant and current, with the important exception of the nomenclature used to denote sex and gender. Therefore, the PGC has reclassified the recommendations for standardized pedigree nomenclature as a Practice Resource with the addition of the Focused Revision detailed below. A Focused Revision is a brief addendum that focuses on content identified as outdated in the previously published document, without changing the main purpose or intent of the Practice Resource (Kalia & James, 2020).

3 | INTRODUCTION

Recommendations for the use of standardized human pedigree nomenclature were first published in the *American Journal of Human Genetics* and the *Journal of Genetic Counseling* in 1995 (Bennett et al., 1995a, 1995b). Minor revisions to the original recommendations were published in the *Journal of Genetic Counseling* in 2008 (Bennett et al., 2008).

Beginning in early 2020, we reevaluated pedigree nomenclature for its continued relevance to the practice of genetic counseling, particularly with respect to the growing awareness of the nonbinary nature of sex and gender, as well as respect for the importance in clinical settings of a person's self-identified gender and sexuality.

In assessing the nomenclature, we reviewed the current use of the recommended pedigree symbols in clinical practice, publications, and electronic health records. We recognize that individuals served through genetic counseling have ownership of their health data and medical narratives. The creation of personal and family health documentation is becoming the shared creation of health providers with their patients. Patients who have complete access to their medical records are more likely to become engaged in efforts to improve and maintain their health (Mikk et al., 2017). As people gain access to their electronic health records, it is important to adopt practices that respect patient differences and identities.

We reviewed the medical literature for critiques of, and proposed alternatives to, the 2008 nomenclature. In addition, we requested input from the Assisted Reproductive Technologies/Infertility Special Interest Group (ARTI-SIG) of the NSGC to assess whether the pedigree nomenclature needed to be revised given the advances in reproductive technology since 2008.

The use of pedigree nomenclature requires distinguishing sex from gender. Broadly speaking, sex is defined by morphology or biology (phenotype, karyotype, etc.) while gender refers to social constructions of roles, behaviors, expressions, and identities of men, women, boys, girls, and gender diverse people. Gender is usually viewed in terms of gender identity and gender expression. Gender identity concerns a person's internal sense of self and how they fit into the world from the perspective of gender, which may or may not align with sex assigned at birth (e.g., man, woman, gender-diverse, etc. See Table 1). Gender expression refers to how

TABLE 1 Recommended definitions and inclusive terminology related to gender, sex, and sexuality (Advocates for Intersex Youth, n.d.; A Gender Identity, n.d.; Barnes et al., 2020; Lee et al., 2016; Lyninger, 2019)

Term	Definition
Cis/cisgender	An individual whose gender identity aligns with the sex they were assigned at birth.
Gender diverse	An umbrella term that is used to describe gender identities that demonstrate a diversity of expression beyond the binary framework.
Gender expression	How someone expresses their gender identity, e.g., through name, pronouns, clothing, hair styles, etc., which may or may not correspond with their gender identity.
Gender identity	A person's sense of self and how they fit into the world, from the perspective of gender, which may or may not align with sex assigned at birth.
LGBTQIA2S+	An acronym standing for Lesbian, Gay, Bisexual, Transgender, Queer/Questioning, Intersex, Asexual, Two-Spirit, and other gender identities and sexual orientations. There are many variations of this acronym.
Nonbinary	A person who does not identity as either only male or only female, but instead identifies as something between or outside of these identities.
Sex	A category often assigned at birth based on biological attributes (e.g., the appearance of genitalia or secondary sex characteristics).
Trans/ Transgender	A person whose gender identity or gender expression does not align with the sex they were assigned at birth. People who are transgender can use the terms trans man, trans woman, transmasculine, transfeminine, nonbinary, gender nonconforming, genderqueer, etc. to describe their gender identity. The terms MtF (male to female) and FtM (female to male) should not be used.
Variations of Sex Characteristics (VSC)	A broad description of varied conditions which lead to differences in the development of the urogenital tract, external genitalia, development of secondary sex characteristics, and other clinical characteristics. Sometimes referred to as intersex, differences of sex development, or by using the name of a specific variation.

someone expresses their gender identity (e.g., through name, pronouns, clothing, hair style, etc.), which may or may not correspond with their gender identity. Gender identity and biological sex are unrelated to an individual's sexuality, i.e., a person's identity in relation to the gender or genders to which they are typically attracted.

