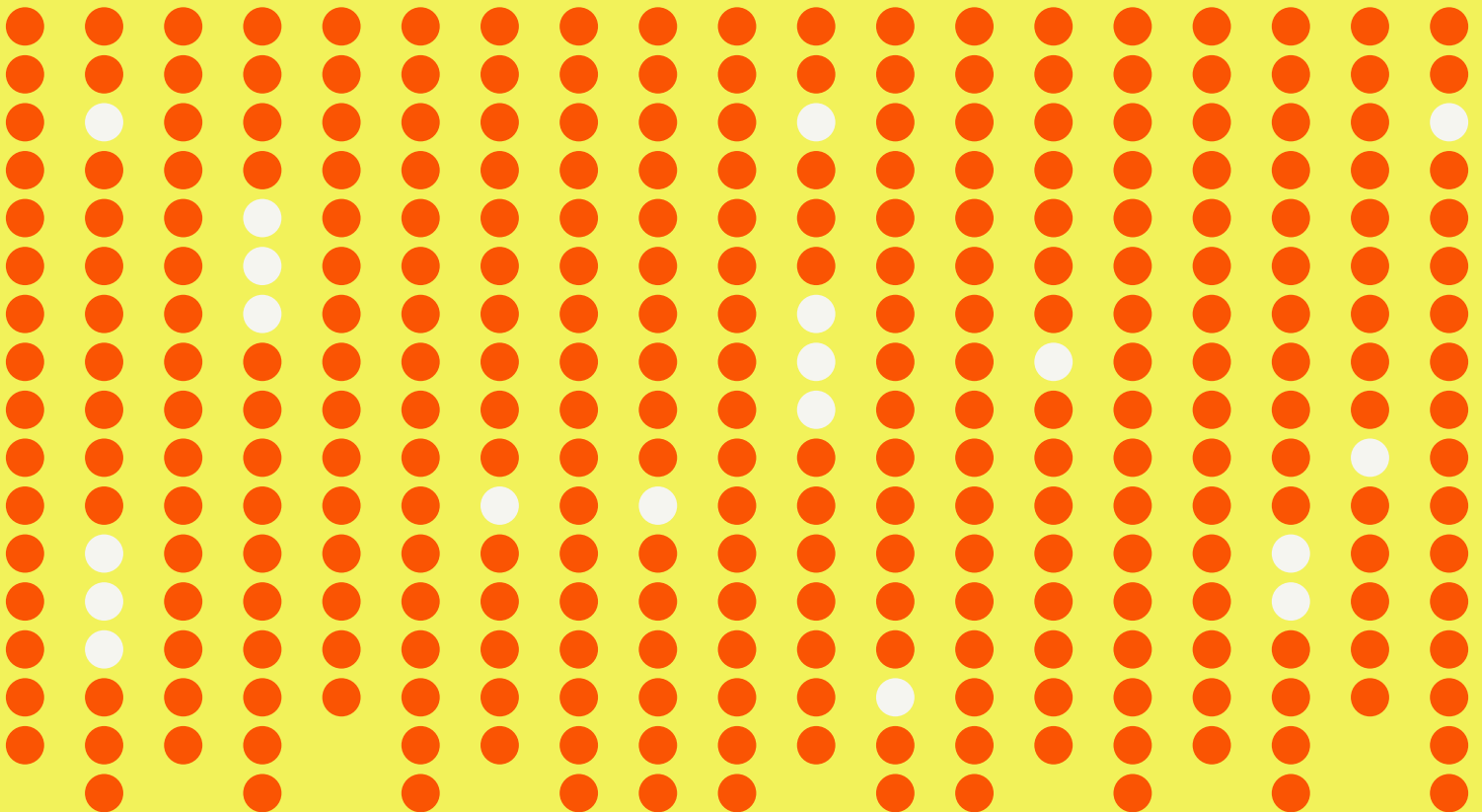


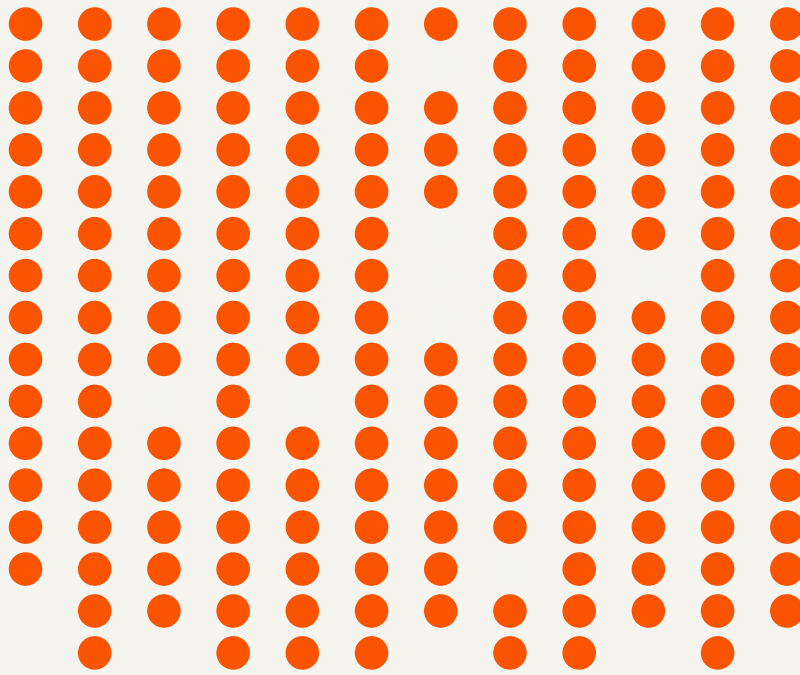


November 2023

# Demographic Reporting and Mix in Clinical Trials

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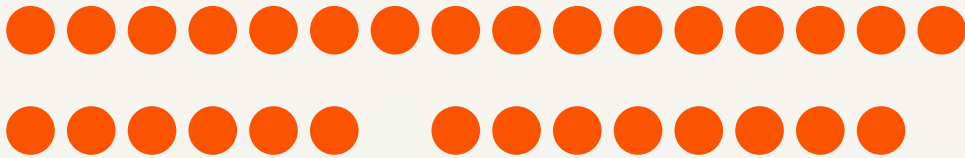


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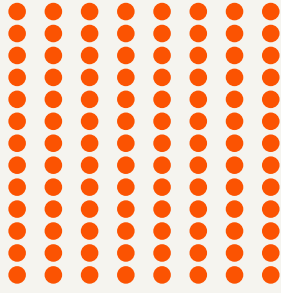
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# Background

Clinical trial enrollment can vary based on demographics. Cancer drug trials, for example, have been shown to skew disproportionately toward young, White, male participants (Murthy et al. 2004, Varma et al. 2023). There can also be variability in a treatment’s impact and effectiveness across different demographic groups. As another example, many medications have meaningful pharmacological differences based on sex and race (Kaiser 2005, Soldin and Mattison 2009, Whitley and Lindsey 2009, Pierson et al. 2021).

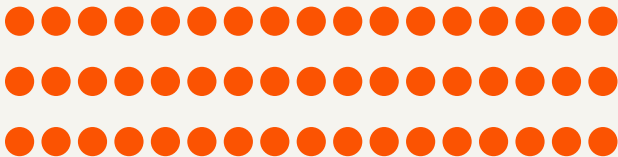
Gaps in the amount of trial data collected for a demographic group could lead to that group receiving treatments that were developed on a knowledge base that was not completely applicable. This means that disparities in trial enrollment could result in disparities in the quality of care available in the future as treatments are recommended, prescribed, and used on the basis of imperfect information for understudied populations. There is also evidence that under-recruitment of a population depresses subsequent investment in drugs to treat that population, as it becomes more costly for developers to determine whether an investment in a drug for that group will be worthwhile. The uncertainty around returns makes firms less likely to invest (Michelman and Msall 2022).

A broad accounting of how frequently demographics are publicly reported—and how those demographics vary across clinical trials—is missing from the current literature and related discussion. This report seeks to fill that gap by quantifying the number of studies with and without demographic information (sex, ethnicity, or race). For studies that include demographic information, we investigate how the demographic distributions vary across studies and compare these distributions to the general population. This provides a baseline for where the sector currently stands and context for future changes in demographic reporting and balance.

# Data

We use the Clinical Trials Transformation Initiative's Aggregate Analysis of ClinicalTrials.gov (AACT) database to analyze ClinicalTrials.gov registration data (AACT 2022) as of May 15, 2022. The AACT data are publicly available and updated daily for online queries. AACT also releases static database copy files (a full snapshot of all data retrieved from ClinicalTrials.gov as of a given date) for download. All analyses that follow were conducted using the May 15, 2022, static copy. The AACT database is well described on its website and in associated literature; in short, the AACT is an accurate snapshot of the data recorded on ClinicalTrials.gov (AACT 2022, Tasneem et al. 2012).

ClinicalTrials.gov is the central online public database for clinical research studies involving human participants and encompassing both clinical trials and observational studies. In clinical trials, an intervention aimed at treating or preventing a condition is actively administered to the study population by the investigator for a predetermined duration. In observational studies, by contrast, patients receive treatment according to clinical decisions, and health outcomes are recorded over time. Drug trials (clinical trials of pharmaceuticals and biological products) are a subset of clinical trials, and clinical trials also include studies of devices, surgical techniques, and non-pharmacological interventions, such as diet, exercise regimens, community health interventions, or cognitive behavioral therapy.



## What Information Is Reported and When?

When a trial is initially registered on ClinicalTrials.gov, certain data are always reported. These include the study title, a description of the study, details about the study protocol, and the condition targeted by the treatment. Registration is the mechanism that causes a study to appear in the ClinicalTrials.gov database.

While the initial registration includes basic information about the target population (such as whether the study will only include female subjects), detailed demographic information about the study population is not included at this stage. That information is included in a subsequent data submission: the posting of study results. When results are posted, they include the number of individuals in each treatment arm, their outcomes, and information on their demographics (to the extent that such information was collected).

To review the demographics in a clinical trial using the AACT data, the trial needs (i) to be registered on ClinicalTrials.gov, (ii) to have posted the study results, and (iii) to include relevant demographic information as part of the posted results. Only registered studies can be analyzed, as unregistered studies do not appear in the data. Given this population of registered studies, the following analyses summarize which studies eventually post their results, the frequency with which each demographic is reported in posted results, and finally—for the studies that meet the above criteria—what the demographic balance looks like.

