

- Uptake of gender diversity reporting remains limited, despite efforts to reduce sex and gender disparities in clinical research^{1,2}
- The US Food and Drug Administration recognizes sex and gender as distinct terms; however, the recent guidelines for enhancing diversity of clinical trial populations assume sex and gender to be concordant³
- In the United States, an estimated 390 adults in every 100,000 identify themselves as transgender. There remains a significant gap in inclusion of this underserved and understudied population in clinical trials^{4,5}
- As a proxy to evaluating gender diversity in clinical trials, we analyzed trends around gender- and sex-based eligibility reporting in clinical trials registered in the ClinicalTrials.gov database

Study Selection

- ### Trends in Studies With Gender-Based Eligibility Over Time

- Most studies were related to HIV (41%). Other therapeutic areas were also represented, including hormone replacement therapy, social behavior, sex reassignment, cardiometabolic conditions, human papillomavirus, and mental health, among others (**Figure 3**)
 - The vast majority of studies were sponsored by academic and medical institutions (72%) but very few were industry sponsored (3%) (**Figure 4**)
- ## Sex and Gender Reporting on ClinicalTrials.gov
- After applying the exclusion filters (**Figure 1, Approach II**), 13 records remained and were further analyzed
 - In our analysis, we evaluated the following (**Figure 5**):
 - Sex- and gender-based eligibility listed under the “Study Details” tab
 - Detailed eligibility criteria reported under the “Tabular View” tab
 - Sex and gender breakdown included in the “Study Results” tab

- The scope of this study included clinical studies conducted from 2005 to the present that are listed on ClinicalTrials.gov
- A 2-pronged comprehensive search strategy was used for identifying studies where gender-based selection was applied (**Figure 1**)
 - Approach I assessed trend distribution over time, therapeutic areas, types of intervention, and funding source (**Figure 1**)
 - Approach II evaluated records with study results available (n=13) to gather deeper insights into gender reporting trends and to understand associated challenges (**Figure 1**)

Records identified through database searching (n=3210)

Identification

Aim – To explore recent trends in gender- vs sex- based eligibility in clinical trial records

Database searched – ClinicalTrials.gov

Search string – “transgender” OR “two-spirit” OR queer OR intersex OR “Trans-male” OR “Trans man” OR “Trans-female” OR “Trans woman” OR Genderqueer OR “Gender non-conforming” OR “non-binary”

Approach I

Records excluded (n=581)

- Studies with start date before 2005

Records screened (n=2629)

Records excluded (n=2527)

- Non-specific matches to search terms, including trans-nasal, trans-axial, trans-epidermal, etc.

Full records assessed for number of studies over time, therapeutic areas, and funding source (n=102)

Approach II

Records excluded (n=2968)

- Studies with start date before 2005
- Study status did not include
 - Recruiting
 - Active, not recruiting
 - Not yet recruiting
 - Completed
 - Enrolling by invitations
- Study results were not available

Records screened (n=242)

Records excluded (n=228)

- Non-specific matches to search terms, including trans-nasal, trans-axial, trans-epidermal, etc.
- Additional records excluded (n=1)
- Eligibility based on sexual orientation

Full records assessed for detailed eligibility criteria and gender-based breakdown (n=13)

Filtering

Screening

Inclusion

Approach I

Funding Source	Percentage
Academic/Medical Institutions	72%
Academic/Medical Institutions + NIH	16%
Academic/Medical Institutions + U.S. Federal Government	3%
Industry	3%
NIH + Industry	1%
U.S. Federal Government	1%

NIH, National Institutes of Health.

Year	Number of people
2008	1
2012	1
2013	4
2014	2
2015	7
2016	7
2017	12
2018	10
2019	18
2020	28
2021	12

Category	Percentage
HIV	41%
Hormone Replacement Therapy	21%
Social Behavior	14%
Sex Reassignment	7%
Cardiometabolic	5%
HPV	4%
Mental Health	3%
Substance Abuse	2%
Socioeconomic	1%
SARS-CoV2	1%
Reproductive Health	1%

HIV, human immunodeficiency virus; HPV, human papillomavirus; SARS-CoV2, severe acute respiratory syndrome-coronavirus 2.

Gender-based eligibility
A type of eligibility criteria that indicates whether eligibility to participate in a clinical study is based a person's self-representation of gender identity or gender (yes, no). Gender is distinct from sex.