Variations of sex characteristics (VSC), sometimes referred to as intersex (Crocetti et al., 2021), are distinct from gender identity, gender expression, and sexuality. People with VSC may identify as male, female, gender-diverse, etc.

Table 1 is a reference for common terminology and inclusive language for gender, sex, and sexuality (Advocates for Intersex Youth, n.d.; A Gender Identity, n.d.; Barnes et al., 2020; Crocetti et al., 2021; Lee et al., 2016; Lyninger, 2019). Terminology used in this article is based on the assessment of our literature review of the currently preferred terminology and will undoubtedly continue to change.

4 | RECOMMENDED CLARIFICATIONS AND REVISIONS

Our review of medical publications since 2008 was consistent with our previous report (Bennett et al., 2008) and did not identify any systematic alternative pedigree nomenclature. The NSGC ARTI-SIG did not suggest any changes to the symbols used in assisted reproductive technology (ART) (refer to Section 4.3). In this publication, we do not recommend creating any new pedigree symbols.

However, this publication represents an important update because it offers critical clarification regarding the use of symbols and language regarding sex assigned at birth and gender, and the difference between the two terms, with a view to ensuring safe and inclusive practice for those who are gender diverse or transgender. Our goals are to affirm individual identities while maintaining biologically, clinically, and genetically meaningful information.

In addition, we provide more examples of common scenarios for assisted reproductive technologies (ART), recommend against making changes to relationship lines between partners and spouses, and eliminated the 'E' notation used to indicate the results of a physical, laboratory, or imaging evaluation (although the results of those evaluations can still be included in the pedigree). We have also modified the way that carriers of recessive conditions are depicted.

The recommended pedigree nomenclature, general instructions, and some examples of their use are shown in Box 1 and Figure1–5.

4.1 | Distinguishing between sex and gender in pedigrees

The 2008 NSGC guidelines recommend the use of squares and circles to indicate 'phenotypic gender' of people who are transgender (Bennett et al., 2008) and, if known, the karyotype could be denoted below the symbol. However, we recognize that 'phenotypic gender' was unclear in the 2008 recommendations – it could be most readily interpreted as relating to gender expression, which is not necessarily related to gender identity. We also acknowledge that most people have not had a karyotype and that sex assigned at birth is typically based on evaluation of external genitalia. Additionally, it was also previously recommended that people with VSC could be represented using the diamond symbol, which was also the symbol used when sex assigned at birth was not known or not clinically relevant; this could potentially result in the diamond symbol being misinterpreted.

BOX 1 Instructions for recording information on a pedigree

1. Distinguish gender from sex. The pedigree symbol represents gender (square, circle, diamond)
   a. Establish gender by asking the proband/consultand
   b. The absence of notation beneath a diamond indicates that sex and/or gender identification of the individual are unknown or not specified
   c. AMAB = Assigned Male At Birth
   d. AFAB = Assigned Female At Birth
   e. UAAB = Unassigned At Birth
   f. Note: for children who have not yet expressed a gender identity, and in the context of pregnancy, stillbirth, and relatives, unless known to be otherwise sex and gender are assumed to align.
2. Limit identifying information to maintain confidentiality and privacy.
3. Key/legend should contain all clinical information relevant to pedigree interpretation (e.g., define fill/shading).
4. For clinical (non-published) pedigrees include:
   a. Name of proband/consultand
   b. Family names/initials of relatives for identification, as appropriate
   c. Name and title of person recording pedigree
   d. Historian (person relaying family history information)
   e. Date of intake/update
   f. Indication for taking pedigree (e.g., abnormal ultrasound, familial cancer, developmental delay, etc.)
   g. Ancestry of both sets of grandparents, when clinically relevant
5. Recommended order of information placed below symbol (or to lower right)
   a. Age; can note year of birth (e.g., b.1978) and/or death (e.g., d. 2007)
   b. Evaluation results, e.g. genome sequencing, gene panel, karyotype, ultrasound, etc.
   c. Pedigree number (e.g., I-1, I-2, I-3), typically used in research or publication