## Reporting Requirements

Reporting requirements for ClinicalTrials.gov have changed over time. A detailed history of ClinicalTrials.gov can be found at the following site: <https://classic.clinicaltrials.gov/ct2/about-site/history>. ClinicalTrials.gov launched in 2000 as a public information resource under the requirements of the Food and Drug Modernization Act of 1997.

Several key policy changes surrounding required reporting have occurred since ClinicalTrials.gov launched. The first is that in 2004, the International Committee of Medical Journal Editors (ICMJE) required the registration of clinical trials as a prerequisite for publication. This requirement was only for registration, not the eventual posting of results.

The second major policy change was the Food and Drug Administration Amendments Act of 2007 (FDAAA), which required certain types of trials to register with ClinicalTrials.gov, set requirements for results reporting, and introduced civil penalties for noncompliance. The exact rules for reporting (in terms of who was required to report and in what timeframe) remained in flux until 2017, when the “Final Rule” for the FDAAA was fully implemented. In the intermediate timeframe between 2007 and 2017, stricter reporting requirements were gradually enacted. The full text of the Final Rule can be found in the Federal Register (Clinical Trials Registration and Results Information Submission 2016; <https://www.federalregister.gov/documents/2016/09/21/2016-22129/clinical-trials-registration-and-results-information-submission>).

The Final Rule applies to all “Applicable Clinical Trials” (ACTs). To be considered an ACT, a study must meet the following conditions: (1) be a clinical study; (2) assess a drug, biologic, or device that

the FDA regulates; (3) not be a Phase 1 or device feasibility study; and (4) be related to eventual FDA approval, related to eventual US exporting, or conducted in a US facility.

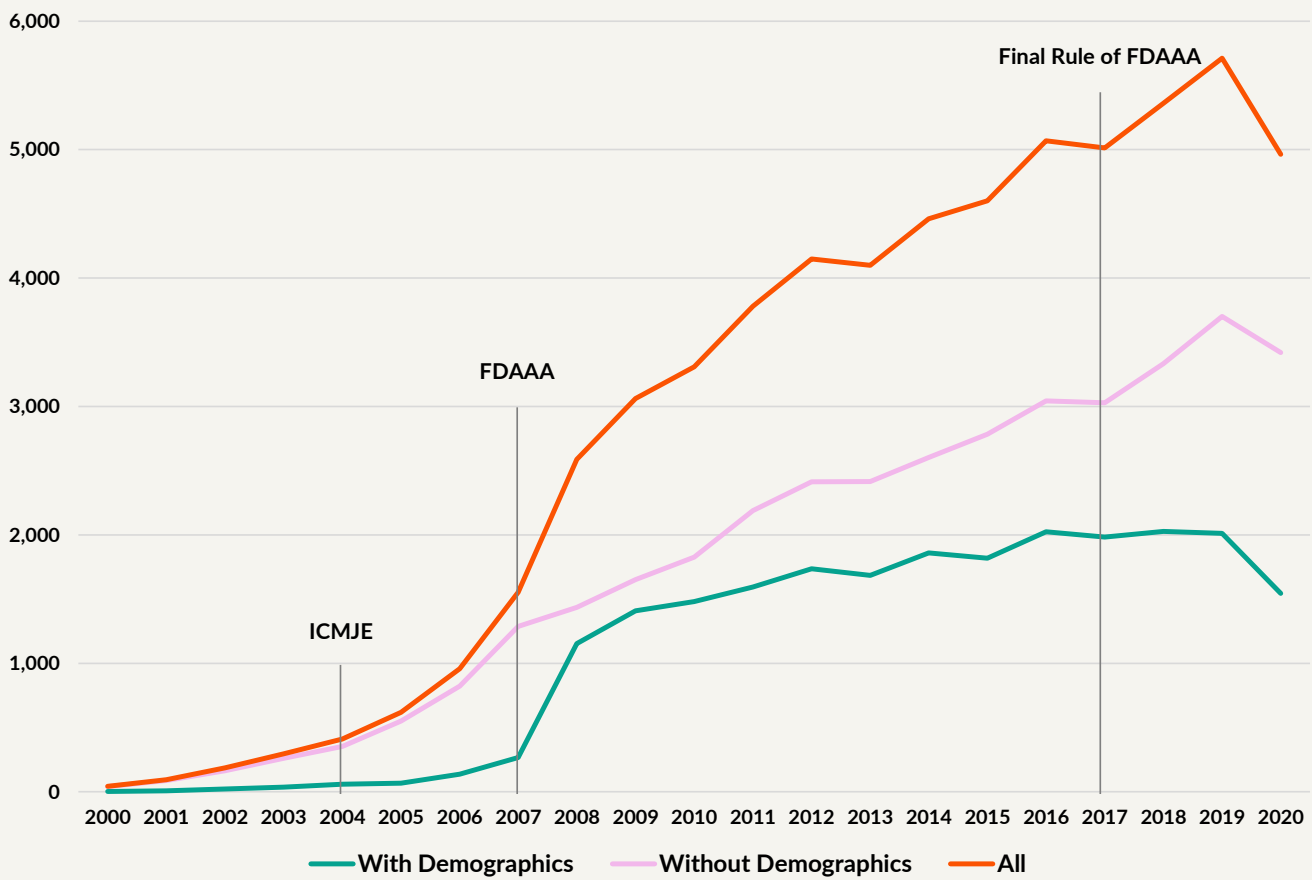
For all ACTs, results are generally required to be submitted within one year of study completion, but some exceptions allow for a delay. For example, if a drug, biologic, or device will continue to be developed (or may continue to be developed), then the responsible entity can delay reporting of results until either final approval or clearance is being sought or until development of the product is terminated. This would mean that results for a registered Phase 2 study might not be reported to ClinicalTrials.gov until the separately registered Phase 3 study was complete, or that unsuccessful Phase 3 results might not be reported to ClinicalTrials.gov until the sponsor decided to abandon future development. These exceptions to the one-year deadline allow for potentially long delays in reporting results.

The third major policy change came from the National Institutes of Health (NIH) and was timed to coincide with the full implementation of the FDAAA Final Rule. NIH policy was adjusted so that as of January 18, 2017, any clinical trial funded by the NIH, regardless of whether it is an ACT under the FDAAA Final Rule, is required to be registered with and submit results to ClinicalTrials.gov.

## Sample Inclusion Criteria

Figure 1 shows the time-trend for US clinical studies reported annually to ClinicalTrials.gov, as well as the time-trends for the number of studies that did and did not include demographics (a study may not include demographic information either because no results have yet been reported or because it reported results that did not include demographics).

**Figure 1. Annual Counts of US Clinical Studies in ClinicalTrials.gov**



Source: Milken Institute (2023); AACT Database (2022)

The ICMJE required the registration of clinical trials as a prerequisite for publication in 2004, which was immediately followed by an acceleration of the number of trials reported, but not the number of reported trials that included demographic information. There was another rapid increase in the number of reported trials and an increase in the proportion of studies that reported any demographic information after the initial enactment of the FDAAA.

The registration and results-reporting requirements were fully implemented in 2017 with the full enactment of the Final Rule. Under the Final Rule, sex or gender is required to be reported, and

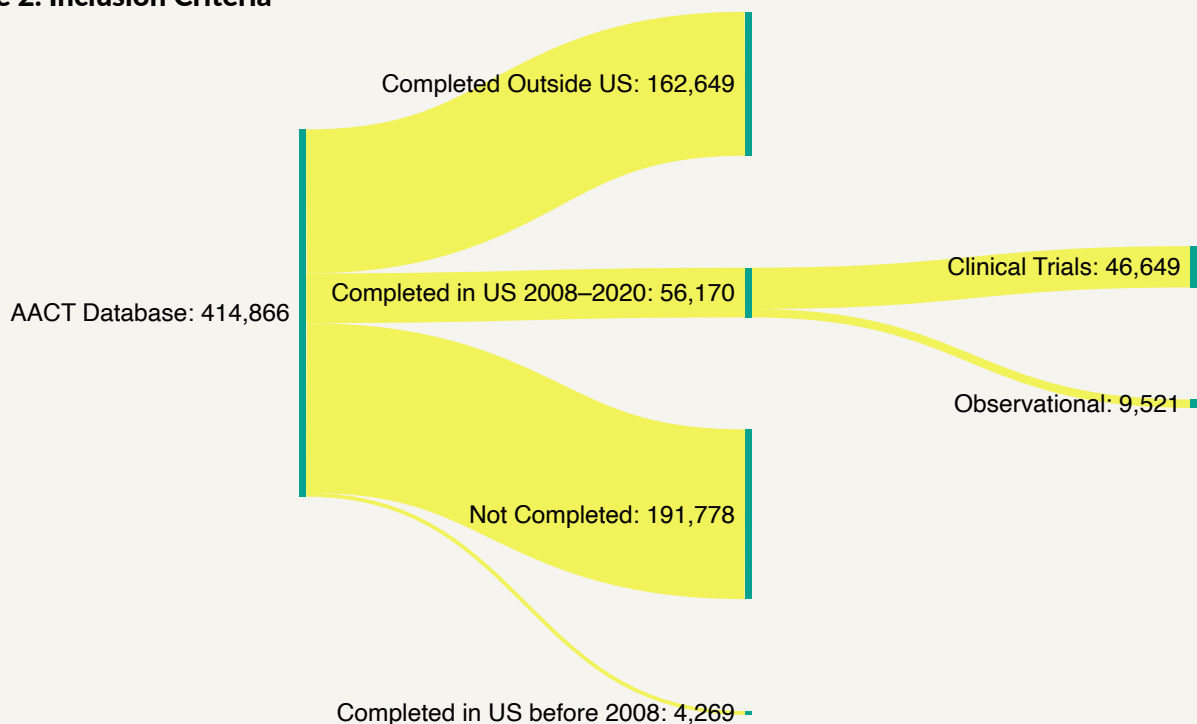
The ICMJE required the registration of clinical trials as a prerequisite for publication in 2004, which was immediately followed by an acceleration of the number of trials reported, but not the number of reported trials that included demographic information.

race/ethnicity is required if the study’s completion date is on or after January 18, 2017. That said, the language of the rule leaves some ambiguity. Some demographic information is required “if collected under the protocol,” which seems to imply that if the study protocol does not include the collection of demographic information, then reporting is not required. In 95.8 percent of studies in our final sample, the reported variable is sex (biologic designation), as opposed to 4.2 percent of studies where the reported variable is gender (individual identity). We will refer to this variable as sex, with the understanding that in some cases what was reported was actually gender. When gender was collected in lieu of sex, and a study participant reports as neither male nor female, we do not include that study participant in our counts for calculating male/female balance (these observations make up less than 0.001 percent of the data).

