

2021 NIMH TRIENNIAL REPORT CERTIFYING ADHERENCE TO THE NIH POLICY ON THE INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH AS REPORTED FOR FISCAL YEARS 2019 – 2021

Background/Overview

The National Institutes of Health (NIH) Revitalization Act of 1993 (P.L. 103-43) mandated that the advisory council of each Institute prepare a biennial report describing the manner in which the Institute has complied with requirements regarding the inclusion of women and minorities in clinical research. Enacted December 13, 2016, the 21st Century Cures Act (P.L. 114-255) contained measures to assess, report, and improve inclusion of key demographic groups (groups that reflect diversity of sex, age, and minority status) to advance understanding health disparities between different demographic groups. The 21st Century Cures Act also amended the frequency of the Report of the NIH Director on the inclusion of women and minorities from biennial to triennial. The NIH is mandated (NIH Revitalization Act of 1993, P.L. 103-43 (Public Health Service Act sec. 492B, 42 U.S.C. sec. 289a-2)) to ensure that women and minorities are included in NIH-funded clinical research in a manner that is appropriate to the scientific question under study, and that NIH-defined Phase III clinical trials are designed in a manner sufficient to examine differential effects of interventions on both women and men, as well as individuals of diverse racial and ethnic groups. As a result, the NIH established policies and guidelines for inclusion of women and minorities in clinical research.¹

This report details the National Institute of Mental Health's (NIMH) strategies for maintaining compliance with these inclusion policies and guidelines and provides data on extramural and intramural clinical research and Phase III clinical trials. As the NIH inclusion guidelines apply to studies both within and outside the United States, data are presented for all NIMH studies (both domestic and foreign). The data reflect the breadth of the clinical research supported by NIMH to fulfill its mission to transform the understanding and treatment of mental illnesses through basic and clinical research, paving the way for prevention, recovery, and cure. The NIMH clinical research portfolio includes large-scale clinical trials and observational studies, as well as smaller studies in basic, translational, and services research.

Strategies for Ensuring Compliance

NIMH follows several steps to ensure compliance with the NIH inclusion policy and guidelines. NIH policies and changes to the policies are disseminated via NIH Guide Notices. In grant applications² involving human subjects research, applicants are required to include plans for the inclusion of women and minorities and individuals across the lifespan. Applicants can seek assistance from program officials in developing inclusion plans. Once the grant application is received by NIMH, the implementation of inclusion guidelines involves the participation of review, program, policy, and grants management staff.

Upon receipt of the grant application, inclusion is first addressed by peer review. Individuals serving on NIH scientific review groups are given specific [guidance](#) for evaluating applications for the appropriateness of the proposed plan for inclusion by age, sex/gender, racial, and ethnic minority enrollment goals, as well as the recruitment plans that explain how the applicant will

¹ For further information about the guidelines, please see https://grants.nih.gov/grants/funding/women_min/guidelines.htm

² Refer to the Public Health Service (PHS) Human Subjects and Clinical Trial Information Form Instructions for complete guidance on what should be addressed (<https://grants.nih.gov/grants/how-to-apply-application-guide/forms-e/general/g.500-phs-human-subjects-and-clinical-trials-information.htm#top>).

meet these goals. For NIH-defined Phase III clinical trials, reviewers further assess enrollment goals for plans to conduct analyses of intervention effects among sex/gender, racial minority groups, and ethnic minority groups. Scientific review groups make recommendations as to the acceptability of the proposed study population with respect to the inclusion policies. Unacceptable inclusion plans must be reflected in the priority score of the application and documented in the summary statement. Applications with unacceptable inclusion plans receive a bar to funding which must be resolved prior to award of the grant or cooperative agreement. In the case of a bar to funding, the program official associated with the grant application notifies the grant applicant. The program official reviews the revised inclusion plan (and if applicable, the inclusion enrollment report) and works with the NIMH Office of Clinical Research (OCR) to ensure the revisions adequately address the inclusion concerns. Once satisfactory, the inclusion plan is returned to the NIMH program official and the Division of Extramural Activities Grants Management Branch, and the bar to funding is lifted. This response is kept in the official grant file, along with a record of administrative actions taken.

