

How Exclusion of Women and African-Americans Undermines the Value of Treatment Research

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Poll Question #1

- What is your primary role in VA?
 - student, trainee, or fellow
 - clinician
 - researcher
 - manager or policy-maker
 - Other

Logic of the evidence-based medicine movement

- High-quality, well-controlled research can identify what works
- Everyday clinical practice in many areas (e.g., alcohol treatment) is often ineffective
- Translation of science into practice will improve health care provision and outcomes

Do parachutes provide protection from “gravitational challenge”?

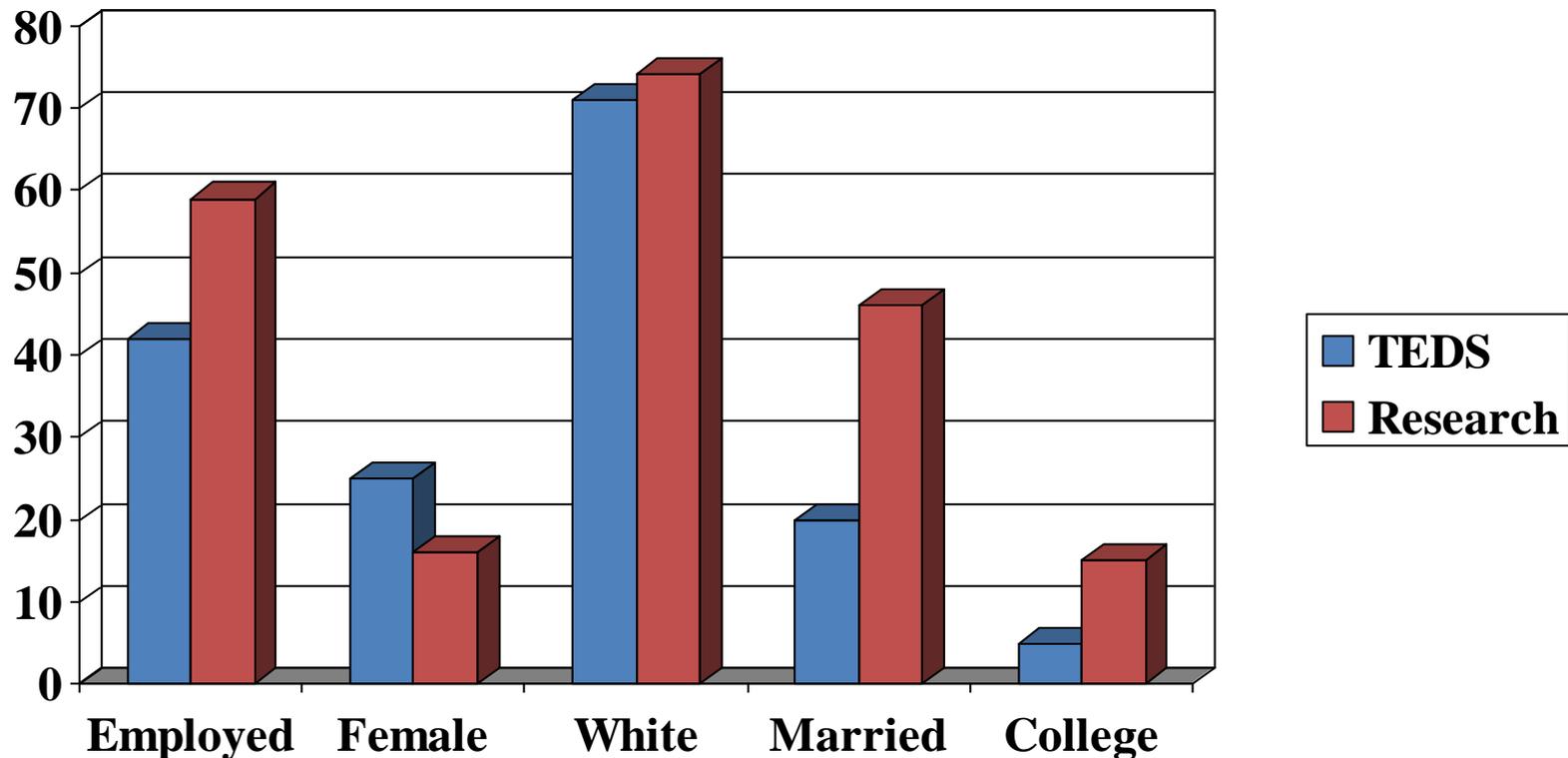


G.C. Smith and J. P. Pell, 2003 BMJ, 327: 1459-1461

“Lies, damned lies and
evidence-based medicine”

--D.P. Kernick The Lancet 1998; 351:1824

Demographics of researched vs real-world alcohol patients in U.S.



Could eligibility criteria in treatment outcome research be a place where we could lessen this problem?

- Impose rules unlike clinical practice
- Create unrepresentative samples by design
- Are in part under researchers' control

Moncrieff & Drummond (1998)

- Reviewed methodological quality of 25 highly-cited trials of alcohol treatment
- Mentioned that half of studies failed to report number of patients excluded
- Of reported studies, mean = 50% with a range of 4-92%

Questions for research program on eligibility criteria and alcohol patients

- What criteria do alcohol treatment researchers use and how often?
- How do criteria affect the composition of samples?
- Do criteria affect the outcomes of treatment research studies?

Study 1: What eligibility criteria do alcohol treatment researchers use and how often?

Data Source: Finney meta-analysis

- All 683 English-language alcohol treatment outcome studies that:
- Included a follow-up
- Had at least 5 adult patients per condition
- Appeared between between 1980 to 1998 (Dissertations, journals and books)

Methods

- Data are the verbatim published text
- Coded by independent raters
- Test for rater drift each 50 studies
- Range of agreement 95-100%, Kappa 0.94