Our analysis sample includes US clinical studies completed between January 1, 2008 and December 31, 2020. This sampling window captures the timeframe during which a non-negligible number of trials reported demographic information and during which the proportion of studies reporting such information was relatively stable.

As of May 15, 2022, the AACT database included 414,886 registered studies. We exclude 4,269 US studies that were completed prior to 2008 (1 percent of the data), 162,649 studies that were completed outside of the US (39 percent of the data), and 191,778 studies that were registered but not yet completed (46 percent of the data). This leaves 56,170 clinical studies completed at the US-located facilities between 2008 and 2020. Of these studies, 83 percent (46,649) are clinical trials, and 17 percent (9,521) are observational studies. Figure 2 illustrates the study inclusion criteria.

**Figure 2. Inclusion Criteria**



Source: Milken Institute (2023); AACT Database (2022)

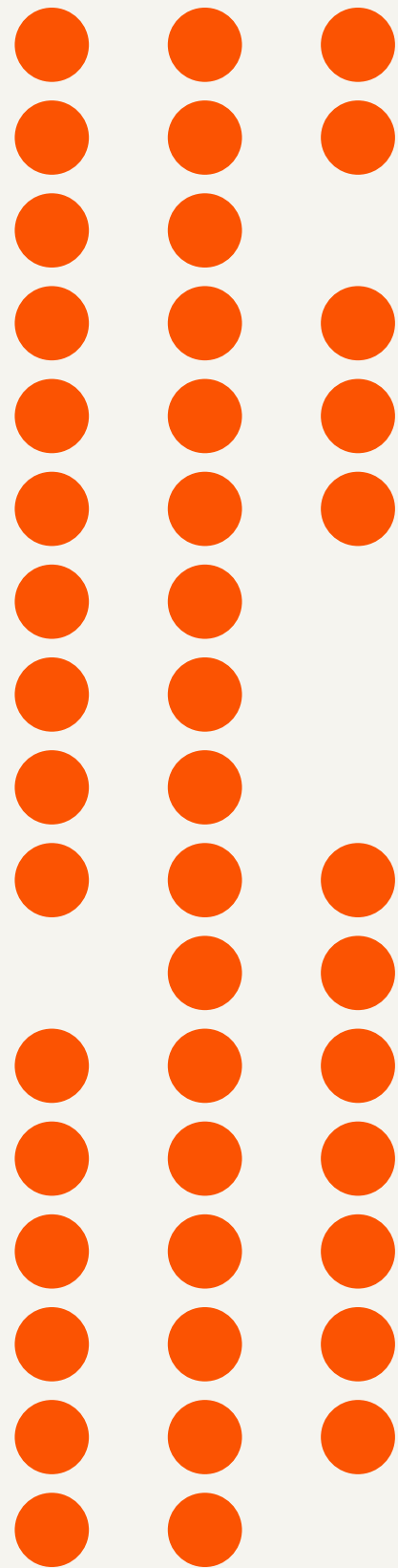


# Variables of Interest

From the AACT database, we collect information on the size of each study (the number of participants), whether results were reported, and whether demographic information was included as part of the reported results. Where demographic information was included, we also collect the demographic breakdown of the study population. We look across three different demographics: sex, ethnicity, and race. We also collect information on the general characteristics of the study, such as the study’s primary purpose, the phase, and the disease class being studied.

We categorize diseases using the Clinical Classification Software provided by the Healthcare Cost and Utilization Project. The Appendix shows the 22 clinical classifications used to sort diseases based on ICD-10-CM (<https://hcup-us.ahrq.gov/toolssoftware/ccsr/dxcsr.jsp#download>).

The AACT database uses string variables for disease conditions; therefore, classification is done via string matches to the description of ICD-10-CM or the Medical Subjects Headings for each disease category in the US National Library of Medicine. Categorization was successful for approximately 95 percent of clinical studies. Clinical studies have multiple records for reporting conditions; thus, studies can be counted in multiple bins when distributions are tabulated by disease. When classifying by disease, we exclude studies with “healthy participants” or “general descriptions” as the name of the disease for disease classification.



# Reporting of Results and Demographics

Among the 46,649 clinical trials in our sample, 21,473 (46 percent) had reported their results, and 25,176 (54 percent) had not. Of the 9,521 observational studies, 943 (10 percent) had reported results, as opposed to 8,578 (90 percent) that had not (see Figure 3).

We focus the rest of this discussion on clinical trials, as the rate of reporting for observational studies is too low to provide a reasonable representation of this class of studies. Reporting patterns for clinical trials have changed over time. Figure 4 shows how quickly results were reported for studies completed in each year between 2008 and 2020. The lines show what percentage of clinical trials completed in a given year reported results to ClinicalTrials.gov within two years, within four years (this category includes those that reported within two years), and that have not yet reported their results (this includes studies that will never report and studies that have delayed their reporting past May 15, 2022).

Results reporting has, on average, grown faster over time. A portion of the more recent increase in no results being submitted is likely due to not enough time having elapsed for slower reporters to have uploaded their results. Thus, studies completed in 2020 would only include one-and-a-half year's worth of uploaded results, whereas studies completed in earlier years would have longer time windows for possible reporting.

**Figure 3. Results Reporting Rate by Study Type**

Figure 3A. Clinical Trials (N = 46,649)

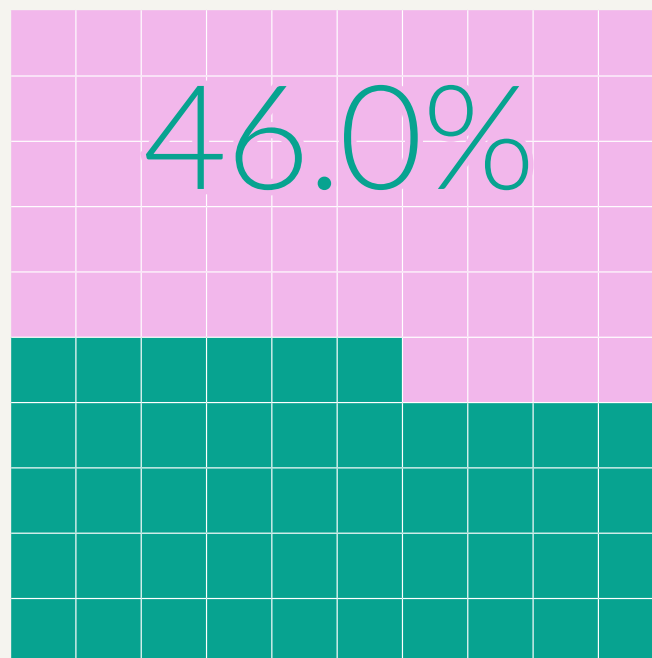
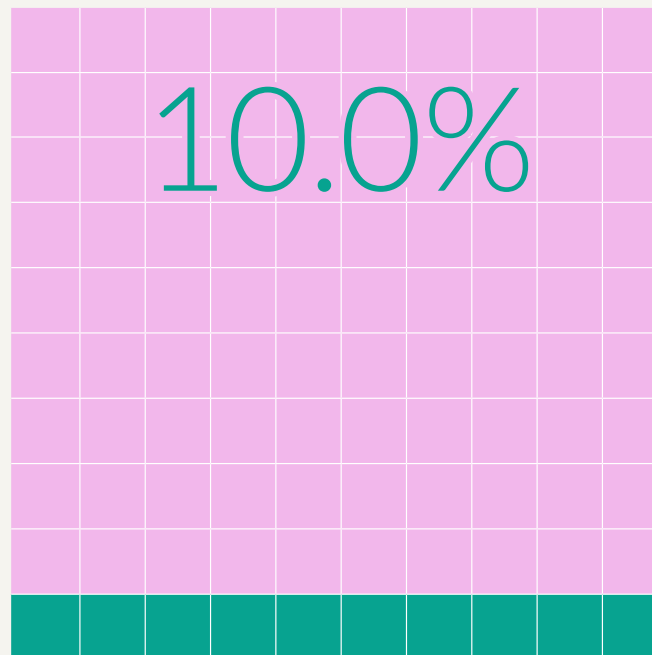
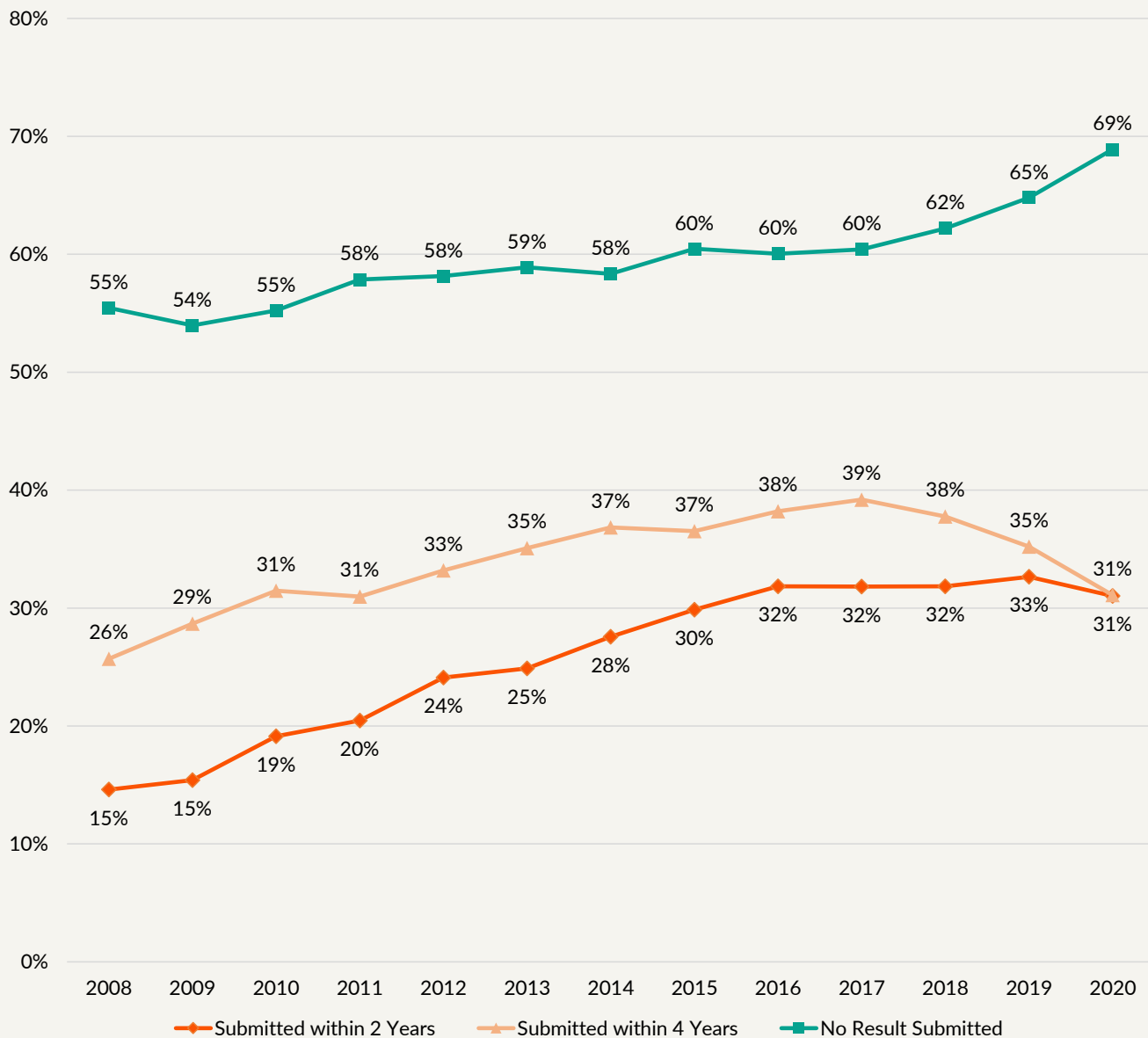