As noted above, program officials are also involved in the implementation of the NIH inclusion policies/guidelines. For all grants that include participation of human subjects, program officials review the inclusion plan in the application and indicate whether it is scientifically appropriate. NIMH program officials monitor actual enrollment progress in annual progress reports and provide consultation to investigators when necessary. For NIH-defined Phase III clinical trials, program officials monitor the requirement for sex/gender, race, and ethnicity analyses in applications and annual progress reports. In addition to program officials' activities over the life of the grant, grants management staff ensure that appropriate terms and conditions of award are included in the Notice of Award, and that this information is appropriately documented in the official grant file.

All intramural clinical research studies require investigators to provide plans for the appropriate inclusion of women and minorities and individuals across the lifespan, and/or a justification whenever representation is limited or absent, as part of their NIH protocol reviews. Intramural Institutional Review Boards (IRBs) review research protocols for compliance with inclusion guidelines and conduct annual monitoring. With each annual review and renewal, the investigator documents the number, sex/gender, and race and ethnicity of participants accrued during the past year; any issues with accrual are addressed by the investigator at the IRB annual review and evaluated by the pertinent IRB. The NIH Clinical Center's Office of Protocol Services (OPS) maintains centralized systems for capturing accrual data including sex/gender, ethnic, and racial status. OPS coordinates annual reporting of participant's demographic data to the NIH Office of Extramural Research (OER) and the NIH Office of Research on Women's Health (ORWH).

For NIMH extramural clinical research studies, OCR monitors the entry of inclusion data, performs quality assurance tasks, prepares aggregate reports for the National Advisory Mental Health Council and the NIH ORWH, and provides up-to-date training on procedures for ensuring the accuracy of inclusion data, as well as on the use of the electronic Human Subjects System (HSS). OCR provides this training through individual assistance and the provision of training materials to staff. In addition, NIMH program officials/program directors and scientific review officers had the opportunity to attend the 2020 Inclusion Training for Program Staff and the 2020 Inclusion Training for Review Staff in April 2020. Staff may access the archived training on the NIH staff intranet. There are additional training opportunities for NIMH staff to learn about addressing inclusion, such as the NIH Integrated Core Curriculum series and training on HSS facilitated by the NIH OER.

Analysis and Interpretation of Data

The appended tables show enrollment data for FY 2019 to FY 2021. Included in the tables are enrollment data for all extramural and intramural clinical research. Inclusion data are reported using the Office of Management and Budget's (OMB) revised 1997 racial and ethnic categories, which are required for the collection, tabulation, and presentation of race and ethnicity data within the Federal Statistical System.³ When assessing inclusion data, it is important to keep in mind that the number of individuals in sex/gender, racial, and ethnic subgroups included in a particular study depends upon the scientific questions addressed in the study and the prevalence or incidence among these subgroups of the disease, disorder, or condition under investigation.

To preview the significant trends in the inclusion data for FY 2019 to FY 2021, there was an overall increase in participant enrollment in NIMH-funded extramural and intramural clinical research. Between FY 2019 and FY 2021, there was a sharp increase in participant enrollment in NIH-defined Phase III clinical trials. Notably, however, increases were not evident across all racial and ethnic minority groups. For example, there was a proportional decrease in African American enrollment into extramural research studies and Phase III clinical trials. As noted below, NIMH is aware that the COVID-19 pandemic significantly impacted the research enterprise and likely influenced trends evident in this data.

Table 1 displays the total inclusion enrollment records⁴ (IERs) for NIH-defined extramural and intramural clinical research for FY 2019, FY 2020, and FY 2021. The total number of IERs increased slightly from FY 2019 to FY 2021. On average, 59 percent of the IERs had enrollment; IERs without enrollment increased across the fiscal years. IERs without enrollment include studies that were not yet recruiting participants during the given fiscal year. Also, due to the COVID-19 pandemic, institutions conducting clinical research experienced delays in study timelines and for some, a complete halt of operations, which significantly impacted enrollment into clinical research studies across the fiscal years.

