Addressing Transgender Erasure in HIV Clinical Trials: The Scorecard for Transgender and Gender-Diverse Inclusion

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We sought to offer a structured framework for evaluating transgender and gender-diverse (TGD) inclusion in HIV clinical trials, with actionable criteria for trial design and conduct, and to quantify and characterize TGD inclusion in pivotal HIV studies as supporting evidence of the need for this framework.

We devised a tool (scorecard) consisting of 14 scoreable indicators for TGD-responsive HIV research with input from global TGD communities. We tested the scorecard in a cross-sectional review of 41 randomized controlled HIV biomedical efficacy trials to measure TGD responsiveness. Studies were selected to represent the spectrum of groundbreaking HIV therapeutic and prevention studies enrolling participants in countries around the world from 1991 to 2023. We found that TGD individuals represent a reported 2532 (1.4%) of 178 893 participants in the selected HIV clinical trials.

Scorecard indicators reveal a dearth of HIV research responsive to the needs of TGD communities. The lack of TGD representation in HIV clinical trials indicates a historical erasure of TGD communities with potential public health consequences. The scorecard might guide future HIV research to be more responsive to the needs of TGD people. (*Am J Public Health*. Published online ahead of print August 7, 2025:e1–e10. https://doi.org/10.2105/AJPH.2025.308134)

AJPH Published online ahead of print August 7, 2025

Transgender and gender-diverse (TGD) people are a key population in the global HIV response. Estimates suggest that global HIV incidence is 66 times higher for transgender women (TGW), 7 times higher for transgender men (TGM), and unknown for gender nonbinary (GNB) people relative to the adult population overall.[1] Global HIV prevalence among TGD people is 9.2% on average and as high as 58% in some locations.[2] Despite these disparities, TGD people are underrepresented in HIV research. Trials conducted among cisgender people may not be generalizable to TGD people; TGD communities face unique social, biological, and epidemiological conditions, many of which remain underexplored.[3–5]

The exclusion of TGD individuals from clinical trials prevents opportunities for TGD communities to receive investigational interventions and may also hinder access to approved medical products. In the DISCOVER study, the exclusion of people assigned female at birth had the unintended consequence of limiting regulatory approval of a novel HIV prophylactic regimen to people assigned male at birth only; cisgender women, TGM, and GNB people assigned female at birth remained excluded from clinical guidelines for this HIV prevention option at the time of the writing of this article.[6] This example illustrates how a lack of diversity in clinical trials can burden medical decision-making in clinic settings where questions about managing safety and certain pharmacological interactions (e.g., approved medications and exogenous hormone therapy) may not be supported by data. Considering HIV's disproportionate impact on TGD communities, HIV research must be optimized to better respond to the needs of TGD people.

We sought to devise an evidence-based guidance tool to support the inclusion of TGD people and their priorities in the design and implementation of future HIV clinical trials. We also sought

to provide further supporting evidence of the need for such a tool by measuring the extent to which a cross section of HIV clinical trials have been inclusive of and responsive to the needs of TGD communities. Here we present the HIV Research Scorecard for TGD Inclusivity (hereafter Scorecard) and findings from our review of TGD representation in 41 global HIV clinical trials conducted over the past 30 years.

METHODS

The Manifesto to Align HIV Prevention Research with Trans and Gender Diverse Realities[7] was released in 2021. This document represents the culmination of literature reviews, surveys, workshops, and interviews with more than 35 TGD individuals including communities of people with HIV, health care providers, and researchers in 27 countries around the world. Contributors were queried on research gaps and needs among TGD communities, resulting in recommendations for aligning HIV research with the lived experiences of TGD individuals and communities.

The manifesto's recommendations were recognized as a strength, but its expansive format was a potential limitation of its impact. To support the practical application of the manifesto, we removed narrative text, reduced the document to its recommendations, combined overlapping components, and ultimately synthesized it into a single-page scorecard consisting of 14 yes-or-no indicators spanning 4 domains of clinical trials: study design, study implementation, study reporting, and language. Together, these indicators constitute the Scorecard (Figure 1).

We tested the Scorecard in a cross-sectional review of HIV clinical trials. Eligibility criteria for the review included randomized controlled biomedical efficacy trials inclusive of therapeutic and prevention studies. We excluded HIV cure studies because of the lack of large, randomized efficacy studies with critical findings in this arena. Eligible studies were further narrowed down to include the most recognizable trials with breakthrough pivotal findings essential to the field, including the first trials to formally demonstrate that antiretroviral therapy regimens conferred clinical and survival benefits, the studies underpinning treatment as prevention ("undetectable equals untransmittable"), the majority of HIV vaccine efficacy studies, studies demonstrating proof of concept for broadly neutralizing antibodies for prevention, studies leading to the approval of oral and injectable preexposure prophylaxis, and a selection of additional novel preexposure prophylaxis studies incorporating a variety of microbicide and long-acting injectable formulations.