The diagram illustrates the relationship between different types of eligibility criteria and their breakdown into 'Yes' and 'No' counts. It is organized into four main columns: Sex-based eligibility, Gender-based eligibility, Detailed gender-based eligibility, and Gender-based breakdown. Red arrows indicate the flow of information from the criteria tables to the breakdown counts.

Sex-based eligibility

Study Details	Tabular View	Study Results
Eligibility Criteria		
Ages Eligible for Study:	18 Years to 49 Years (Adult)	
Sexes Eligible for Study:	All	
Gender Based Eligibility:	Yes	
Gender Eligibility Description:	We did no confirmation of biological sex and accepted all participants as they self-identified	
Accepts Healthy Volunteers:	Yes	

Gender-based eligibility

Study Details	Tabular View	Study Results
Eligible Criteria		
Inclusion Criteria:	1. aged 18-49 at the start of the study 2. self-identity as transgender women 3. self-identity as sexually active with more than one partner in the prior 90 days 4. at least one sexual partner in the last 90 days had a penis 5. has a smartphone 6. resides in the U.S.	
Exclusion Criteria:	Anyone not meeting inclusion criteria	
Sexes Eligible for Study:	All	
Gender Based Eligibility:	Yes	
Gender Eligibility Description:	All participants must identify as transgender women	

Detailed gender-based eligibility

Study Details	Tabular View	Study Results
Sex/Gender		
Sex/Gender, Customized	Measure Type: Count of Participants	Number Analyzed 47 participants
Unit of Measure: Participants		
Female	3	6.4%
Male	35	74.5%
Transfemale or Transwoman	6	12.8%
Transmale or Transman	0	0.0%
Genderqueer or Gender Nonconforming	3	6.4%
Other Gender Identity	0	0.0%

Gender-based breakdown

Sex-based eligibility	Gender-based eligibility	Detailed gender-based eligibility	Gender-based breakdown
Yes=13	Not listed=8	No=4	Yes=8
	No=2	Yes=2	No=2
	Yes=3	Yes=3	No=1
			Yes=2

Transgender individuals Assigned female sex at birth
Gender nonconforming Transman
Two-spirit
Genderqueer
Nonconforming
Transgender Women (TGW)
Transmale
Trans Masculine
Female-to-male (FTM)
Diverse transgender identity
Transgender female
Male-to-female (MTF)
Transfeminine

- Although gender-based eligibility was applied, it was not consistently reported in the ClinicalTrials.gov records that were analyzed
- There was no standardized methodology for reporting on gender (definition)
- Study limitations:
 - The ClinicalTrials.gov search algorithm is not optimized for these searches
 - Gender breakdown in the “Study Results” tab of ClinicalTrials.gov was not identified by the search string applied

References

1. Chen B, Jin H, Yang Z, Qu Y, Weng H, Hao T. An approach for transgender population information extraction and summarization from clinical trial text. *BMC Med Inform Decis Mak*. 2019;19(Suppl 2):62. 2. Chan PS. Invisible gender in medical research. *Circ Cardiovasc Qual Outcomes*. 2019;12(4):e005694. 3. Enhancing the diversity of clinical trial populations – eligibility criteria, enrollment practices, and trial designs: Guidance for industry, U.S. Department of Health and Human Services, Food and Drug Administration, Center for Drug Evaluation and Research, and Center for Biological Evaluation and Research. November 2020. Accessed March 23, 2021. <https://www.fda.gov/regulatory-information/search-fda-guidance-documents/enhancing-diversity-clinical-trial-populations-eligibility-criteria-enrollment-practices-and-trial>. 4. Meerwijk EL, Sevelius JM. Transgender population size in the United States: a meta-regression of population-based probability samples. *Am J Public Health*. 2017;107(2):e1-e8. 5. Jones NC, Otto AK, Ketcher DE, Permut JB, Quinn GP Schabath MB. Inclusion of transgender and gender diverse health data in cancer biorepositories. *Contemp Clin Trials Commun*. 2020;19:100597.

Acknowledgements

This study was supported by Cadent Medical Communications, a Syneos Health™ group company. The authors thank Nicholas Kenny, Chief Scientific Officer of Syneos Health™, for his insight and experience on clinical trial diversity.

Disclosures

All authors are employees of Cadent Medical Communications, a Syneos Health™ group company.