Table 2 displays the sex/gender by racial and ethnic distribution of participants in NIH-defined extramural and intramural clinical research in FY 2019, FY 2020, and FY 2021. Participant enrollment increased and sex/gender enrollment remained relatively consistent with slightly more females enrolled than males across the fiscal years. The large increase in participant enrollment from FY 2019 to FY 2020 may be accounted for by an extramural clinical research study which launched in FY 2020 and enrolled a large number of participants. Across FY 2019 to FY 2021, total racial and ethnic minority enrollment gradually decreased. This may be explained, in part, by a decrease in Black or African American participant enrollment during this time. Although the overall number of Black or African American participants increased between FY 2019 and FY 2020, due to the overall participant enrollment increase, the percentage of Black or African American participants decreased. The percentage of Black or African American participants further decreased in FY 2021.

The next largest racial and ethnic minority group is Asian, followed by More Than One Race, American Indian/Alaska Native, and Hawaiian/Pacific Islander. The percentage of participants who reported Hispanic ethnicity marginally increased from FY 2019 to FY 2020 and remained consistent in FY 2021. Percentages for Unknown/Not Reported race and ethnicity increased

³For more information about revised racial and ethnic categories required by OMB revisions to Statistical Policy Directive 15, see https://nces.ed.gov/programs/handbook/data/pdf/Appendix_A.pdf.

⁴The inclusion enrollment report is used to report both planned and cumulative (or actual) enrollment, and the sex/gender, race, ethnicity, and age of enrollment of the study participants.

from FY 2019 to FY 2020 and remained consistent in FY 2021. These increases from FY 2019 to FY 2020 for Unknown/Not Reported race and ethnicity may be accounted for by an intramural large-scale online study, an extramural project that is building a genetic bank in underrepresented populations, and a large extramural pragmatic trial implementing collaborative care for perinatal depression.

Tables 3 displays the sex/gender by racial and ethnic distribution of participants in NIH-defined extramural and intramural Phase III clinical trials for FY 2019, FY 2020, and FY 2021. In FY 2019, FY 2020, and FY 2021 NIMH supported 48, 39, and 67 NIH-defined extramural and intramural Phase III clinical trials, respectively. Participant enrollment in Phase III clinical trials notably increased from FY 2020 to FY 2021. The large increase may be accounted for by two extramural research studies (approximately 47 percent)—one large-scale trial utilizing mobile technology in college populations with mental disorders and a pragmatic trial evaluating strategies for the implementation of an eHealth HIV prevention program. There were slight fluctuations in female representation from FY 2019 to FY 2021. From FY 2019 to FY 2021, Black or African American participant enrollment accounted for about 67 percent of enrollment into Phase III clinical trials, the largest racial minority group in Phase III clinical trials. In FY 2019, the large percentage for Black or African American participant enrollment in Phase III clinical trials may be accounted for by an extramural trial evaluating a community support worker intervention for HIV which completed enrollment that year. Although the number of Black or African American participants remained relatively consistent in FY 2019 and FY 2020, due to the overall increase in participant enrollment, the percentage for Black or African American participants decreased. Similarly, in FY 2021, the number of Black or African American participants significantly increased; however, the overall Phase III clinical trial participant enrollment increased sharply which accounts for the reduction in this group's enrollment percentage.

Participants who reported American Indian/Alaska Native and Hawaiian/Pacific Islander increased across the fiscal years. Across FY 2019 to FY 2021, there were increases in the percentage of individuals who reported Hispanic ethnicity. The large increase in enrollment among individuals who reported Hispanic ethnicity from FY 2020 to FY 2021 may be accounted for by three extramural projects—a large-scale trial utilizing mobile technology in college populations with mental disorders, a pragmatic trial evaluating strategies for the implementation of an eHealth HIV prevention program, and a trial evaluating the effects of internet-based cognitive behavioral therapy in college students with mental disorders.

As noted above, NIH-defined Phase III clinical trials should be designed in a manner sufficient to provide for valid analyses of whether the variables being studied affect women or members of racial and ethnic minority groups differently than other trial participants. Recipients conducting applicable⁵ NIH-defined Phase III clinical trials must ensure results of valid analyses⁶ by sex/gender, race, and/or ethnicity are submitted to [Clinicaltrials.gov](https://clinicaltrials.gov). NIH-defined

⁵Applicable clinical trial is the term used in Title VIII of the Food and Drug Administration Amendments Act (FDAAA) of 2007 (P.L. 110-85) to designate the scope of clinical trials that may be subject to the registration and results reporting requirements in FDAAA. Clinical trials that are subject to the regulation are, in general, clinical trials of drug, biological, and device products regulated by the Food and Drug Administration (FDA). A pediatric post-market surveillance study of a device product required by the FDA is also subject to the regulation.