To improve the representativeness of our sample, we also chose to include studies with a variety of results (e.g., those demonstrating efficacy, futility, and superiority). On the basis of these criteria, a literature review, and database searches on ClinicalTrials.gov[8] and the clinical trials database maintained by AVAC,[9] we selected 41 studies to evaluate for TGD responsiveness using the Scorecard's 14 indicators. Table 1 presents the 41 studies included in this review; citations for the selected studies are available in the appendix (available as a supplement to the online version of this article at http://www.ajph.org). Source documents for our review included study protocols, study publications, study records hosted on ClinicalTrials.gov, conference presentations, and e-mail correspondence with investigators involved in selected trials.

RESULTS

The 41 trials included in this analysis reported a cumulative total of 178 893 study participants. We categorized participants as TGD when source documents explicitly identified TGD participation (e.g., number of "transgender women") or provided data on participants' sex assigned at birth that could be cross referenced with self-reported gender identity (e.g., participants assigned female sex at birth and identifying as male were classified as TGM). We classified cisgender participants in the same manner (i.e., the number of participants explicitly identified in source documents as "cisgender" or participants whose reported sex matched their reported gender identity). In one study, participants could select more than one gender identity; we were able to collapse multiple selections into a single category for all participants in that study (e.g., participants who selected "gender queer" and "gender variant" were categorized as gender nonbinary).

On the basis of the information available, 2532 (1.4%) participants could be categorized as TGD. Within this group, the largest percentage was made up of 2042 (80.6%) TGW, followed by 398 (15.7%) GNB individuals and 92 (3.6%) TGM. Cisgender people represent 42 905 (24.0%) of total participants, including 29 668 cisgender men and 13 237 cisgender women. The remaining 133 456 (74.6%) participants could not be categorized as TGD or cisgender because of ambiguous definitions of the study population (see the Study Design section), the studies' failure to

AJPH Published online ahead of print August 7, 2025

HIV Research Scorecard for Trans and Gender-Diverse Inclusivity

		YES 1 pt	NO/Not Available 0 pt
Study Design			
1.	Eligibility criteria explicitly include gender nonbinary individuals.		
2.	Eligibility criteria explicitly include transgender men.		
3.	Eligibility criteria explicitly include transgender women.		
4.	If gender nonbinary individuals, trans men, or trans women are not included, their exclusion is explicitly justified.		
5.	Specific and measurable goals are set for the enrollment of TGD participants, either in absolute numbers or as a percentage of total participants.		
6.	Gender-affirming hormone use is accounted for as a variable (e.g., in eligibility criteria, safety monitoring, efficacy, drug-drug interactions, etc.).		
Study Implementation			
7.	TGD status is ascertained in data collection using best practices (e.g., DAIDS TGD Working Group[a] or similar).		
8.	Outreach, marketing, and recruitment strategies and materials clearly exemplify TGD eligibility and inclusion.		
9.	TGD staff are included among the core study team and/or among research site staff.		
10.	Sites selected to recruit for the study have proven experience working with TGD communities.		
11.	The study includes a community engagement plan that involves partnerships with organizations serving TGD communities to foster engagement.		
Study Reporting			
12.	Participant TGD status is readily ascertained in study publications, presentations, and reporting using best practices (e.g., DAIDS TGD Working Group[a] or similar).		
13.	TGD-specific safety and efficacy analyses are reported in study findings.		
Language			
14.	All study-related documents, outreach materials, and study-led communications adhere to best practices in gender-inclusive language as outlined in the *NIAID HIV* Language Guide.[b]		

SCORE TOTAL = YES + NO =

A. 11-13 points B. 8-10 points C. 4-7 points D. 1-3 points F. 0 points

FIGURE 1— HIV Research Scorecard for Transgender and Gender-Diverse (TGD) Inclusivity

[a]National Institute of Allergy and Infectious Diseases Division of AIDS Cross-Network Transgender and Gender-Diverse Working Group. Data collection: gender identity, sex assigned at birth, intersex status, and sexual orientation. https://www.hanc.info/resources/sops-guidelines-resources/community.html#trans.
[b]National Institute of Allergy and Infectious Diseases. NIAID HIV Language Guide. https://www.thebody.com/hiv/niaid-hiv-language-guide.

collect or clearly report demographic data (see the Study Reporting section), 5 ambiguous participant responses (i.e., self-reporting "female sex at birth" and "transgender male to female" gender identity or vice versa), and 30 participants who declined to report their gender identity. Focusing only on the 45 437 participants who could be categorized, TGD individuals represented 5.6% of participants, as compared with 94.4% cisgender individuals.