Figure 3B. Observational Studies (N = 9,521)



Source: Milken Institute (2023); AACT Database (2022)

**Figure 4. Speed of Results Reporting for Clinical Trials**



Source: Milken Institute (2023); AACT Database (2022)

## Drug Trial and Non-drug Trial Reporting

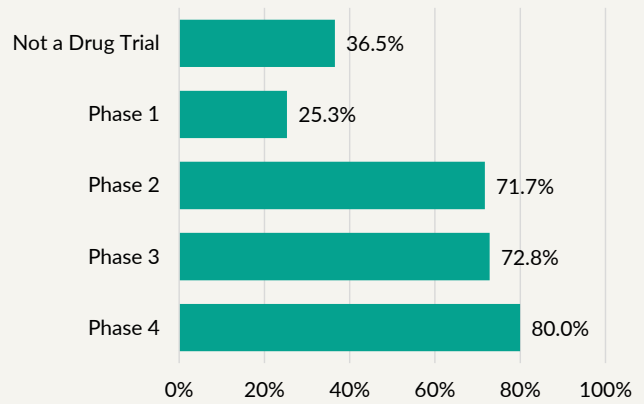


In addition to being slightly more common, drug trials are much more likely to report their results than other types of clinical trials. Out of 20,649 clinical trials that were not drug trials, 7,538, or 36.5 percent, reported results, as opposed to

13,935 out of 26,000, or 53.6 percent, of drug trials. Within drug trials, reporting of results was far more common for later phases: Just over a quarter of Phase 1 trials reported results, whereas more than 70 percent of Phase 2-4 trials reported results (see Figure 5).

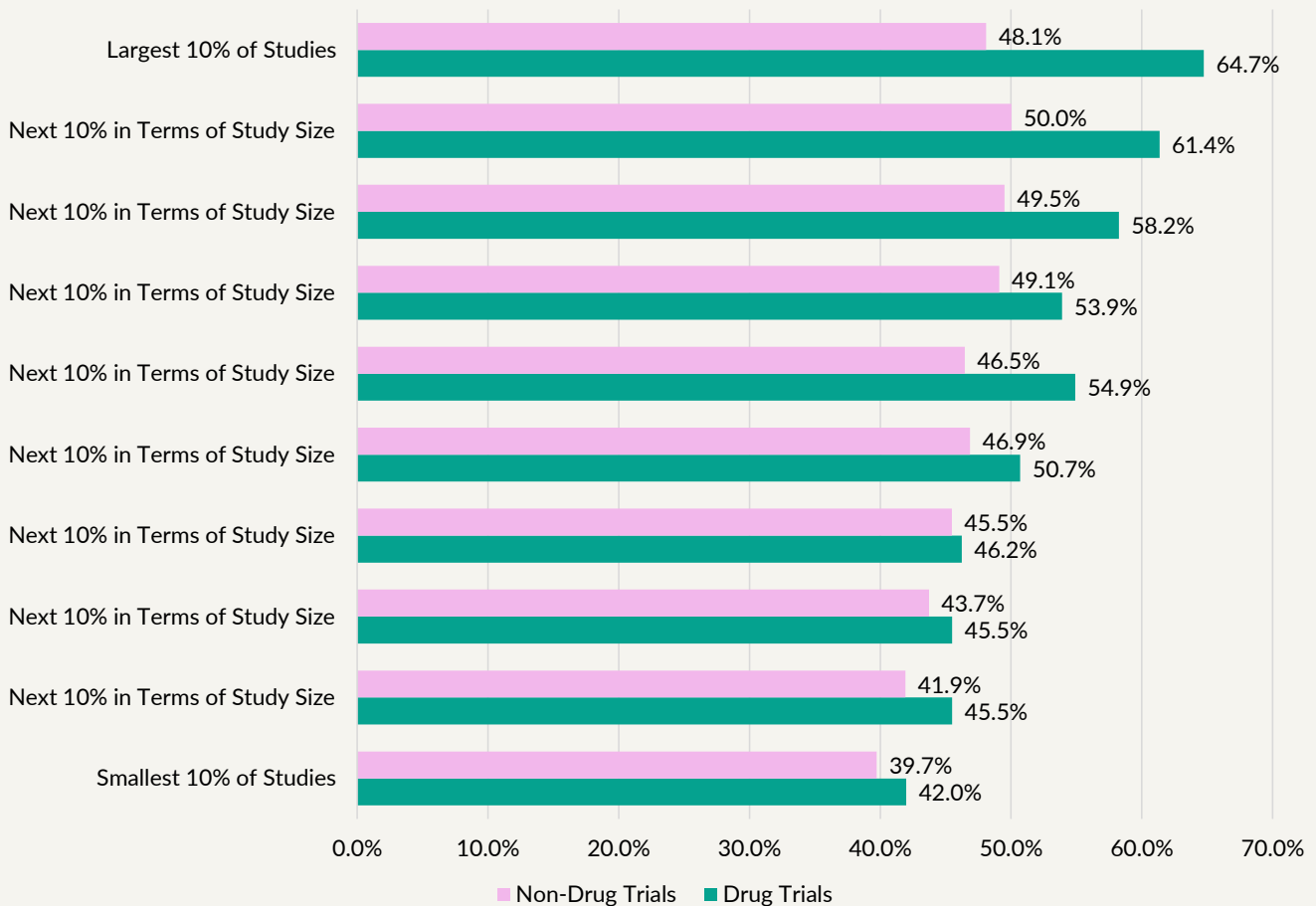
Drug trials are also more likely to report results when they have larger enrollment (which is correlated with the study phase). As drug trials are larger, they are almost uniformly more likely to have reported results to ClinicalTrials.gov, as shown in Figure 6. This general pattern also exists for non-drug trials but is slightly less pronounced.

**Figure 5. Results Reporting by Study Phase**



Source: Milken Institute (2023); AACT Database (2022)

**Figure 6. Results Reporting by Study Enrollment**



Source: Milken Institute (2023); AACT Database (2022)

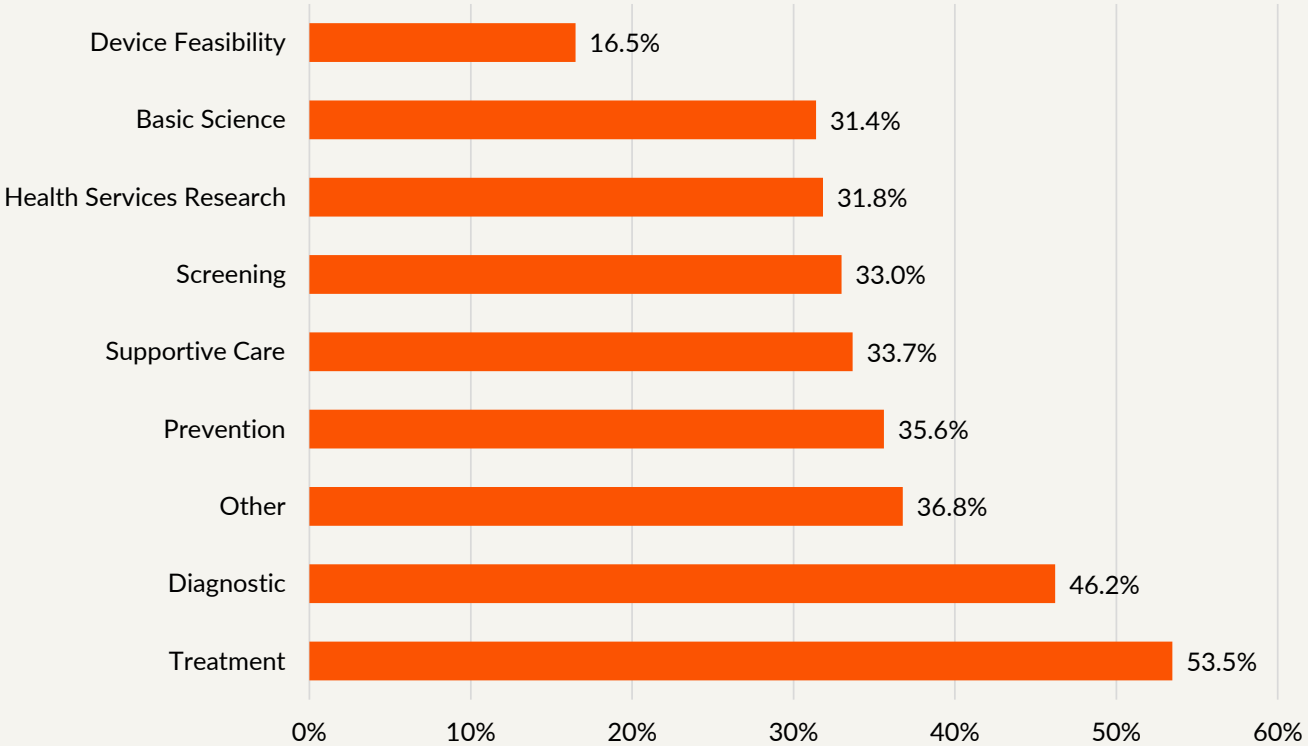
# Study Topic and Results Reporting



Reporting rates for clinical trial results varied considerably according to the topic of the study. This was true for both the primary purpose of the study and the disease addressed by the study. Figure 7 shows the rate of results reporting based on the primary reported purpose of the study. Clinical trials centered on diagnostics and treatment were the most likely to upload results, whereas device feasibility studies (which are exempt from results-reporting requirements under the FDAAA and Final Rule) and basic science studies were the least likely to upload results.