⁶This term means an unbiased assessment. Such an assessment will, on average, yield the correct estimate of the difference in outcomes between two groups of subjects. Valid analysis can and should be conducted for both small and large studies. A valid analysis does not need to have a high statistical power for detecting a stated effect. The principal requirements for ensuring a valid analysis of the question of interest are: allocation of study participants of both sexes/genders (males and females) and from different racial and/or ethnic groups to the intervention and control groups by an unbiased process such as randomization; unbiased evaluation of the outcome(s) of study participants;

Phase III clinical trials that required valid analyses by sex/gender and race and/or ethnicity for FY 2019, FY 2020 and FY 2021 were 92 percent, 95 percent, and 87 percent, respectively. An alternative way to review inclusion data is by Research, Condition, and Disease Categorization (RCDC). The total number of participants enrolled in projects associated with listed research, condition, or disease category can be displayed by sex/gender, race, and ethnicity. RCDC category reports for inclusion data for NIMH are available upon request. After March 1, 2022, the reports can be found at <https://report.nih.gov/RISR/>.

Tables

1. Table 1. FYs 2019-2021 Total Inclusion Enrollment Records (IERs) for NIH-Defined Extramural and Intramural Clinical Research
2. Table 2: FYs 2019-2021 Enrollment for All NIH-Defined Clinical Research, Sex/Gender by Race and Ethnicity
3. Table 3. FYs 2019-2021 Enrollment for NIH-Defined Extramural and Intramural Phase III Clinical Research, Sex/Gender by Race and Ethnicity

and use of unbiased statistical analyses and proper methods of inference to estimate and compare the intervention effects by sex/gender, race, and/or ethnicity.

Tables

Table 1. FYs 2019-2021 Total Inclusion Enrollment Records (IERs) for NIH-Defined Extramural and Intramural Clinical Research

Fiscal Year	Total IERs	IERs Without Enrollment	IERs With Enrollment	US Site IERs	Non-US Site IERs	Female Only IERs	Male Only IERs	IERs Excluding Male only and Female only*
2019	1,696	565	1,131	982	149	103	53	975
2020	2,040	864	1,176	1,011	165	110	60	1,006
2021	2,196	1,012	1,184	1,026	158	119	58	1,007

*Inclusion Enrollment Records (IERs) excluding male-only and female-only include unknown sex/gender, and combination of unknown and any sex/gender(s).

Table 2: FYs 2019-2021 Enrollment for All NIH-Defined Clinical Research, Sex/Gender by Race and Ethnicity

Fiscal Year	Sex Gender	Minority	% Minority	Total Enrollment	% Total	AI/AN	% AI/AN	Asian	% Asian	AA	% AA	PI	% PI	White	% White
2019	Female	88,022	61.4	143,310	51.8	679	0.5	15,883	11.1	56,090	39.1	363	0.3	57,539	40.2
2019	Male	77,090	61.1	126,173	45.6	579	0.5	16,490	13.1	46,321	36.7	402	0.3	51,032	40.4
2019	Unknown	269	3.7	7,212	2.6	23	0.3	38	0.5	89	1.2	3	0.0	399	5.5
2020	Female	113,377	58.8	192,740	53.8	1,576	0.8	23,511	12.2	65,758	34.1	317	0.2	77,878	40.4
2020	Male	87,368	57.4	152,323	42.5	1,083	0.7	25,597	16.8	45,136	29.6	285	0.2	61,116	40.1
2020	Unknown	655	5.0	13,092	3.7	24	0.2	91	0.7	265	2.0	15	0.1	727	5.6
2021	Female	102,541	50.6	202,731	53.9	1,666	0.8	20,121	9.9	55,378	27.3	362	0.2	93,268	46.0
2021	Male	84,485	51.1	165,244	43.9	1,313	0.8	22,029	13.3	41,729	25.3	305	0.2	74,757	45.2
2021	Unknown	1,309	15.9	8,255	2.2	38	0.5	272	3.3	493	6.0	5	0.1	1,665	20.2