The first study reporting TGD enrollment was the Preexposure Prophylaxis Initiative (iPrEx) study, which began enrolling participants in 2007. Therefore, all identifiable TGD enrollment took place during the second half of the analyzed period from 2007 to 2023, when most of the studies occurred (n = 32). All 2532 TGD participants were distributed across 12 studies (Figure 2).

AJPH Published online ahead of print August 7, 2025

TABLE 1— Summary of Findings From Cross-Sectional Scorecard Review of 41 Pivotal Global HIV Clinical Trials, 1991–2023

	Score	Indicators Achieved	TGD Enrollment[a]
A-grade studies (11–13 points)			
PURPOSE 2 (2022–2023)	12/13	1, 2, 3, 5, 6, 7, 8, 9, 10, 11, 12, 14	728/3271 (209 GNB, 43 TGM, 476 TGW)
IMPOWER-024 (2021–2022)	11/13	1, 3, 4, 5, 6, 7, 8, 10, 11, 12, 14	42/494 (20 GNB, 22 TGW)
B-grade studies (8–10 points)			
HPTN 083 (2016–2020)	10/13	3, 5, 6, 8, 9, 10, 11, 12, 13, 14	570/4566 (570 TGW)
HVTN 706 (2019–2021)	10/13	1, 2, 3, 6, 7, 8, 9, 10, 11, 12	323/3887 (70 GNB, 14 TGM, 239 TGW)
HVTN 704/HPTN 085 (2016–2018)	8/13	2, 3, 6, 7, 8, 9, 10, 11	254/2699 (60 GNB, 17 TGM, 177 TGW)
C-grade studies (4–7 points)			
REPRIEVE (2015–2019)	6/13	1, 2, 3, 7, 12, 13	129/7770 (37 GNB, 7 TGM, 85 TGW)
DISCOVER (2016–2017)	5/13	3, 6, 12, 13, 14	74/5387 (74 TGW)
HVTN 702 (2016–2019)	5/13	1, 2, 3, 7, 12	21/5404 (2 GNB, 3 TGM, 16 TGW)
iPrEx (2007–2009)	5/13	3, 6, 8, 12, 13	339/2499 (339 TGW)
PARTNER 2 (2010–2017)	5/13	2, 4, 7, 12, 14	3/1564 (3 TGM)
IMPOWER-022 (2021–2022)	4/13	4, 7, 12, 14	0/730
PURPOSE 1 (2021–2023)	4/13	4, 7, 12, 14	0/5345
D-grade studies (1–3 points)			
HVTN 505 (2009–2013)	3/13	3, 6, 12	44/2496 (44 TGW)
HVTN 703/HPTN 081 (2016–2018)	3/13	4, 7, 12	0/1924
HVTN 502 (2005–2007)	2/13	2, 3	Ambiguous/3000
IPERGAY (2012–2014)	1/13	3	Ambiguous/400
HPTN 084 (2017–2020)	1/13	12	5/3224 (5 TGM)
F-grade studies (0 points)			
ACTG 175 (1991–1992)	0/13	None	Ambiguous/2467
ACTG 320 (1996–1997)	0/13	None	Ambiguous/1156
ASPIRE (2012–2015)	0/13	None	Ambiguous/2629
Bangkok Tenofovir Study (2005–2010)	0/13	None	Ambiguous/2413
CAPRISA 004 (2007–2010)	0/13	None	Ambiguous/889
FACTS 001 (2011–2014)	0/13	None	Ambiguous/2059
FEM-PrEP (2009–2011)	0/13	None	Ambiguous/2120
HPTN 052 (2005–2010)	0/13	None	Ambiguous/3526
HPTN 071 (2013–2017)	0/13	None	Ambiguous/48302
HVTN 503 (2007)	0/13	None	Ambiguous/801
HVTN 705 (2017–2019)	0/13	None	Ambiguous/2600
MTN 003 (2009–2011)	0/13	None	Ambiguous/5029
Opposites Attract (2012–2016)	0/13	None	Ambiguous/686
PARTNER 1 (2010–2014)	0/13	None	Ambiguous/1776
Partners PrEP (2008–2010)	0/13	None	Ambiguous/9494
PrEPVacc (2020–2023)	0/13	None	Ambiguous/1512
PROUD (2012–2014)	0/13	None	Ambiguous/544
Ring Study (2012–2016)	0/13	None	Ambiguous/1959
Ritonavir Study (1995)	0/13	None	Ambiguous/1090
RV 144 (2003–2005)	0/13	None	Ambiguous/16 402
SMART (2002–2006)	0/13	None	Ambiguous/5472
START (2009–2013)	0/13	None	Ambiguous/4685