Gender	Sex		
	Male	Female	Unassigned at Birth
Man/Boy	 56y	 AFAB 34y	 UAAB 28y
Woman/Girl	 AMAB 56y	 34y	 UAAB 28y
Non-binary/Gender Diverse	 AMAB 56y	 AFAB 34y	 UAAB 28y

FIGURE 1 Sex and gender in pedigree nomenclature

	Identifies as Man/Boy	Identifies as Woman/Girl	Identifies as Non-Binary/Gender Diverse	Sex and/or gender are not known or not specified
Multiple individuals, number known	 2	 2	 2 AMAB	 2
Multiple individuals, number unknown or not specified	 n	 n	 n AMAB/ AFAB	 n
Deceased individual	 d. 1981	 d.4 mo	 d.86 AFAB	 d. 2002
Stillbirth (SB)				 SB 34wk AFAB
Clinically affected individual (define shading in key/legend) Affected individual (> one condition)			 AMAB AFAB	
Proband (Always affected with condition)	 P	 P	 P AMAB	
Consultand (Shade, if affected)	 b.12/23/1954	 31y	 44y AFAB	
Documented evaluation, records reviewed			 AMAB	
Asymptomatic/presymptomatic carrier (no clinical symptoms now, but could later exhibit symptoms), typically for dominant conditions (document condition(s) in legend)			 AMAB	

FIGURE 2 Common pedigree definitions, symbols, and abbreviations

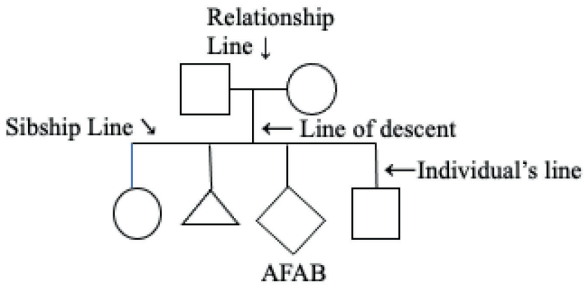
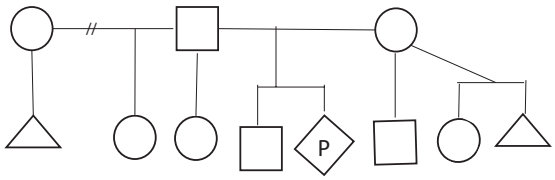
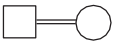
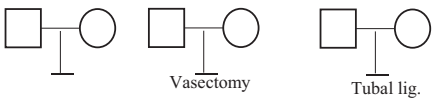
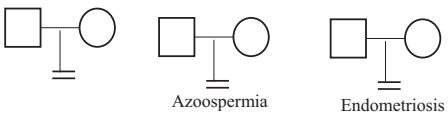
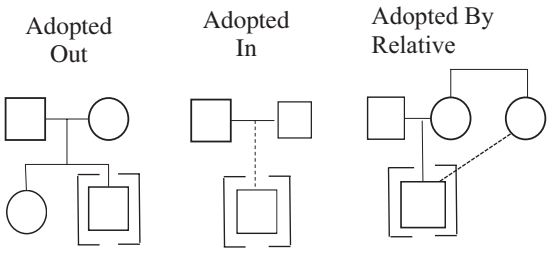
Definitions		Comments
		Siblings should be listed from left to right in birth order (oldest to youngest)
Relationships		A break in a relationship line indicates the relationship no longer exists. Multiple previous partners do not need to be shown if they do not affect genetic assessment.
Consanguinity		If degree of relationship not obvious from pedigree, it should be stated (e.g., third cousins) above relationship line.
Twins, Triplets, etc. In the absence of a "?" or a connecting line, assumed to be dizygotic		
No children by choice or reason unknown. Indicate reason if known.		
Infertility (indicate reason if known)		
Adoption Brackets used for all adoptions. Adoptive and biological parents denoted by dashed and solid lines of descent, respectively.		