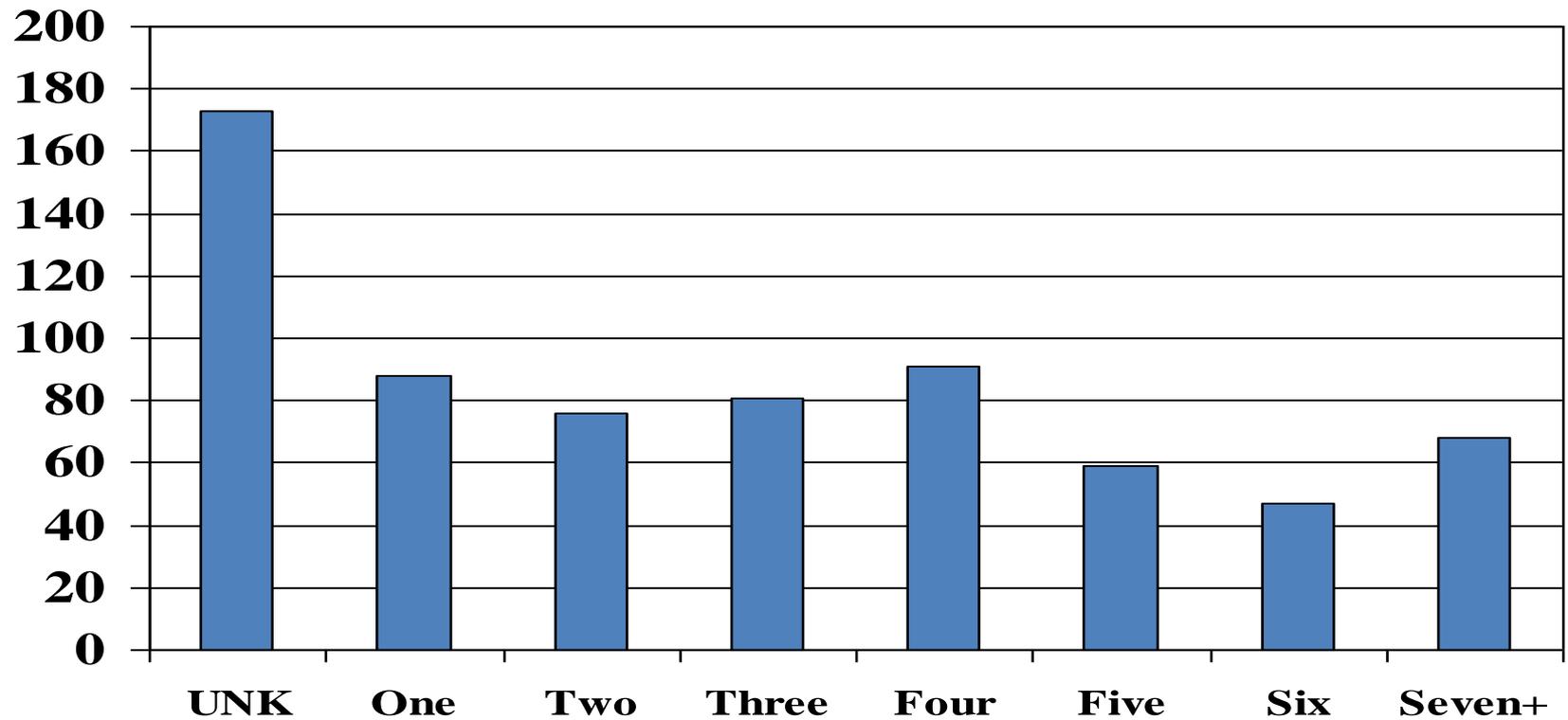
Psychiatric Category

- Cannot be psychotic
- Cannot have co-occurring “psychiatric problems”
- Cannot pose a threat to self or others
- Cannot be taking psychiatric medication

Compliance/motivation category

- Must agree up front to attend all treatment
- Cannot be “difficult” or “uncooperative”
- Must agree to be available for a follow-up research interview
- Must be motivated to change

Number of eligibility criteria used in 683 alcohol treatment studies



Prevalent criteria

- Psychiatric/emotional problems (37.8%)
- Alcohol treatment (31.8%)
- Medical conditions (31.6%)
- Compliance/motivation (31.5%)
- Neuro-cognitive problems (23.0%)
- Illicit drug use (22.7%)
- Social/Residential Stability (19.6%)

National differences in average rate of eligibility criteria

- UK 2.41
- Anzus 2.48
- USA 2.84
- Scandinavia 3.22
- Canada 3.25
- Ger/Fra/Ita 3.79

Major predictors of greater exclusivity in study design

	<u>b-weight</u>	<u>SE</u>	<u>p</u>
Constant	0.60	0.27	.03
Decade of Publication	0.77	0.11	.000
US NIAAA Funding	1.22	0.25	.000
Private Sector Funding	0.82	0.41	.047
Randomized design	1.39	0.19	.000
Inpatient/Residential TX	-.21	0.18	ns

Note. Positive weight means increased exclusiveness

Summary of study #1 key findings

- Eligibility criteria widely used, poorly described
- Alcohol treatment research is getting more exclusive (less representative)
- Eligibility criteria more common with particular designs and funders

Study 2: Are certain populations disproportionately excluded?

For Details See: Humphreys, K., Weingardt, K., & Harris, A. (2007). The influence of subject eligibility criteria on compliance with National Institutes of Health guidelines for inclusion of women, minorities and children in treatment research. Alcoholism: Clinical and Experimental Research, 31, 988-995.