Continued

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TABLE 1— Continued

	Score	Indicators Achieved	TGD Enrollment[a]
TDF2 (2007–2009)	0/13	None	Ambiguous/1219
VAX 004 (1998–1999)	0/13	None	Ambiguous/5403

Note. ACTG = AIDS Clinical Trials Group; HPTN = HIV Prevention Trials Network; HVTN = HIV Vaccine Trials Network; MTN = Microbicide Trials Network; TGD = transgender and gender diverse; GNB = gender nonbinary; TGM = transgender men; TGW = transgender women. In the first column, the years in parentheses represent the study's enrollment period. Numbers in the Indicators Achieved column correspond to Scorecard indicators 1–14 shown in Figure 1. "Ambiguous" in the TGD Enrollment column represents the 133 456 (75%) participants who could not be categorized as TGD or cisgender on the basis of the information available (see Results).
[a]Number of participants identified as TGD/total number of participants enrolled.

Study Design (Scorecard Indicators 1–6)

Scorecard indicators 1 through 3 determined whether GNB individuals (indicator 1), TGM (indicator 2), and TGW (indicator 3) were discretely and explicitly included in study eligibility criteria. Most studies used ambiguous terminology, if at all, to define the study population, such as "men," "women," "females," and "males," without clarifying whether these terms referred to gender identity, sex assigned at birth, or current anatomy and without using clarifying terms such as "cisgender" and "transgender." Only 3 studies explicitly included GNB individuals, 6 studies explicitly included TGM, and 11 studies explicitly included TGW. Eligibility did not always correspond to enrollment; several studies included TGD individuals in eligibility criteria but did not report any TGD enrollment, whereas other studies did not include TGD individuals in eligibility criteria but later reported TGD enrollment.

Scorecard indicator 4 evaluated whether justification for exclusion was stated in studies that did not explicitly include TGD individuals. Five studies scored positively on this indicator, including 3 studies designed specifically for cisgender women. Each of these 3 studies had its own separate "sibling study" designed to include TGD participants as a means of addressing similar research questions. For example, the PURPOSE 1 study was designed exclusively for cisgender

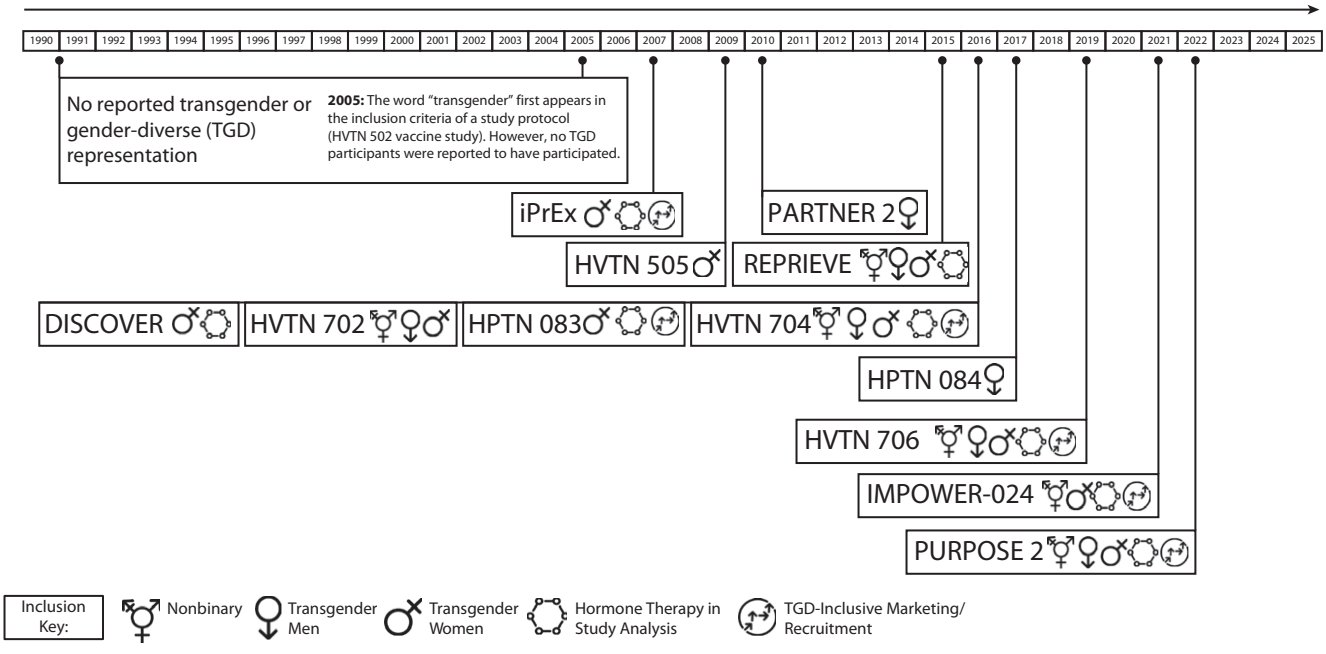

FIGURE 2— Timeline of Transgender and Gender-Diverse Representation in 41 Pivotal Global HIV Clinical Trials, 1991–2023