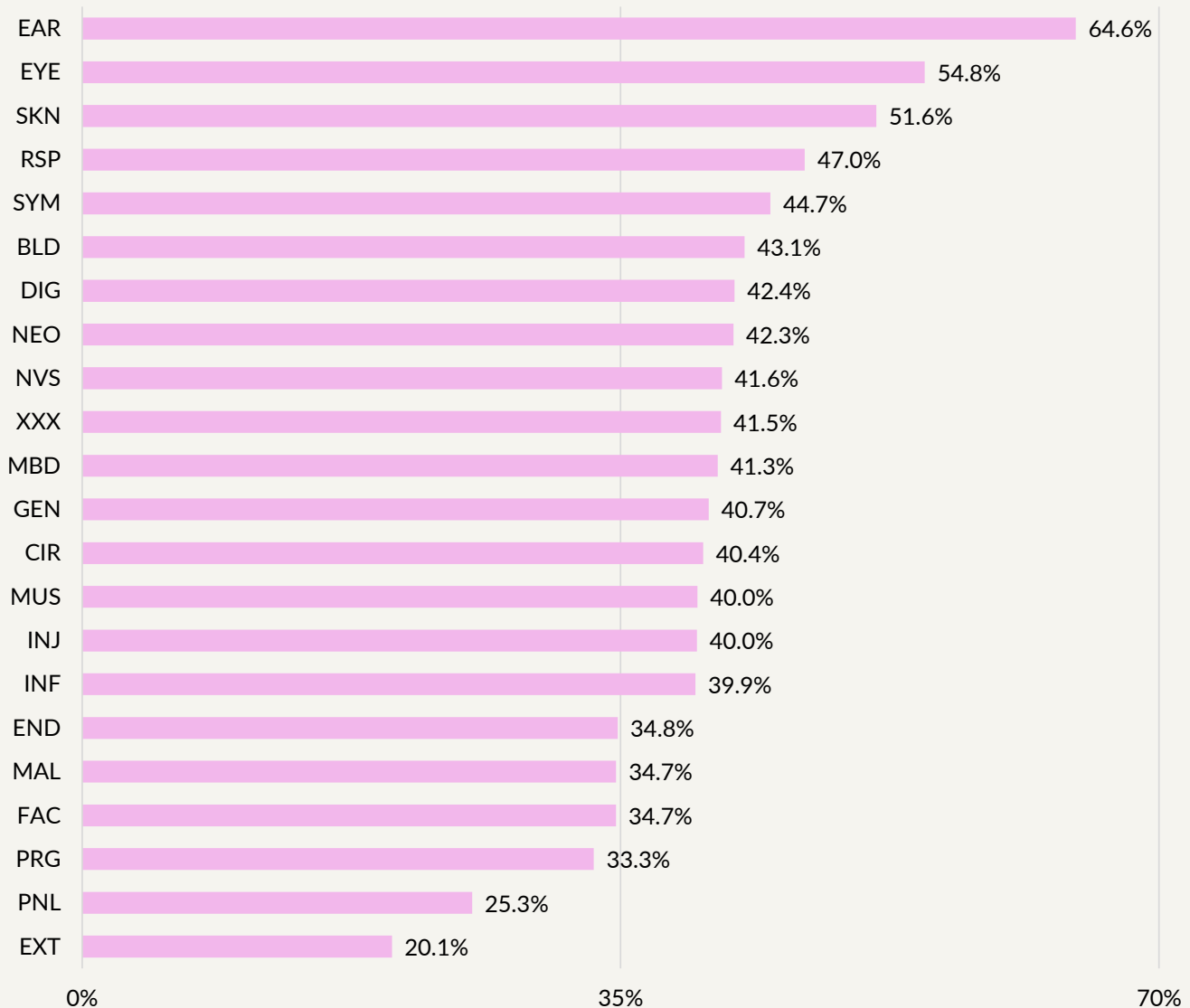
There are also sizable differences in the rate at which results are uploaded to ClinicalTrials.gov based on the disease the study was addressing. Rates of results reporting by disease type are shown in Figure 8. Diseases of the ear and mastoid process (EAR), of the eye and adnexa (EYE), and of the skin and subcutaneous tissue (SKN) were the most likely to upload results, reporting results in more than half of all relevant clinical trials. The least likely to upload were clinical trials related to external causes of morbidity (EXT); pregnancy, childbirth, and the puerperium (PRG); and conditions originating in the perinatal period (PNL).

**Figure 7. Results Reporting by Primary Purpose of Study**



Source: Milken Institute (2023); AACT Database (2022)

**Figure 8. Results Reporting Based on Disease**



Source: Milken Institute (2023); AACT Database (2022)

## Presence of Demographic Information in Reported Results

Almost all sampled studies registered with ClinicalTrials.gov that report results include at least some demographic information. Of the 21,473

clinical trials that reported results, all but 81 (less than one-half of 1 percent) included counts of participants by sex, race, or ethnicity. Sex was the most common: Of the 21,473 clinical trials that reported results, all but 135 (slightly over one-half of 1 percent) included counts of participants based on sex. For clinical trials, reporting information on the race or ethnicity of the study population was far less common than reporting information on sex.

Although sex was reported as part of the results in more than 99 percent of studies that reported results, race was only reported as part of the results half of the time (or in 22.9 percent of all clinical trials), and ethnicity was only reported as part of the results 34.3 percent of the time (or in 15.8 percent of all clinical trials); this is shown in Figure 9. Another important feature of reporting data on race is that the variable for the race of participants is not uniform across studies, and the possible responses recorded for this variable can differ considerably. In some cases, this is due to the study being restricted to certain subgroups by design; in other cases, it is due to differences in how the variable is constructed.

For each phase in drug trials, with non-drug trials reported separately, Figure 10 reports the frequency with which sex, race, or ethnicity is reported, given that the study reported its results to ClinicalTrials.gov. Race and ethnicity are consistently reported less frequently across all study phases. These demographics are also noticeably less likely to be reported in Phase 4 trials relative to other phases. Non-drug trials tend to be less likely to report race or ethnicity than drug trials in general.

Although sex was reported as part of the results in more than 99 percent of studies that reported results, race was only reported as part of the results half of the time (or in 22.9 percent of all clinical trials)