FIGURE 3 Pedigree line definitions

The National Comprehensive Cancer Network (2022) recommends using a circle within a square for a transgender man who was assigned female at birth (AFAB) and a square within a circle for a transgender female who was assigned male at birth (AMAB). It is unclear whether people who are transgender were consulted in the generation of the NCCN recommendations. Since the NCCN recommendations were published, they have been criticized; the circle-within-a-square and square-within-a-circle nomenclature is not favored by members of the transgender community (Barnes et al., 2020; Lyninger, 2019; Sheehan et al., 2020).

It is essential that the pedigree representation of people who are gender-diverse, transgender, and who have VSC is affirming to the individual and should also be correctly documented in the pedigree. Along these lines, we recommend that, whenever possible, the

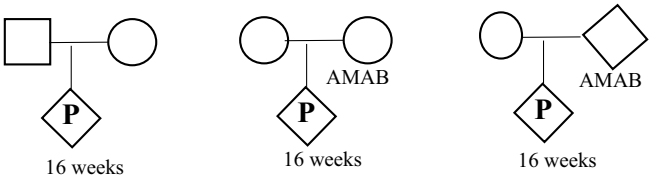
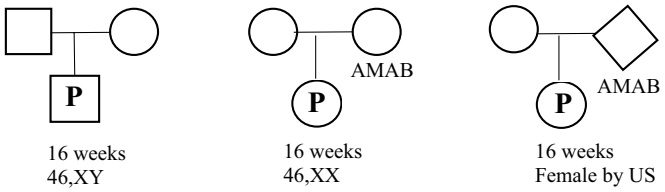
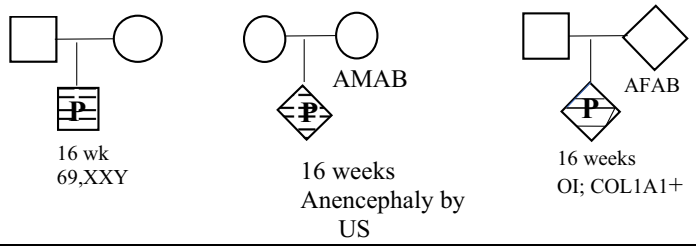
Instructions Note gestational age, if known, under each symbol. If affected, use shading and explain in key.	
Pregnancy (P) Fetal sex unknown	
Pregnancy (P) Fetal sex known (indicate how sex determined)	
Affected Pregnancy	
Spontaneous abortion (SAB)	
Affected SAB	
Ectopic (ECT)	
Termination of pregnancy (TOP)	
Affected TOP	

FIGURE 4 Pedigree symbols related to pregnancy, miscarriage, and termination of pregnancy.

Instructions:
— D represents egg or sperm donor
— S represents surrogate (gestational carrier)
— When a single individual is both the ovum donor and a surrogate, in the interest of genetic assessment, they should only be referred to as a donor (e.g., 4 and 5); the pregnancy symbol and its line of descent are positioned below the individual who is carrying the pregnancy
— Available family history should be noted on the gamete donor and/or gestational carrier