Fiscal Year	Sex Gender	MTOR	% MTOR	U/NR	% U/NR	Not Hispanic	% Not Hispanic	Hispanic Latino	% Hispanic Latino	U/NR	% U/NR
2019	Female	6,771	4.7	5,985	4.2	125,673	87.7	13,077	9.1	4,560	3.2
2019	Male	5,945	4.7	5,404	4.3	110,277	87.4	11,789	9.3	4,107	3.3
2019	Unknown	68	0.9	6,592	91.4	2,793	38.7	77	1.1	4,342	60.2
2020	Female	8,191	4.2	15,509	8.0	158,945	82.5	20,103	10.4	13,692	7.1
2020	Male	6,377	4.2	12,729	8.4	126,265	82.9	14,398	9.5	11,660	7.7
2020	Unknown	134	1.0	11,836	90.4	3,084	23.6	207	1.6	9,801	74.9
2021	Female	12,928	6.4	19,008	9.4	164,160	81.0	21,105	10.4	17,466	8.6
2021	Male	9,073	5.5	16,038	9.7	132,615	80.3	16,959	10.3	15,670	9.5
2021	Unknown	296	3.6	5,486	66.5	4,164	50.4	339	4.1	3,752	45.5

The data presented in this report show only inclusion data records labeled as prospective data. Inclusion data records labeled as existing data are excluded. [Abbreviations: American Indian/Alaska Native = AI/AN; Black/African American = AA; Native Hawaiian/Pacific Islander = PI; More Than One Race= MTOR; Unknown/Not Reported = U/NR]

Table 3. FYs 2019-2021 Enrollment for NIH-Defined Extramural and Intramural Phase III Clinical Research, Sex/Gender by Race and Ethnicity

Fiscal Year	Sex Gender	Minority	% Minority	Total Enrollment	% Total	AI/AN	% AI/AN	Asian	% Asian	AA	% AA	PI	% PI	White	% White
2019	Female	1,573	93.2	1,688	63.6	1	0.1	3	0.2	1,545	91.5	0	0.0	130	7.7
2019	Male	895	92.7	965	36.4	1	0.1	3	0.3	879	91.1	0	0.0	75	7.8
2019	Unknown	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
2020	Female	1,636	70.0	2,337	71.8	6	0.3	23	1.0	1,510	64.6	10	0.4	739	31.6
2020	Male	805	88.0	915	28.1	3	0.3	14	1.5	715	78.1	1	0.1	140	15.3
2020	Unknown	5	100.0	5	0.2	0	0.0	0	0.0	5	100.0	0	0.0	0	0.0
2021	Female	5,202	59.6	8,728	66.4	88	1.0	684	7.8	3,219	36.9	60	0.7	3,908	44.8
2021	Male	3,099	70.6	4,392	33.4	55	1.3	324	7.4	2,070	47.1	17	0.4	1,535	34.9
2021	Unknown	15	57.7	26	0.2	0	0.0	3	11.5	5	19.2	0	0.0	12	46.2

Fiscal Year	Sex Gender	White	% White	MTOR	% MTOR	U/NR	% U/NR	Not Hispanic	% Not Hispanic	Hispanic Latino	% Hispanic Latino	U/NR	% U/NR
2019	Female	130	7.7	4	0.2	5	0.3	1,666	98.7	22	1.3	0	0.0
2019	Male	75	7.8	6	0.6	1	0.1	954	98.9	10	1.0	1	0.1
2019	Unknown	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
2020	Female	739	31.6	29	1.2	20	0.9	2,264	96.9	71	3.0	2	0.1
2020	Male	140	15.3	13	1.4	29	3.2	832	90.9	72	7.9	11	1.2
2020	Unknown	0	0.0	0	0.0	0	0.0	5	100.0	0	0.0	0	0.0
2021	Female	3,908	44.8	625	7.2	144	1.6	7,451	85.4	1,270	14.6	7	0.1
2021	Male	1,535	34.9	217	4.9	174	4.0	3,732	85.0	660	15.0	0	0.0
2021	Unknown	12	46.2	3	11.5	3	11.5	19	73.1	6	23.1	1	3.8

The data presented in this report show only inclusion data records labeled as prospective data. Inclusion data records labeled as existing data are excluded. [Abbreviations: American Indian/Alaska Native = AI/AN; Black/African American = AA; Native Hawaiian/Pacific Islander = PI; More Than One Race= MTOR; Unknown/Not Reported = U/NR]