### Figure 9. Presence of Race and Ethnicity in Reported Results

Figure 9A. Race in Reported Results

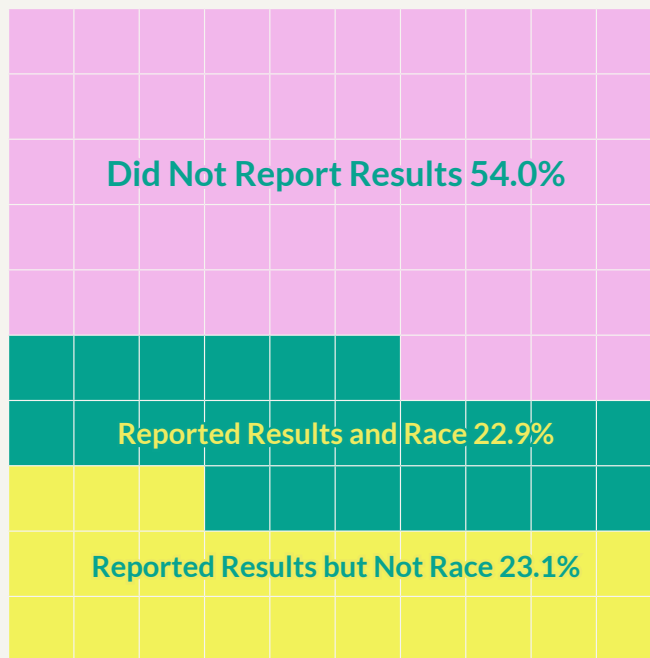
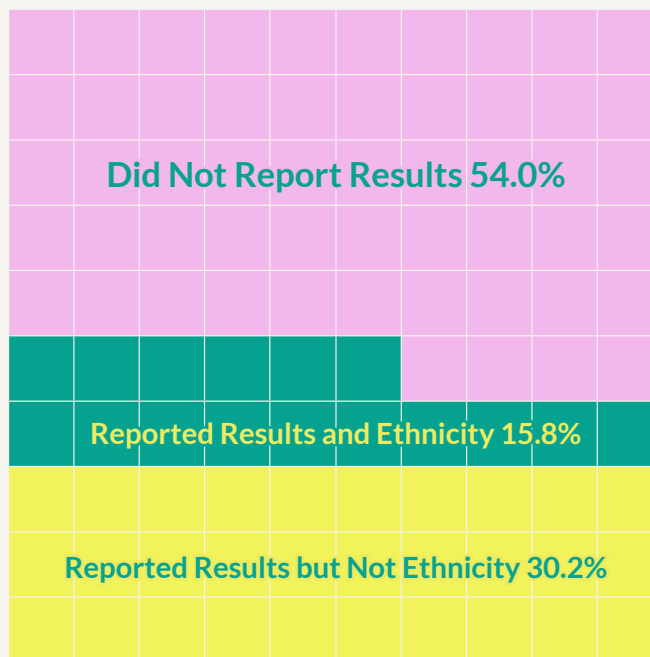
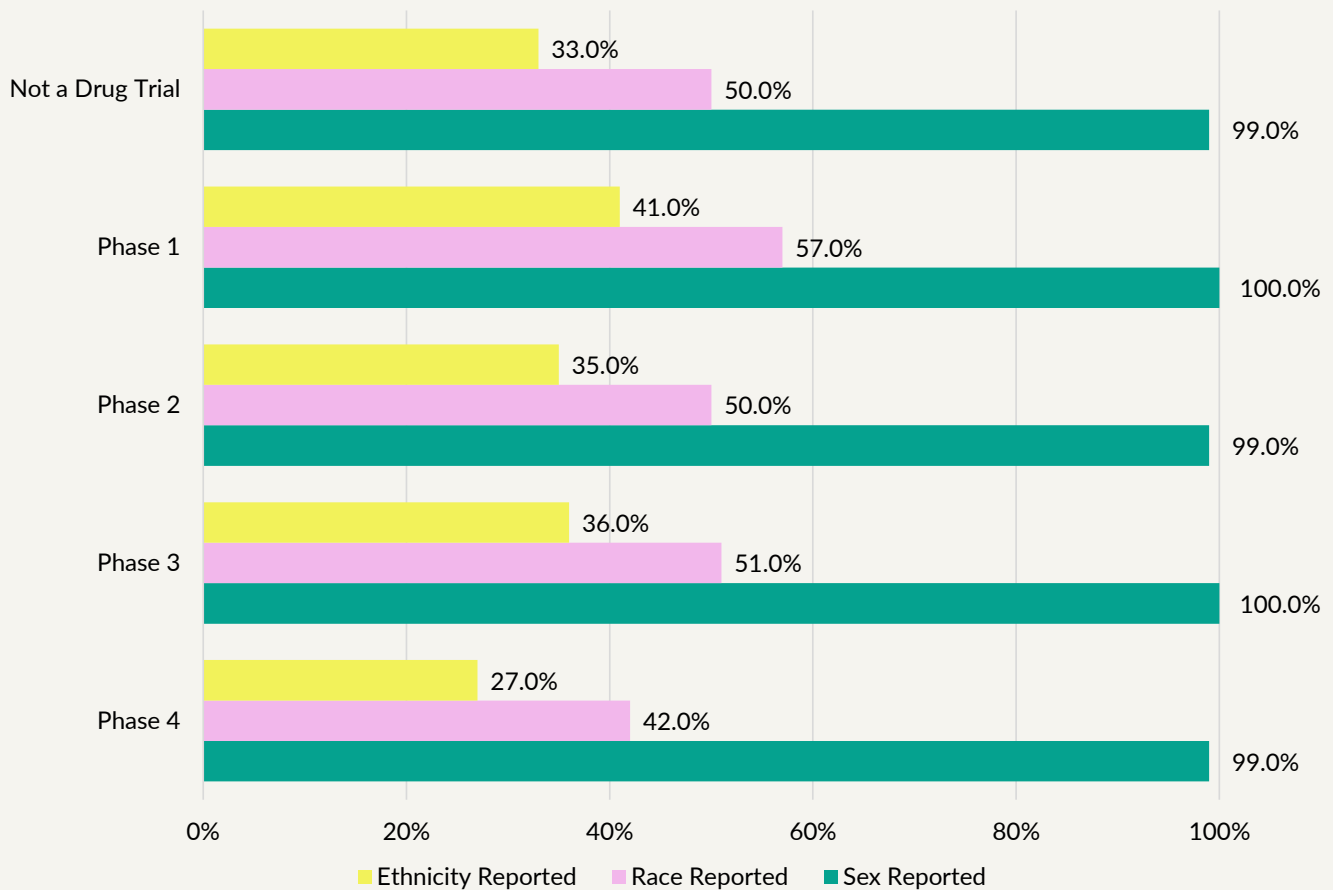


Figure 9B. Ethnicity in Reported Results



Source: Milken Institute (2023), AACT Database (2022)

**Figure 10. Presence of Demographics in Reported Results by Phase of Trial**



Source: Milken Institute (2023); AACT Database (2022)

# Comparison of Collected Demographics to the General Population



The remainder of this report examines the demographic makeup of clinical trials in the AACT that report results and contain demographic information. The sample is restricted to the 46.0 percent of clinical trials that report gender, the 22.9 percent that report race, and the 15.8 percent that report ethnicity. These are smaller subsamples, and there is the possibility of a systematic pattern in which studies report demographics; that is, the demographics reported may not be representative of those in the non-reporting studies. In the following information, we also provide the demographic makeup of the general US population from the 2020 Census as a reference.



It's important to note that, while the Census is a useful guidepost for demographic balance, it does not necessarily include the demographic mix appropriate for a given clinical study. An analyst would want the study demographics to match those of the population impacted by the intervention in question. For example, although the 2020 Census population is 49.5 percent male and 50.5 percent female, a researcher would expect studies of diagnoses related to pregnancy, childbirth, and the puerperium to contain a far greater proportion of female participants, as these diagnoses disproportionately impact women. Similarly, men experience hearing loss at twice the rate of women (Hoffman et al. 2017), so we'd expect a study population randomly selected from people experiencing hearing loss to include more men than women.

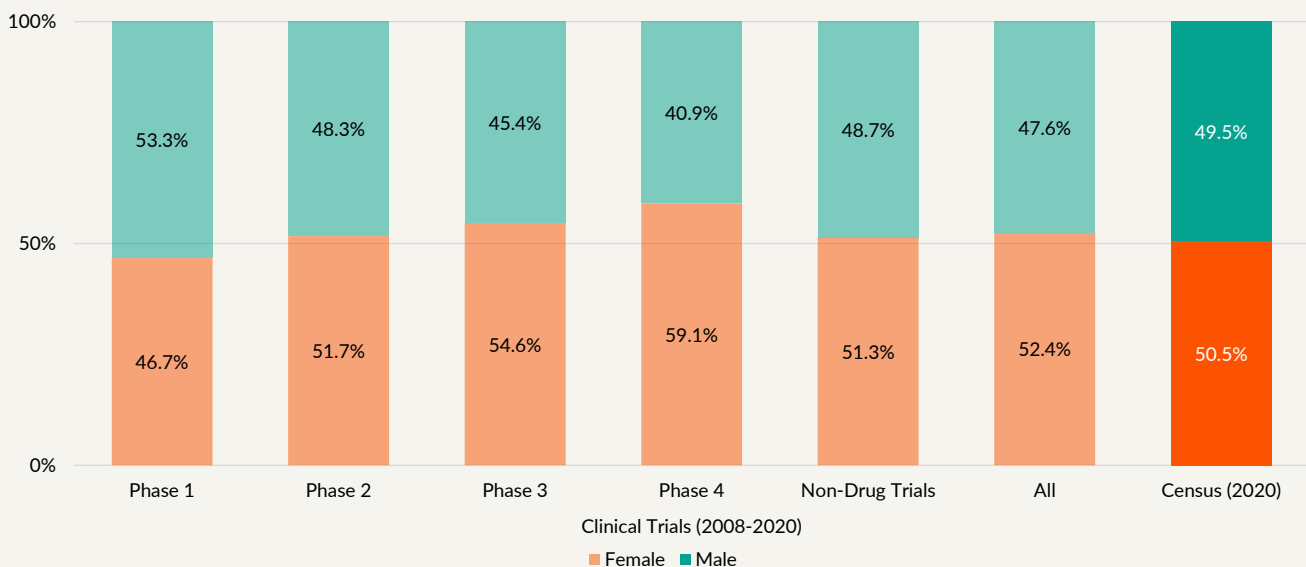
The analyses to follow are meant strictly to document the distribution of demographics in clinical trials relative to a common and widely used benchmark (the US Census) and should not be taken as a measure of the appropriateness of any given study's demographic mix.

## Sex

Figure 11 reports the overall sex distribution for the clinical trials reporting that demographic. These studies included about 3.3 million females (52.4 percent) and 3 million males (47.6 percent), accounting for 52.4 percent and 47.6 percent of participants, respectively. Compared with the most recent US Census, clinical trials in totality are slightly more female-heavy. There is variation based on the phase of the study: Early phases are disproportionately male, but, as phases progress, trials overall become disproportionately female.

The numbers in Figure 11 are calculated by counting the total male and female study participants in each category and dividing by the total number of study participants. This ignores that many studies are single-sex: More than 15 percent of clinical trials reporting demographics to ClinicalTrials.gov include only one sex. Figure 11 also does not consider the extent to which individual studies may over- or under-represent specific groups relative to the Census.

**Figure 11. Distribution of Sex in Clinical Trials**



Source: Milken Institute (2023); AACT Database (2022); US Census Bureau (2020)