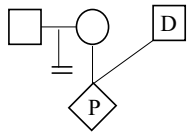
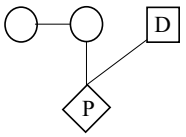
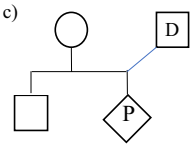
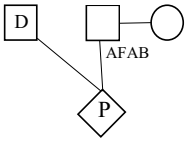
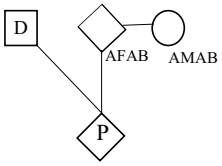
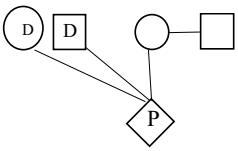
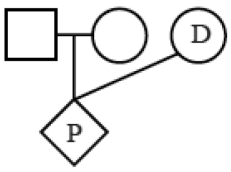
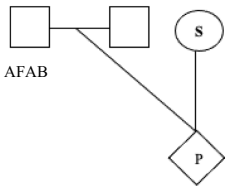
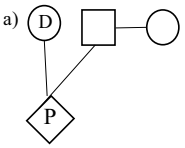
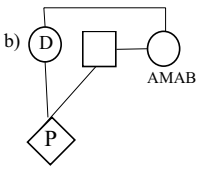
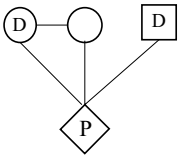
Possible Reproductive Scenarios		Comments
1. Donor gamete (sperm)	a)  b)  c)  d)  e) 	a) Cisgender man, cisgender woman couple in which the woman is carrying a pregnancy conceived using donor sperm. No relationship line is shown between the woman carrying the pregnancy and the sperm donor. b) Cisgender women couple in which one of the women is carrying a pregnancy conceived using donor sperm. c) Unpartnered cisgender woman who has a son and a current pregnancy conceived with the same donor d) Transgender man who is pregnant via a sperm donor and in a relationship with a cisgender woman e) Nonbinary person whose pregnancy was conceived using a sperm donor and who is in a relationship with a transgender woman
	f) 	f) A cisgender heterosexual couple conceives via IVF using donated embryo from donor egg and donor sperm. Pregnancy is carried by the female partner.
2. Donor gamete (ovum)		Cisgender man, cisgender woman couple in which the woman is carrying pregnancy conceived using a donor egg and partner's sperm. The line of descent from the birth parents is solid because there is a biologic relationship that may affect the fetus (e.g., teratogens, maternal disease).
3. Surrogate (S) only		Transgender man, cisgender man couple whose gametes are used to impregnate a woman (surrogate) who carries the pregnancy. The line of descent from the surrogate is solid because there is a biological relationship that may affect the fetus (e.g., teratogens).
4. Surrogate ovum donor	a)  b) 	a) Cisgender man, cisgender woman couple in which a partner's sperm is used to inseminate an unrelated woman who is carrying the pregnancy b) Cisgender man and a trans woman couple in which the cis man's sperm is used to inseminate the other partner's sister who is carrying the pregnancy for the couple.
5. Double gamete donor Pregnancy		A cisgender woman couple conceive a pregnancy using one partner's egg with donor sperm, and the non-donor partner is the gestational parent (as indicated by the vertical line extending down from the non-donor partner to the pregnancy).

FIGURE 5 Assisted reproduction symbols

symbols on the pedigree be used to document *gender*, and not *sex assigned at birth* (Figure 1). We do not recommend using the circle-within-a-square or square-within-a-circle. Instead, as suggested by members of the transgender community (Barnes et al., 2020; Lyninger, 2019), we recommend the use of the symbol corresponding to gender identity (i.e., square for man/boy or circle for woman/girl) with the annotation AMAB (assigned male at birth) or AFAB (assigned female at birth) for people who are transgender. A square with no annotations indicates a cisgender male. Likewise, a circle with no annotations indicates a cisgender female.