Note. HPTN = HIV Prevention Trials Network; HVTN = HIV Vaccine Trials Network.

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women, but its sibling study, PURPOSE 2, explicitly named "cisgender men, transgender women, transgender men, and gender nonbinary people" as the study population; both studies tested the same investigational product for HIV prevention.

The fourth study that scored positively for indicator 4, IMPOWER-024, included GNB individuals and TGW but not TGM. Correspondence with the investigators revealed that planning for another study called IMPOWER-035 had been under way before a clinical hold on the investigational product halted study development. IMPOWER-035 would have included TGM and additional TGD populations, and this was the rationale for excluding TGM from IMPOWER-024. The fifth study, PARTNER 2, was designed specifically for people who identify as "gay men," with the study protocol clarifying that both cisgender and transgender gay men were eligible. We found this rationale to be reasonable for the exclusion of GNB individuals and TGW. The remaining TGD-exclusionary trials did not provide justification for excluding TGD populations, nor were "sibling studies" conducted to investigate similar research questions in TGD populations.

Scorecard indicator 5 evaluated whether studies were designed with TGD-specific enrollment goals (i.e., a number or percentage of TGD participants that the study aimed to enroll). Three studies achieved this indicator. HIV Prevention Trials Network (HPTN) 083 set a goal to enroll at least 10% TGW; 12.5% was achieved. PURPOSE 2 set a goal to enroll 20% TGW; 15% was achieved. Although PURPOSE 2 did not set an enrollment goal for GNB individuals or TGM, the study enrolled 209 (6%) and 43 (1%), respectively. IMPOWER-024 set a goal to enroll at least 100 TGW; the study enrolled 22 TGW, or 4.5% of the total enrolled participants, before it was placed on a clinical hold and subsequently discontinued. IMPOWER-024 also enrolled 20 GNB individuals, although there was no goal set for enrollment of this population.

Scorecard indicator 6 evaluated whether studies were designed to account for gender-affirming hormone use as a variable, for example in eligibility criteria, safety monitoring, efficacy, and drug–drug interactions. Eight studies achieved this indicator and did so in a variety of ways. Some studies determined the impact of hormone use on the efficacy of the investigational product under investigation, and vice versa, whereas others adjusted eligibility criteria to allow TGD participants using hormones to be clinically evaluated according to their gender identity rather than their sex assigned at birth.

Study Implementation (Scorecard Indicators 7–11)

Scorecard indicator 7 evaluated studies' use of gender-inclusive data collection practices, including measures ascertaining participants' gender identity separately from their sex assigned at birth. The Scorecard narrowly defines achievement of this indicator by referencing a 2023 best practices document based on data collection methods established in the early 2000s.[10] Among other criteria, a study's data collection practices must include options for participants to self-identify as GNB, TGM, and TGW unless a clear rationale is stated for any group's exclusion. All studies in our analysis included a measure of "sex," but the first study to consider gender as a discrete measure was HIV Vaccine Trials Network (HVTN) 502, which began enrolling in 2005; still, this study fell short of best practices in that GNB individuals were not considered.

Subsequently, many studies collected data on gender identity and sex assigned at birth, but only 10 studies in our entire analysis satisfied the Scorecard's comprehensive criteria for gender-inclusive data collection, starting with the PARTNER 2 study in 2010. Therefore, less than half of the 23 studies conducted after 2010 met the Scorecard's standards for data collection, and some studies conducted as recently as 2020 did not meet these standards. GNB exclusion was a significant barrier to achieving this indicator. Another 6 studies were found to explicitly include TGD people in study outreach, marketing, and recruitment strategies (indicator 8). Little information was available on indicators 9 through 11, but 4 studies met the criteria for employment of TGD study staff (indicator 9), 5 met the criteria for TGD-competent site selection (indicator 10), and 5 met the criteria for partnership with TGD organizations (indicator 11). Box 1 illustrates examples that explicitly met the stated criteria for indicators 8 through 11.[11–13]

Study Reporting (Scorecard Indicators 12–13)

Fourteen studies (34%) achieved Scorecard indicator 12 by clearly reporting on the gender distribution of study participants in the study results such that TGD representation could be ascertained. However, some of these studies presented only partial data. For example, 2 studies did not collect gender identity data from the first group of participants to enroll; these studies implemented TGD-inclusive data collection measures only after study enrollment had already begun, thereby missing the opportunity to screen some participants.