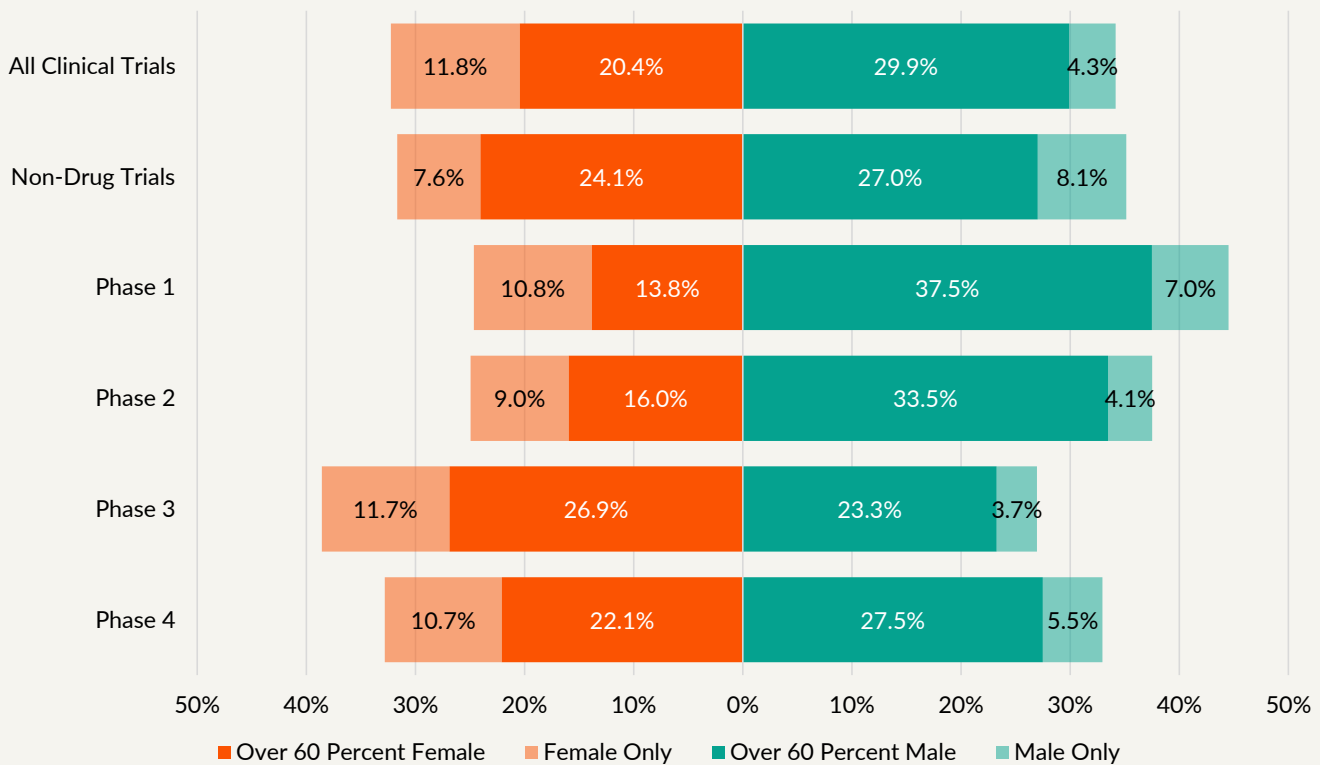
Put differently, the frequency with which clinical trials have differing sex balances is not well captured by the average mix of sexes across all study participants. Figure 12 shows the percentage of studies that have a sex mix more than 10 percentage points different from the one seen in the Census. These studies are broken into four categories: studies that are more than 60 percent male but not completely male; studies that are more than 60 percent female but not completely female; and studies that are one sex exclusively. The majority of studies are outside of a 60/40 sex mix.

Across all clinical trials, there are sizable differences in sex mix. There are many more all-female studies (11.8 percent) than all-male

studies (4.3 percent), but there are also many more studies that are over 60 percent male (29.9 percent of studies) than over 60 percent female (20.4 percent of studies). Studies that fall within a 60/40 sex distribution make up 33.6 percent of all clinical trials, which means that a relatively sex-balanced clinical trial is the exception, not the rule. For drug trials, Phases 1 and 2 have more than double the number of studies that are over 60 percent male relative to studies that are over 60 percent female. Phase 1 also has the smallest proportion of studies that are within a 60/40 sex mix (30.9 percent).

There are also sizable differences in sex mix based on the health issue being studied, which are shown in Figure 13. Some, if not most, of these imbalances

**Figure 12. Prevalence of Clinical Trials That Deviate from the Census**



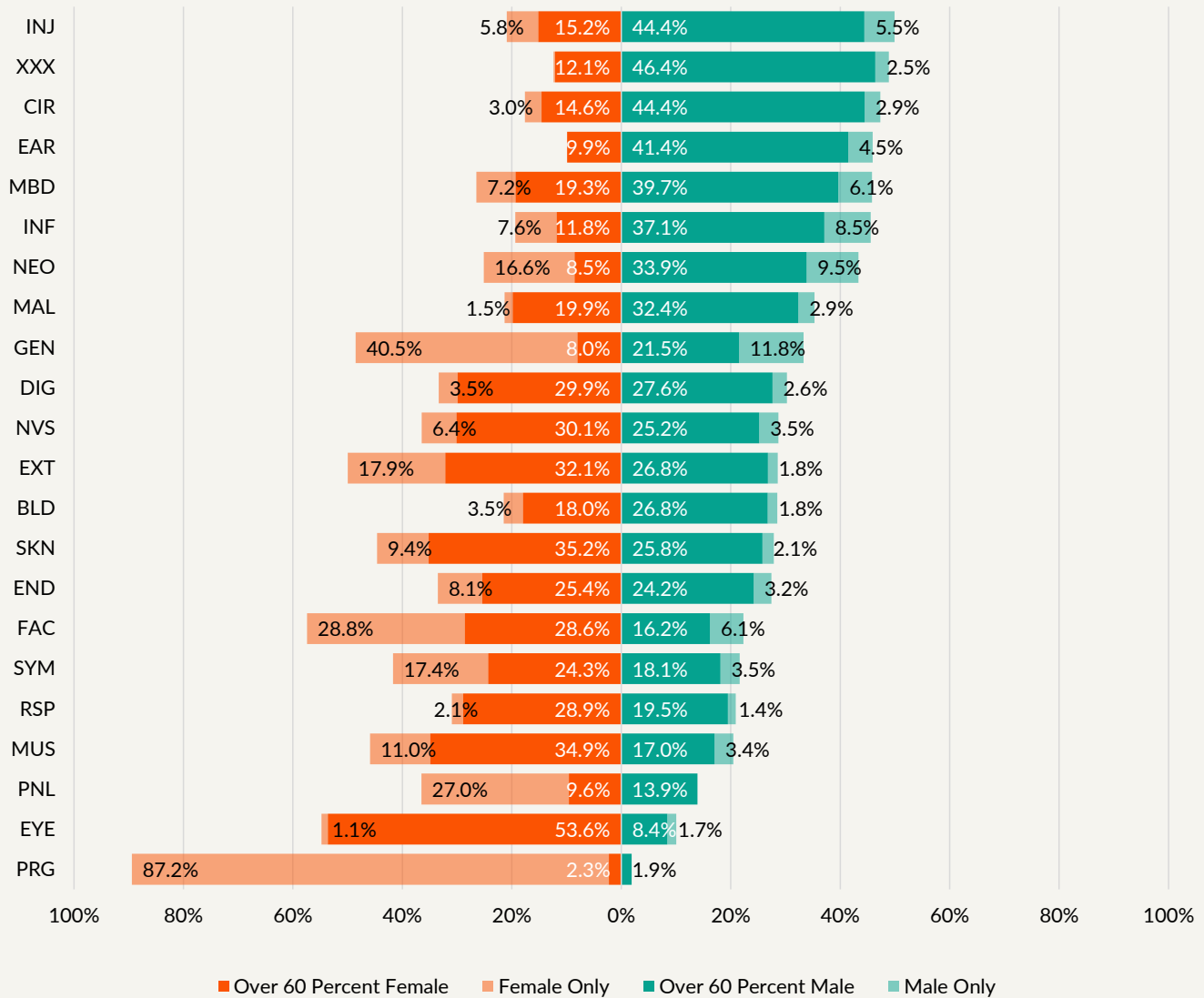
*Note: The category thresholds are based on a 10 percentage-point deviation from the demographic mix found in the 2020 Census and do not necessarily represent underlying disease prevalence by demographic.*

Source: Milken Institute (2023); AACT Database (2022)

are likely due to the nature of the health issue under study. Of studies related to pregnancy, birth, and the puerperium (PRG), 87.2 percent are female-only, probably because the majority of (though not all) research questions on this topic are female-specific, making this the relevant study population.

A noteworthy feature of the data is the sizable spread on both sides of the mix observed in the Census. This means that within a single disease category, there are clinical trials that are heavily male as well as clinical trials that are heavily female. For example, 29.9 percent of studies of diseases of the digestive system (DIG) are over 60 percent

**Figure 13. Prevalence of Clinical Trials That Deviate from the Census by Disease**



*Note: The category thresholds are based on a 10 percentage-point deviation from the demographic mix found in the 2020 Census and do not necessarily represent underlying disease prevalence by demographic.*

*Source: Milken Institute (2023); AACT Database (2022)*

female, and 27.6 percent of studies within the same broad classification of diseases are over 60 percent male. The cause of this pattern could be that there is a wide variety of diseases in this category, each with a very different case mix based on sex, but also possibly due to some studies having unbalanced sampling across sexes.

Within a single disease category, there are clinical trials that are heavily male as well as clinical trials that are heavily female.

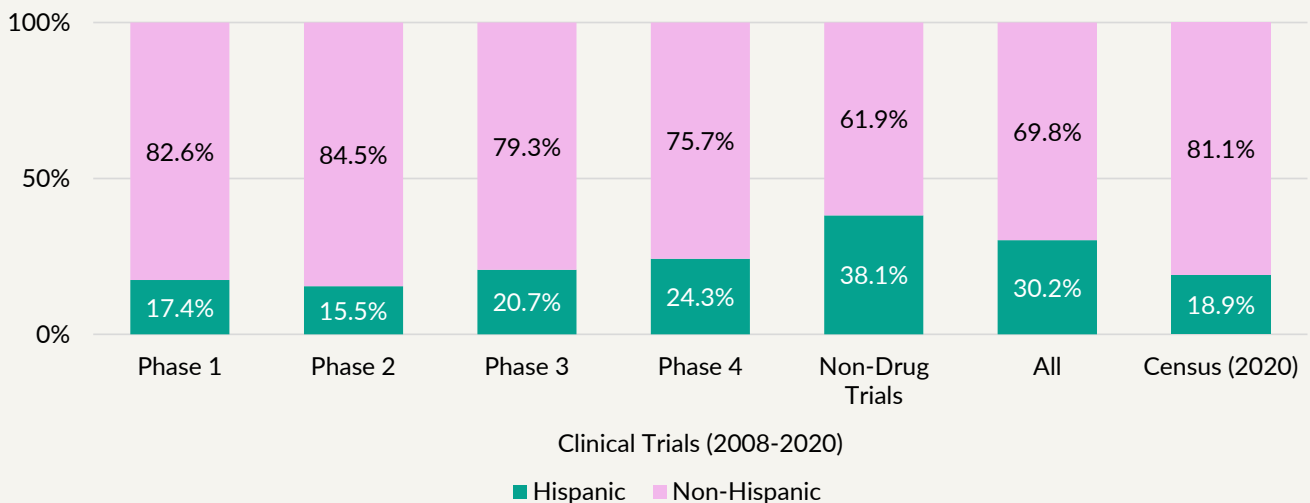
## Ethnicity

As with sex, we give measures of ethnic demographic mix in clinical trials and provide information on the ratio of studies with demographics that differ from the 2020 Census. Again, the Census is intended as a broad guidepost that represents the general US population but is not necessarily the appropriate population mix for studies in all cases, as the demographic mix of a patient population often differs from that of the general population. For example, the Centers for Disease Control and Prevention (CDC 2015) report that the US Hispanic population has a 49 percent lower rate of cancer and a 35 percent lower rate of heart disease than the US non-Hispanic population.