An inverted triangle has been suggested as a way to represent gender-diverse people (Tuite et al., 2020). Due to the historical use of inverted triangles to designate certain prisoner groups in Nazi concentration camps (Elman, 1996), and based on the input of the gender-diverse community (Barnes et al., 2020), we instead recommend the use of the diamond symbol, along with an annotation indicating the sex assigned at birth (i.e., AFAB, AMAB). If no sex was assigned at birth due to parental preference (a practice that is becoming more common because of growing legal recognition in a number of jurisdictions), or due to clinical reasons such as sometimes occur when a child is born with VSC, a diamond with the annotation UAAB (unassigned at birth) should be used (Gold, 2018; Kennedy & Hellen, 2010). Clinically relevant details (e.g., details of diagnosis of VSC, history of gender-affirming surgeries, etc.) can be indicated with annotations and with fill pattern(s) within the symbol and described in the legend, as needed. A karyotype should be listed only if known; it should not be assumed based on the sex assigned at birth. Absent any annotation, a diamond symbol refers to an individual whose gender and sex are not known or not relevant to the clinical circumstances.

Research is needed regarding pedigree preferences for the community of people with VSC to allow fully inclusive recommendations (Advocates for Intersex Youth, n.d.; Crocetti et al., 2021; Lee et al., 2016). For now, using the symbol corresponding to the individual's gender with annotations such as VSC, karyotype if known, or the name of the specific genetic condition seems most appropriate. Shading of the symbol to denote a person with VSC can be used and defined in the legend.

These conventions permit pedigrees to minimize graphic complexity while still maintaining their critical ability to communicate medically and genetically meaningful information. The diamond, the square, and the circle are all equally valid representations of the normal spectrum of human gender identity.

4.2 | General revisions

The 'E' notation (Evaluation) from the previous recommendations has been eliminated because of a lack of general usage in daily pedigree practice and publications. The results of the individual's evaluation(s) can be listed below the individual's symbol, but they do not need to be preceded by an 'E' (Box 1; Figure 2).

The Task Force discussed changing the 'relationship line,' connecting spouses or partners, from a solid to a dotted line to align with the use of a dotted line to denote nonbiological relationships, as with adopted children (Figure 3). Although the logical argument for the change is sound, it was decided that such a change is largely unnecessary and would be disruptive both to practicing clinicians (who currently use a solid line) and electronic medical records and pedigree software. It was also noted that in consanguineous unions, a solid double line denotes a genetic relationship.

4.3 | Representation of assisted reproduction

The author group did not change the symbols used for pregnancy, miscarriage, and termination of pregnancy (Figure 4) or assisted reproductive technologies (ART). Multiple examples of different relationships and the use of donor gametes are shown in Figure 5.

There was discussion among the author group, in consultation with genetic counselors working in the field of ART, about the possible need to document frozen embryos in a pedigree. Per discussion with the ARTI-SIG, many genetic counselors working in ART do not see a need to document frozen embryos in a pedigree; documentation in a chart note is sufficient. Given this expert input, the author group did not devise a pedigree symbol or nomenclature for frozen embryos. However, a recent small study suggested that some ART genetic counselors see utility in developing nomenclature for frozen embryos (Lepard Tassin et al., 2021). Further research should address this question to inform future focused revisions to pedigree nomenclature. In addition, evolving reproductive technologies such as reproductive mitochondrial donation may require revised nomenclature.

4.4 | Genetic counseling practice and gender inclusivity

The genetic counseling environment should be safe and conducive to allowing people to disclose gender identity and sex assigned at birth (de Vries et al., 2020). Sex assigned at birth and gender identity are clinically relevant and critical for accurate and appropriate genetic counseling. For example, for people who are transgender seeking genetic counseling for a family history of cancer, disclosure of sex assigned at birth is vital to assessing cancer risk, prevention, and treatment options (Berro et al., 2020; Ruderman et al., 2021; von Vaupel-Klein & Walsh, 2021; Zayhowski et al., 2019). In addition, many genetic conditions unrelated to sex or reproduction have causative genes located on the X chromosome, and conditions with autosomal inheritance can have altered expression due to sex. Whether a condition was transmitted via the sperm or the egg can also influence clinical expression of some conditions, such as with Huntington disease. Disclosure to healthcare practitioners of a person's sex assigned at birth is crucial in providing accurate

genetic risk assessment and related health and reproductive options (Barnes et al., 2020; von Vaupel-Klein & Walsh, 2021).

