Practical Application of the ICER-developed Clinical Trial Diversity Rating (CDR) Tool

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HTA49

Introduction

- The ICER-developed Clinical trial Diversity Rating tool (CDR) provides a consistent and transparent framework for evaluating the demographic diversity of clinical trial populations.
- Groups such as Health Technology Assessment bodies, clinical trial regulators, policymakers, journal editors, and researchers can use this tool to assess and improve diversity in clinical trials.

Objective

- To report and discuss the practical application of the ICER-developed CDR tool.

Methods

- Case series that examined pivotal trials in eight ICER assessments completed since the introduction of the CDR tool in the 2023 Value Assessment Framework (VAF).
- The CDR tool evaluates clinical trial diversity quantitatively by comparing trial participants to disease-specific prevalence estimates using pre-defined thresholds to rate each trial. See Table 1.
- For multinational trials, we sought information on US-specific enrollment to complete our evaluation of racial and ethnic diversity.

Table 1. Summary of CDR Tool Framework

PDRR	Score
0	0
>0 to <0.5	1
0.5 to 0.8	2
≥0.8	3

Demographic Characteristics	Rating Categories (Total Score)
Race/Ethnicity	Good (11-12), Fair (7-10), Poor (≤6)
Sex	Good (6), Fair (5), Poor (≤4)
Age	Good (3), Fair (2), Poor (≤1)

PDRR: Participant to Disease-prevalence Representation Ratio

Table 2. Example of Clinical Trial Diversity Ratings on Race/Ethnicity, Sex, and Age

	Prevalence[1,2]	ENHANCE-2 Trial[3]	PDRR	Rating
Race/Ethnicity				Fair
White	71.3%	94.7%	1.33	
Black	11.4%	4.3%	0.38	
Asian	1.4%	0.3%	0.18	
Hispanic/Latino	9.6%	5.0%	0.52	
Sex				Good
Female	53.1%	51.8%	0.98	
Male	46.9%	48.2%	1.03	
Age				Fair
≥65 years	79.7%	56.2%	0.69	

The ENHANCE-2 trial is an example from the Chronic Obstructive Pulmonary Disease Review.

1. Health Equity Tracker. Satcher Health Leadership Institute. Morehouse School of Medicine. Accessed January 26, 2024, https://healthequitytracker.org/exploredata?mls=1.copd-3.00
2. Global Burden of Disease Collaborative Network. Global Health Data Exchange. Accessed March 14 2022, https://vizhub.healthdata.org/gbd-results/
3. Anzueto A, Barjaktarevic IZ, Siler TM, et al. Ensifentrine, a Novel Phosphodiesterase 3 and 4 Inhibitor for the Treatment of Chronic Obstructive Pulmonary Disease: Randomized, Double-Blind, Placebo-controlled, Multicenter Phase III Trials (the ENHANCE Trials). Am J Respir Crit Care Med. Aug 15 2023;208(4):406-416. doi:10.1164/rccm.202306-0944OC

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Results

- Representation of age and sex was rated as good or fair in the majority of trials evaluated, whereas representation of race/ethnicity was only rated fair or poor (Table 3).
- Table 4 describes the challenges we faced in implementing the CDR tool, our solutions, and the potential implications

Table 3. Evaluations of Clinical Trial Diversity

ICER Assessment	Trial Name	Race/Ethnicity	Sex	Age
Schizophrenia	EMERGENT-1			
	EMERGENT-2			
	EMERGENT-3			
COPD	ENHANCE-1			
	ENHANCE-2			
MDS	IMerge			
	MEDALIST			
ATTR-CM	ATTR-ACT			
	ATTRibute-CM			
	HELIOS-B			
Acute Pain	NAVIGATE-1			
	NAVIGATE-2			
SPMS	HERCULES			

*Results reflect the data available at the time of ICER's assessment.
ATTR-CM: transthyretin amyloid cardiomyopathy, COPD: chronic obstructive pulmonary disease, MDS: myelodysplastic syndrome, SPMS: secondary-progressive multiple sclerosis

Key
Good representation of demographic category
Fair representation of demographic category
Poor representation of demographic category
Not calculated

Table 4. Challenges and Solutions in Implementing the CDR Tool

Challenges	Our Solution	(Potential) Implications of the Solutions
Global trials generally did not report US-specific enrollment.	We assessed the diversity of the overall study population.	The rating may not provide a true reflection of the racial and representation of US participants.
Lack of reliable US disease-specific prevalence estimates by race and ethnicity.	We used a combination of data sources to estimate disease prevalence.	Introduces uncertainty as representation may be under or over-estimated.
Differences between the clinical trial population (e.g., post-surgical pain) and the population who would ultimately use the drug (e.g., all patients with acute pain).	We rated representation relative to both the clinical trial population and potential real-world population.	Produces two estimates and leaves judgment to the reader.

Key Takeaways

- The CDR tool objectively assesses clinical trial diversity and opens the door for conversations around equity in clinical trials.
- Support from stakeholders by providing US-specific clinical trial data and/or reliable prevalence data would enhance the application of the tool.

Download the ICER Clinical Trial Diversity Rating Tool