AJPH Published online ahead of print August 7, 2025

BOX 1— Examples of Transgender and Gender-Diverse-Responsive Study Implementation: 41 Pivotal Global HIV Clinical Trials, 1991–2023

Scorecard Indicator	Example
8. Outreach, marketing, and recruitment strategies and materials clearly exemplify TGD eligibility and inclusion	The study website and recruitment materials for the AMP study prominently featured language welcoming TGD participants and photographs of TGD models. Testing was also conducted to obtain feedback from TGD communities on the effectiveness of the imagery, language, style, and overall messaging to inform TGD-responsive marketing for studies such as AMP and HPTN 083.[11]
9. TGD staff are included among the core study team or among research site staff	The PURPOSE 2 HIV prevention study included a global community advisory group, consisting of TGD members, as an integral part of the study team. The study website also included a video stating "We also want to make sure that our sites and our site staff are representative of the communities that we're trying to recruit from so people feel comfortable and want to participate."[12]
10. Sites selected to recruit for the study have proven experience working with TGD communities	In the HVTN 706 study, research sites were expected to enroll cisgender men and transgender people. At various sites, assets included previous experience enrolling TGD study participants, participation in TGD sensitivity training for staff, involvement in trusting relationships with local TGD communities, adjustment of study visit schedules to accommodate challenges unique to TGD participants, linking of TGD participants to health services outside of the study, provision of financial support to cover participants' travel expenses, and accommodation of participants facing transphobia.[13]
11. The study includes a community engagement plan that involves partnerships with organizations serving TGD communities to foster engagement	TGD sensitivity training for staff conducting the HPTN 083 study included partnerships with individuals and organizations serving TGD communities. The study protocol also specified the expectation for each site to work with its local community advisory board and outreach teams to develop a community engagement plan that was appropriate for its local context. In addition, the study included a goal to enroll 10% transgender women; outreach and community engagement plans were expected to align with this goal.

Note. AMP = HVTN 704/HPTN 085 study; HPTN = HIV Prevention Trials Network; HVTN = HIV Vaccine Trials Network; TGD = transgender and gender diverse.

Another 2 studies failed to account for GNB participants in their data reporting (and presumably in data collection), but we classified these 2 studies as achieving indicator 12 by virtue of their reporting on the inclusion of TGM and TGW. We also identified inconsistencies with one trial's published data; we were granted approval to conduct an auxiliary study using the trial's deidentified data set to correct the trial's gender distribution and complete the analysis for our review (this study still did not earn a point for indicator 12). Three studies did not report on gender in their original journal publications, but they later published transgender-specific analyses separately from the primary study findings, thereby satisfying Scorecard indicator 12, albeit imperfectly.

Indicator 13 assessed whether studies reported TGD-specific analyses in their findings; 4 studies did so. These studies reported on a variety of safety, efficacy, and pharmacodynamic findings among TGD participants, separately from primary findings on cisgender participants. Given that several studies in our review only recently concluded, scores for indicator 13 may change as more information becomes available.

Language (Scorecard Indicator 14)

Seven studies (17%) achieved Scorecard indicator 14 by using gender-inclusive language that clearly and correctly defined the study population as operationalized by the National Institute of Allergy and Infectious Diseases (NIAID) HIV Language Guide.[14] Three of these studies predated the release of the original NIAID HIV Language Guide in 2020, demonstrating that Scorecard indicator 14 is achievable without the guide; however, this small number of studies suggests that future investigations could benefit from using the Scorecard and referencing the guide. NIAID-approved terminology included "assigned female/male at birth," "cisgender," "transgender," "gender nonconforming," "regardless of gender identity," and "participants of childbearing potential/pregnant participants." Thirty-four studies used terminology that rendered the study population ambiguous or unintentionally excluded TGD populations, as previously described.

Scores

Taking all indicators into account, only 2 studies achieved A-grade scores per the Scorecard's scoring system: PURPOSE 2 achieved 12 of 13 indicators, and IMPOWER-024 achieved 11 of 13. Three studies had B-grade scores with 8 to 10 indicators achieved, 7 studies had C-grade scores with 4 to 7 indicators achieved, 5 studies had D-grade scores with 1 to 3 indicators achieved, and 24 studies (59%) achieved zero

AJPH Published online ahead of print August 7, 2025

indicators (a grade of F). Table 1 summarizes these findings.