Understanding an individual's gender identity is just as medically important to providing genetic counseling as understanding an individual's sex (Berro et al., 2020; Ruderman et al., 2021; Von Vaupel-Klein & Walsh, 2021; Zayhowski et al., 2019). Further, asking questions such as what pronouns the person uses can strengthen the alliance and trust between patient and provider (Barnes et al., 2020; Turban et al., 2017). Along these lines, it is important for electronic medical records, pedigree software, family/medical history questionnaires, and test request forms to allow for the recording of both sex and gender. Conflation of the two can lead to transgender men being overlooked for gynecological care, for example. However, it is also important that genetic counselors consider and address their patients' safety – for example, by discussing with their patients if and how to record this information as part of their permanent medical record in light of the unfortunate potential for exposure to harm (e.g., discrimination and bias in care) (de Vries et al., 2020).

Additional steps can be taken to enhance the care experience with patients. Adding pronouns to the genetic counselor's name badge and soliciting pronouns on clinical paperwork can signal that the genetic counselor understands that gender is nuanced, and that the genetic counselor can be trusted with sensitive information. Paperwork and instructional aids, and the language we use when we counsel, can be made more inclusive and respectful. For example, rather than saying 'you inherit half your chromosomes from mom and half from dad' it can be said 'half your chromosomes are from sperm, and the other half from the egg.' Instead of 'men should get regular prostate checks' try 'people with prostates should get them checked regularly'. Genetic counselors should stay up to date on research in gender identity and acceptable terminology. Professional human genetics organizations such as the National Society of Genetic Counselors, the Association of Genetic Counseling Program Directors, the Association of Professors in Human and Medical Genetics, the American Society of Human Genetics, and the American College of Medical Genetics and Genomics should make ongoing commitments to continuing education and research on gender-related issues (Gender-Inclusive Biology, n.d.; de Vries et al., 2020; Lyninger, 2019; Von Vaupel-Klein & Walsh, 2021).

Gender identity affirmation is essential; it has been correlated with positive mental health outcomes and increased trust in medical providers among youth who are transgender (University of Texas, n.d.). Affirming care also increases the likelihood that people will seek rather than defer medical care when they need it (Clark et al., 2018). The 2008 recommendations include affirming practices such as the inclusion of nonbiological children adopted into a family and the recording of same-sex relationships. The same recognition of an individual's family system and identity should be applied to people who are transgender and gender nonconforming, even when not 'clinically relevant.' Gender identity and sex also play equally critical roles in medical management. For example, accurate cancer risks and screening strategies for transgender people are understudied, and members of the prenatal and fertility care team may not be fully comfortable caring for or sensitive to the needs of people who are transgender (Berro et al., 2020; Ruderman et al., 2021; Von Vaupel-Klein & Walsh, 2021). Finally, standardized symbols for people who are transgender and gender-diverse conveys a more inclusive mindset, not only for patients but for other professionals who use or access patients' pedigrees.

Transgender identities and experiences encompass a broad range of potential scenarios (e.g., a history of gender-affirming surgeries, or people who are both transgender and with VSC); not all relevant information can be communicated in one symbol. As with other complex health information, notation below the symbol can provide clarifying facts; further details can be recorded in the chart note to avoid a cluttered pedigree. This would also be beneficial for people with VSC or those who self-describe as intersex, for whom a square, circle, or diamond symbol is insufficient in communicating potentially complex and unique health information and risk factors (Barnes et al., 2020: Deutsch et al., 2013; Deutsch, 2016; Safer & Tangpricha, 2019; Sheehan et al., 2020; Zayhowski et al., 2019). We recognize that there has been insufficient research about the pedigree nomenclature preferences of people who are intersex to make adequately informed recommendations. Future research must address this gap.