Two key populations of interest

- U.S. National Institutes of Health policy on “burden and benefits” of treatment research
- Every grant proposal rated on representation of women and racial minorities

Research approach (study 2 and 3)

- Operationalize widely used eligibility criteria using the Addiction Severity Index
- Apply them to “take all comers” health services data sets
- Observe how criteria change the composition and outcomes of the sample

Example Operationalization: Psychiatric/Emotional Problem Eligibility Criteria

Degree of exclusivity

High

Moderate

Low

Operationalization

Any of: IP treatment, halluc, suicidality, psychotropic med

Any 2 of above

All of above

Example real world data sets

- National Drug Evaluation Network
- National Veterans Affairs system
- Target Cities studies
- State data systems from Michigan and Washington
- Community Epidemiology Laboratory

One illustrative sample: State of Washington

- 502 alcohol patients admitted to one of 13 programs statewide
- No eligibility criteria for study entry
- 7.3% African-American, 38.0% female
- All assessed with Addiction Severity Index

POLL QUESTION #2

Which sort of exclusion criteria do you think would be most likely to disproportionately exclude African-Americans?

- Psychiatric
- Medical
- Drug use
- Compliance
- Social-Residential

POLL QUESTION #3

Which sort of exclusion criteria do you think would be most likely to disproportionately exclude women?

- Psychiatric
- Medical
- Drug use
- Compliance
- Social-Residential

Proportion of patients ineligible under less and more exclusive operationalization

	Less	More
Neurological	0.6%	1.0%
Psychiatric	14.9%	62.4%
Medical	27.9%	31.3%
Drug use	69.7%	75.5%
Compliance	7.4%	17.7%
Social-Residential	10.4%	53.2%
Average	21.8%	40.2%

Relative risk of being excluded for African-Americans versus patients of other races

Neurological	<i>na</i>
Psychiatric	0.95
Medical	0.86
Drug use	1.08
Compliance	0.44
Social-Residential	1.13

Relative risk of being excluded for Women versus Male patients

Neurological	1.09
Psychiatric	1.11
Medical	1.01
Drug use	1.15
Compliance	0.47
Social-Residential	1.14

Summary of findings

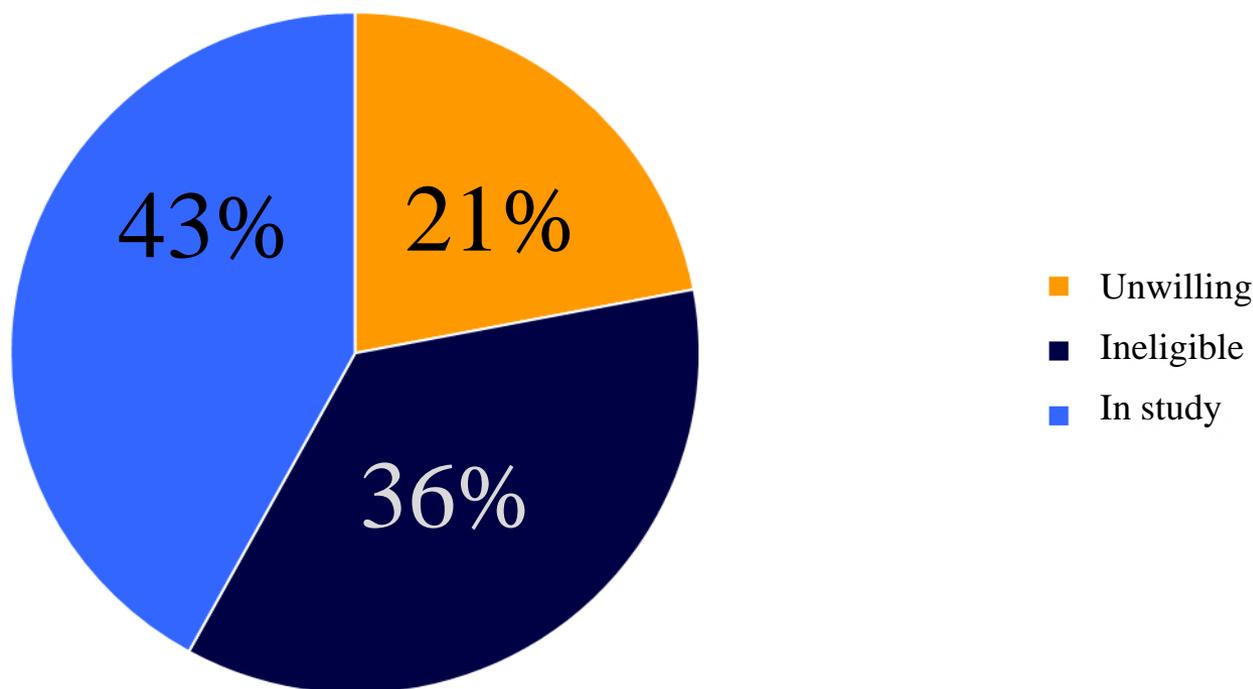
- Not all criteria are of concern (neurological)
- Social-residential and drug use criteria exclude high proportions of patients, especially women and African-Americans
- Other criteria (e.g., compliance) may work in the opposite direction