DISCUSSION

Findings from this analysis of 41 milestone HIV clinical trials representing more than 30 years of HIV research confirm that TGD people and their priorities are critically underrepresented in HIV research despite the disproportionately high burden of HIV faced by TGD communities around the world.[1,2] Of a total of 178 893 participants, only 2042 transgender women, 398 nonbinary individuals, and 92 TGM represented TGD communities in 41 of the most influential HIV clinical trials conducted to date. The public health implications of this research gap are grave, including a dearth of HIV interventions appropriately designed, marketed, and availed to TGD communities urgently in need of these interventions as soon as they are available to other populations.

Before 2005, the word "transgender" was absent from such trials. No standard for TGD responsiveness is achievable without the recognition of the existence of TGD people. Since 2005, a trend toward greater inclusivity has been observed, owing largely to data collection practices established in the early 2000s[10] and momentum derived from a rich history of HIV activism embodied in seminal work such as The Denver Principles.[15] For example, bold activism leading up to the iPrEx study in 2007 resulted in trials that were discontinued and the lasting transformation of research ethics and the role of community involvement in research, as emblazoned in the Good Participatory Practice research guidelines.[16,17]

Research advocacy led by TGD scholars and activists has also drawn attention to the specific needs of TGD communities, a tradition that continues to this day.[4,5,18] Each of these milestones has likely contributed to the change that began in 2007 when the first TGD enrollment was reported. However, evidence suggests that some advancements have been sporadic rather than sustained. More than two thirds of studies conducted since 2007 have still failed to account for GNB people, TGM, and TGW through data collection methodologies, including studies conducted as recently as 2020; recognition of the existence of TGD communities remains a challenge.

Furthermore, very few studies have included TGD-focused research questions or study practices that directly respond to ongoing HIV-related priorities for TGD communities, such as interactions with gender-affirming hormones.[19] The extent to which these priorities are integrated in future trials will likely characterize the next era of TGD-responsive research. In our experience, the success of TGD-inclusive trials has relied heavily on the influence of investigators who specialize in TGD research—including researchers who are transgender—and a commitment to the meaningful involvement of TGD communities in the research process.

The findings outlined here support our recommendation for HIV researchers and advocates to use the Scorecard to operationalize commitment to TGD representation. Investigators, industry sponsors, study participants, community engagement staff, and advocates have a role to ensure that TGD communities are meaningfully included. When used proactively as a study design tool, the Scorecard has the potential to ensure that future HIV clinical trials either include TGD individuals or justify the rationale for their exclusion (Scorecard indicators 1–4). Researchers may also have to carefully consider safety concerns in settings with severe anti-TGD hostility where TGD enrollment could jeopardize the safety of participants and/or research staff, although these concerns must always be weighed against the harms of excluding TGD individuals. These decisions should be informed in consultation with ethicists, legal counsel, and, importantly, engagement with local TGD communities and researchers.

Researchers can use the Scorecard to ensure that, at a minimum, study populations can be accurately characterized (Scorecard indicators 7 and 12). Nearly three fourths of the participants in our analysis—133 456 individuals—could not be categorized as TGD or cisgender. TGD individuals were probably included among these participants, although they were likely assumed to be cisgender by default. This miscategorization undermines the integrity of these studies and their important findings; data that do not accurately reflect the study population compromise a study's validity and applicability to all, not just TGD communities. This vast amount of missing data highlights the need for the Scorecard to support scientific integrity, improve on the generalizability of study results, and potentially improve access to important HIV treatment and prevention measures while identifying areas for further research.

Furthermore, the failure to correctly capture demographic data erases TGD people and their contributions to science and impedes their right to benefit from science.[20] TGD individuals give their time, expertise, bodies, blood, and tissues to research. When research fails to accurately account for TGD communities, it exacerbates health disparities and

AJPH Published online ahead of print August 7, 2025

diminishes TGD individuals' ability to realize scientific progress for their own communities, progress that TGD people continuously help to advance despite the erasure of their contributions. The practice of collecting TGD-inclusive participant data has only recently been established; researchers need guidance and support for the integration of these critical measures.[21] The Scorecard provides a clear and simple checklist to ensure consideration of such practices, which in turn has the potential to enhance clinical trials and their benefits for everyone, TGD and cisgender alike.