4.5 | Representation of carriers of autosomal recessive and X-linked conditions

Previous guidelines recommended that the symbol for a heterozygous carrier of an autosomal or X-linked condition be identified by a dot in the center of the appropriate symbol shape. However, there is growing awareness that heterozygous carriers of a number of homozygous conditions can manifest symptoms either of the recessive condition (Barton et al., 2022; Farrell et al., 2021), or different symptoms altogether, such as a carrier of a single pathogenic *ATM* variant who develops breast cancer. In this situation, a single dot in the center of the symbol could incorrectly suggest that a patient did not have breast cancer, or the fill-pattern for breast cancer might obscure the underlying dot. Furthermore, with the growing trend and the American College of Obstetricians and Gynecologists (ACOG) recommendation that carrier screening before and during pregnancy for recessive conditions include more than 100 conditions, it is not uncommon for a patient to be a carrier for two or more recessive conditions (Gregg et al., 2021). A single dot would not accurately communicate that information, nor would multiple dots allow for distinguishing which conditions the patient was a carrier for. In addition, in a pedigree where different relatives might be carriers of various combinations of the pathogenic variants in question, dots do not allow one to distinguish which conditions a relative might be a carrier of.

Therefore, we recommend that the dot no longer be used to indicate carrier status. Instead, we recommend that the symbol be divided; however, many subsections are necessary, and we use a

unique fill pattern in each subsection to indicate the different carrier results and/or clinical manifestations (Figure 2). As with all pedigree symbols, the fill patterns would be explained in the legend. For example, the symbol of someone who is a carrier of a single *HEXA* pathogenic variant and a single *CFTR* pathogenic variant would be divided in half, and a horizontal line fill could be used for the left half of the symbol and a vertical line fill could be used for the right half of the symbol. Similarly, someone who carries a single *ATM* pathogenic variant who also has breast cancer would have their symbol divided in half, with each half of the symbol having a different fill pattern.

5 | SUMMARY

In this revision, the Pedigree Nomenclature Task Force offers definitional clarity regarding the use of symbols and language with regard to sex and gender; the pedigree symbols represent gender rather than sex assigned at birth. We recommend changes to the symbols used to depict people who do not identify as cisgender. For people who are binary transgender, we recommend the use of the symbol corresponding to gender identity (i.e., square for man/boy or circle for woman/girl) with AMAB (assigned male at birth), AFAB (assigned female at birth), or UAAB (unassigned at birth) written below the symbol to indicate the sex assigned at birth. For people who are gender-diverse, we recommend the use of a diamond with AMAB, AFAB, UAAB written below to indicate the sex assigned (or not) at birth. For people with VSC, we recognize the lack of data on which to base recommendations, but suggest the use of the square, circle, or diamond as appropriate to reflect the individual's gender, with shading of the symbol and definition in the legend, and annotations such as karyotype if known, or the name of the specific genetic condition.

The use of these symbols, with appropriate and relevant clinical details noted below the symbol, can effectively and sensitively communicate clinical and personal information about people seeking genetic counseling. We recommend that genetic counselors take steps to provide an environment in which patients feel safe revealing their gender and sex assigned at birth. Everyone should feel safe, comfortable, respected, and accepted when seeking genetic counseling. An essential component of this is the use of appropriate symbols sensitive to an individual's gender identity.

In addition, we recommend modifications to the way that carrier status is depicted; instead of using a 'dot,' the status can be noted by the fill pattern within the symbol and defined in the legend.

Finally, we suggest that the nomenclature should continue to be reviewed periodically to make sure it is relevant and useful to clinical practice and consistent with changing social values.

AUTHOR CONTRIBUTIONS

Robin Bennett: Conceptualization; writing – original draft; writing – review and editing. **Kathryn Steinhaus French:** Conceptualization; writing – original draft; writing – review and editing. **Robert G. Resta:** Conceptualization; writing – original draft; writing – review and editing. **Jehannine Austin:** Conceptualization; writing – original draft; writing – review and editing.

CONFLICTS OF INTEREST

Robin Bennett declares no financial conflicts of interest. Kathryn Steinhaus French declares no financial conflicts of interest. Robert Resta declares no financial conflicts of interest. Jehannine Austin declares no financial conflicts of interest.

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