Other related findings

- In both public and private systems, exclusion is related to:
- Being African-American
- Being low income
- Having more severe comorbidities

Source: Humphreys, K., & Weisner, C. (2000). Am J Psychiatry, 157, 588-594.

Less than half of drug dependent patients are eligible and willing to participate in RCTs



Depression Studies Also Have Low Enrollment Rates

- Study of 216 consecutive real-world depression patients in outpatient care
- Applied 28 eligibility criteria from an ongoing double-blind RCT
- 215 patients ineligible
- The 1 eligible patient refused to participate!

Studies of study exclusion rates for other disorders

<u>Disorder</u>	<u>% Excluded</u>
Cancers	~50%-70%
CVD	~65%-85%
Panic disorder	~50%
SCZ	~80%
Alzheimer's	~90-95%

Summary of study #2 findings and related work

- A high proportion of real-world alcohol patients are ineligible under most common criteria
- Those excluded tend to be from socially marginal groups which NIH mandates be included
- Not correctable by over-sampling

Study 3: Can eligibility criteria change the outcomes a study obtains?

For details see: Humphreys, K., Harris, A.S., & Weingardt, K. (2008). Subject eligibility criteria can substantially influence the results of alcohol treatment outcome research. Journal of Studies on Alcohol and Drugs, 69, 757-764.

Logic of Study 3

- Bias in outcome estimates is a function of two factors:
- Size of excluded group
- Difference between outcomes of excluded and included patients
- Can test bias using same method as Study 2

Washington State as example

- Patients followed up at 6 months
- ASI Alcohol Composite Index Improvement used as outcome
- Mean improvement 0.28 on a 0-1 scale

Effects on ASI composite score of applying criteria

Psychiatric	8.7% worse outcomes
Medical	10.1% worse outcomes
Drug use	7.2% better outcomes
Compliance	5.8% better outcomes
Social-Residential	15.6% better outcomes

What this means practically

- A treatment with a true success rate of 50%
- Could look like a treatment with a 60% rate if the researcher excluded non-compliant and homeless patients
- Or like a treatment with a 40% rate if the researcher didn't exclude patients with medical/psychiatric co-morbidities

Implications

- Research studies can be designed to generate substantially different outcomes than does everyday practice
- Integration of studies across the literature must consider eligibility criteria

Other key point

- Review of RCTs in influential medical journals by Van Spall et al
- Less than half of eligibility criteria employed were well-justified
- Current status of criteria appears to be that they “go without saying”

Implications across all studies

- Eligibility criteria should be better tailored and reported
- Need to shift to viewing them as like any other methodological decision
- Drug use criteria may not be justifiable
- High bar should be set for those criteria that exclude marginalized groups and/or dramatically changes study conclusions

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Thank you for your attention
Questions/Comments?

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