The Scorecard also supports crucial TGD-specific considerations. It encourages reflection on statistical plans, enrollment criteria, and a variety of recruitment strategies to ensure that an adequate number of TGD participants are included and that TGD-specific study objectives are reached, such as answers to important questions about interactions between investigational drugs and hormones or significant differences in safety, efficacy, adherence, acceptability, or other measures. Standards for adequate statistical power to conduct TGD-specific analyses are not well established (this is an area for further development), but the Scorecard prioritizes transparency (indicator 13). If a study lacks statistical power to test results by stratification, this information should be reported, and investigators should account for the extent to which this constitutes a study limitation. On their own, concerns about statistical power should not be used to justify exclusion of TGD communities. The previously referenced DISCOVER study illustrates how exclusion—not inclusion—can result in a lack of statistical power that undermines the basic ethical principles of research and, ultimately, public health goals.[6]

Furthermore, TGD inclusion matters even if traditional thresholds for statistical power are not feasible. Examples include studies reporting no clinically relevant interactions between the study drug and exogenous hormone use, differences in behavioral characteristics such as substance use, and differences in exploratory measures such as adherence and acceptability. Studies including TGD participants also promote trust, community awareness, and readiness to engage in research and public health initiatives. To explore TGD-specific research questions in greater detail, TGD-specific studies should be considered. For example, HPTN 091, an open-label study designed exclusively for transfeminine adults, tested the impact of co-locating gender-affirming care services with HIV prevention services.[22] (HPTN 091 was not included in our cross-sectional review because it was not an efficacy study and therefore did not meet the inclusion criteria. However, it represents an important milestone as the first study in the HIV Prevention Trials Network designed exclusively for transfeminine participants.)

Even studies without HIV-related endpoints can help in the response to conditions faced by TGD communities that are pertinent to the ecological model of HIV, such as economic hardship and psychological distress.[23] TGD-specific trials, demonstration projects, and modeling work are essential to close key knowledge gaps and answer the research questions most salient to the lived experience of TGD populations. Our cross-sectional review also justifies the need for a more comprehensive systematic review of TGD representation in clinical trials for HIV and other health conditions disproportionately affecting TGD communities, wherein an adaptation of the Scorecard could also be of use.

Finally, the last of the Scorecard's indicators, language, is integral to eliminating the exclusion of TGD people in scientific data, findings, and communications. For example, the trials leading to the approval of cabotegravir for HIV prevention, HPTN 083 and HPTN 084, included 570 TGW and 5 TGM, respectively. However, these studies are sometimes colloquially referred to as "the men's study" and "the women's study," respectively, omitting the substantial contributions of TGD people to the approval of the first long-acting injectable for HIV prevention. Furthermore, it is critical to recognize the multitude of terms describing gender diversity outside of the hegemonic understandings of gender in Europe and North America. We underscore the importance of adapting the language of HIV research to local contexts. As HIV research evolves to better respond to the epidemic, so too must our language evolve to be more gender inclusive.[24]

The lack of TGD representation in HIV clinical trials stands as a historical erasure of TGD communities with potential public health consequences. The Scorecard may guide future HIV research to be more responsive to the needs of TGD people. Importantly, use of the Scorecard during clinical trial development and implementation may enhance access to investigational HIV interventions in clinical trials and to approved products for the treatment and prevention of HIV. Inclusion of TGD people in HIV clinical trials may also provide information on differences in the safety and efficacy of interventions. The Scorecard is poised to set in motion an era of HIV research that meaningfully responds to the needs of TGD people. We invite researchers and advocates to use the Scorecard when designing and evaluating future HIV trials.

AJPH Published online ahead of print August 7, 2025

Doing so will allow the unique needs of TGM, TGW, and gender-diverse populations to be better understood and ultimately better served. AJPH

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PUBLICATION INFORMATION

Full Citation: Minalga B, Feuer C. Addressing transgender erasure in HIV clinical trials: the scorecard for transgender and gender-diverse inclusion. *Am J Public Health*. Published online ahead of print August 7, 2025:e1–e10.

Acceptance Date: March 17, 2025.

DOI: https://doi.org/10.2105/AJPH.2025.308134

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ACKNOWLEDGMENTS

This work was supported by the Coalition to Accelerate and Support Prevention Research and made possible by the generous support of the American people through the US President's Plan for AIDS Relief (PEPFAR) and the US Agency for International Development (USAID). Brian Minalga declares funding through National Institute of Allergy and Infectious Diseases award 2 UM1 AI068614-15 to the Fred Hutchinson Cancer Center.

We thank Leigh-Ann Van der Merwe, Richard Jefferys, Meagan O'Brien, Diana Tordoff, and Manju Chatani for contributing to this project.

Note. The contents of this work are the sole responsibility of the authors and do not necessarily reflect the official views of PEPFAR, USAID, the National Institutes of Health (NIH), or the US government.

CONFLICTS OF INTEREST

The authors have no conflicts of interest to disclose.

HUMAN PARTICIPANT PROTECTION

No human participants were included in this project.

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AJPH Published online ahead of print August 7, 2025