The analyses that follow are simply meant to document the distribution of ethnicity reported in clinical trials relative to a common benchmark; they should not be taken as a measure of the appropriateness of any given study’s demographic mix.

The demographic mix of clinical trials that reported ethnicity is shown in Figure 14. These studies accounted for approximately 1.6 million total participants, of whom 474,847 (30.2 percent) were Hispanic and approximately 1.1 million (69.8 percent) non-Hispanic. There are variations in demographics based on the type of study, with early-phase drug trials enrolling a smaller

**Figure 14. Distribution of Ethnicity in Clinical Trials**



Source: Milken Institute (2023); AACT Database (2022); US Census Bureau (2020)

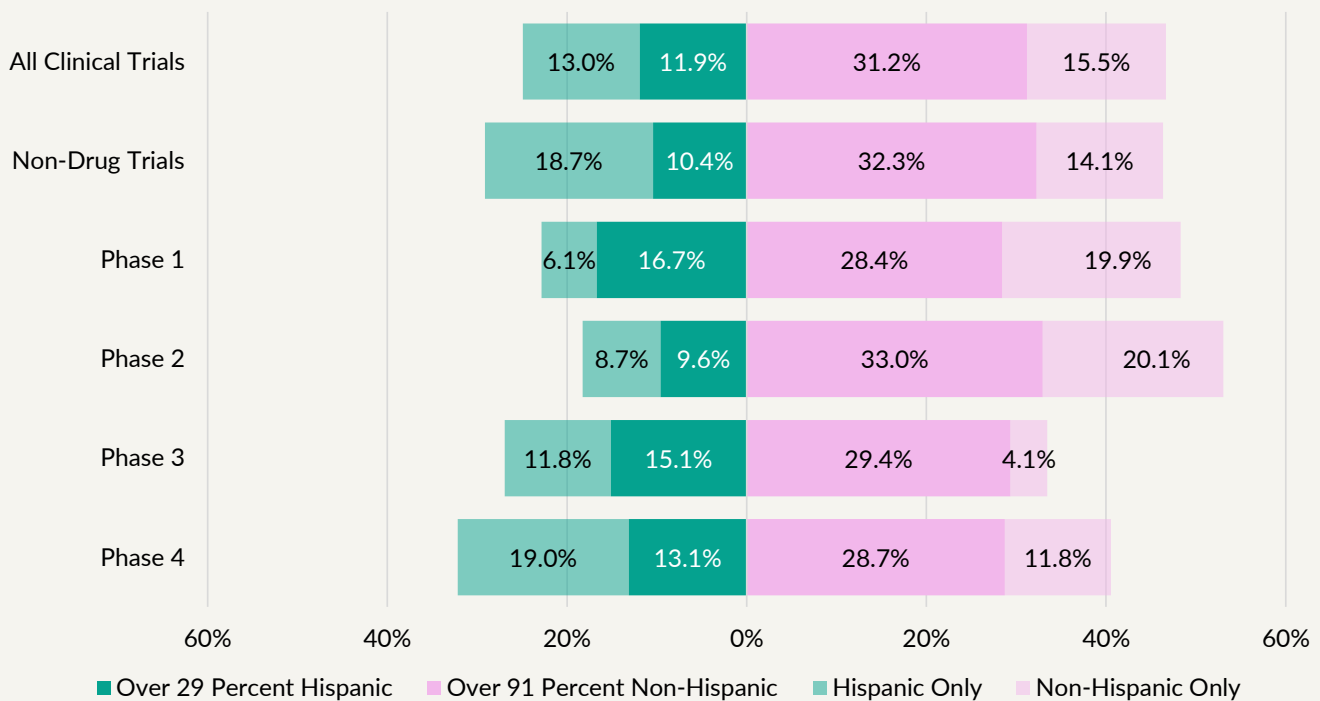
proportion, and later-phase drug trials and non-drug trials enrolling a larger proportion, of Hispanic participants.

A summary of studies with a demographic mix 10 percentage points outside of the mix seen in the 2020 Census is reported in Figure 15. When compared to sex, similarity to the Census based on ethnicity is slightly less: 28.4 percent of clinical trials that report ethnicity to ClinicalTrials.gov have a mix of participants falling within 10 percentage points of the population distribution in the 2020 Census, compared to 33.6 percent of clinical trials for sex. For studies that are not within 10 percentage points of the Census, 13 percent are Hispanic-only studies, and 15.5

percent are non-Hispanic only. Non-Hispanic over-sampling relative to the Census is most prevalent in Phase 2 and non-drug trials, whereas Hispanic over-sampling relative to the Census is most frequent—though still less prevalent than non-Hispanic over-sampling—in Phase 1 trials.

There is, again, a considerable amount of variation in representation based on the disease that is the focus of the study, which is shown in Figure 16. And again, a significant amount of this variation is likely due to underlying disease prevalence. For example, more than 65 percent of studies of neoplasms (NEO) have a study population more than 91 percent non-Hispanic or completely non-Hispanic. So do more than 55 percent of studies of diseases

**Figure 15. Prevalence of Clinical Trials That Deviate from the Census**



*Note: The category thresholds are based on a 10 percentage-point deviation from the demographic mix observed in the 2020 Census and do not necessarily represent underlying disease prevalence by demographic.*

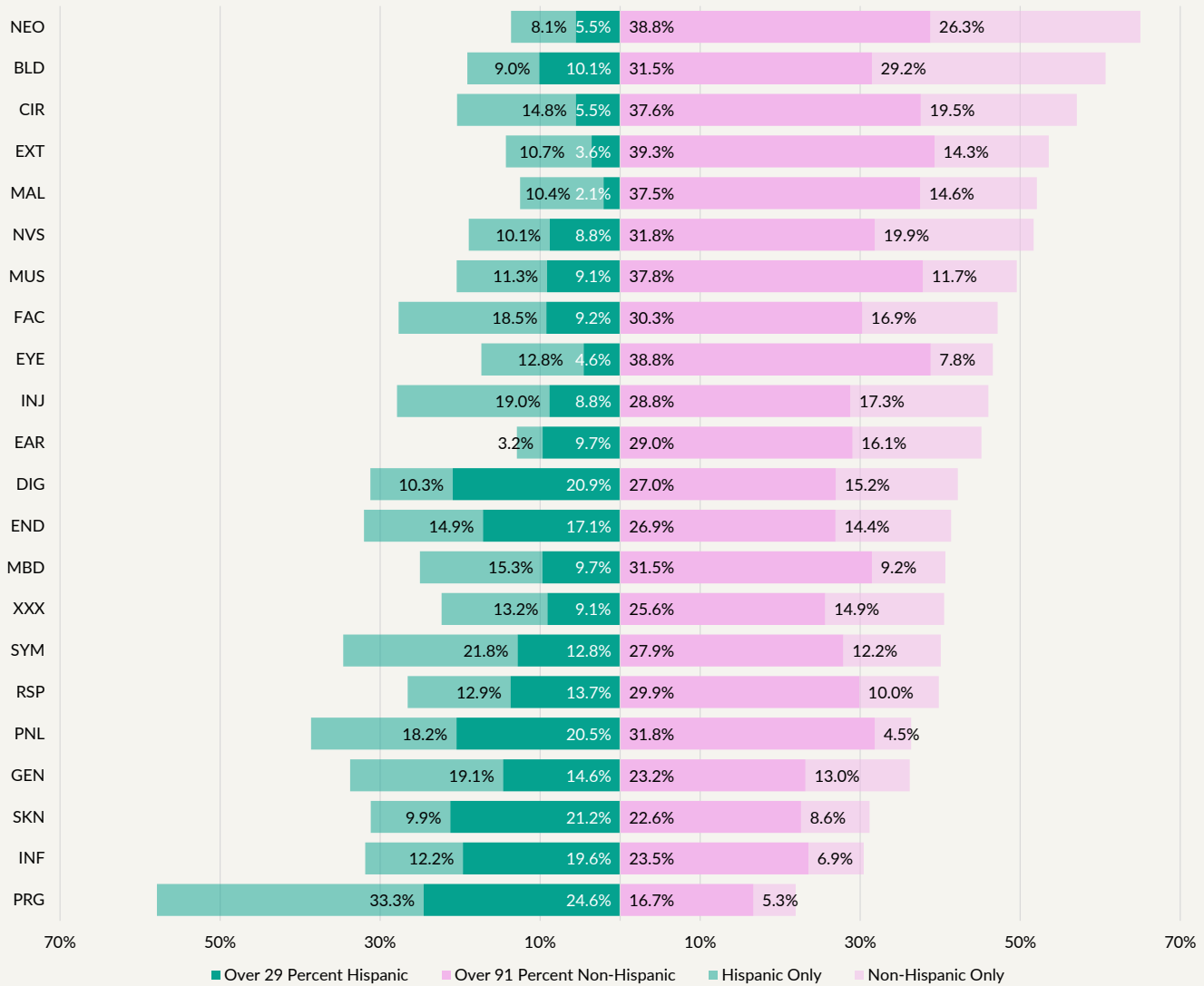
*Source: Milken Institute (2023); AACT Database (2022)*

of the circulatory system (CIR). This pattern of studies, including a smaller Hispanic population than the Census would predict, is consistent with the lower rate of cancer and heart disease in Hispanic populations reported by the CDC (2015).

As with sex, several disease classifications have studies with either a larger or a smaller Hispanic

sample than the Census would predict. The reason for this pattern could be that there is a wide variety of diseases in each classification, each with a very different case mix based on ethnicity, but it could also be due to unbalanced sampling across ethnicities.

**Figure 16. Prevalence of Clinical Trials That Deviate from the Census**



*Note: The category thresholds are based on a 10 percentage-point deviation from the demographic mix found in the 2020 Census and do not necessarily represent underlying disease prevalence by demographic.*

*Source: Milken Institute (2023); AACT Database (2022)*

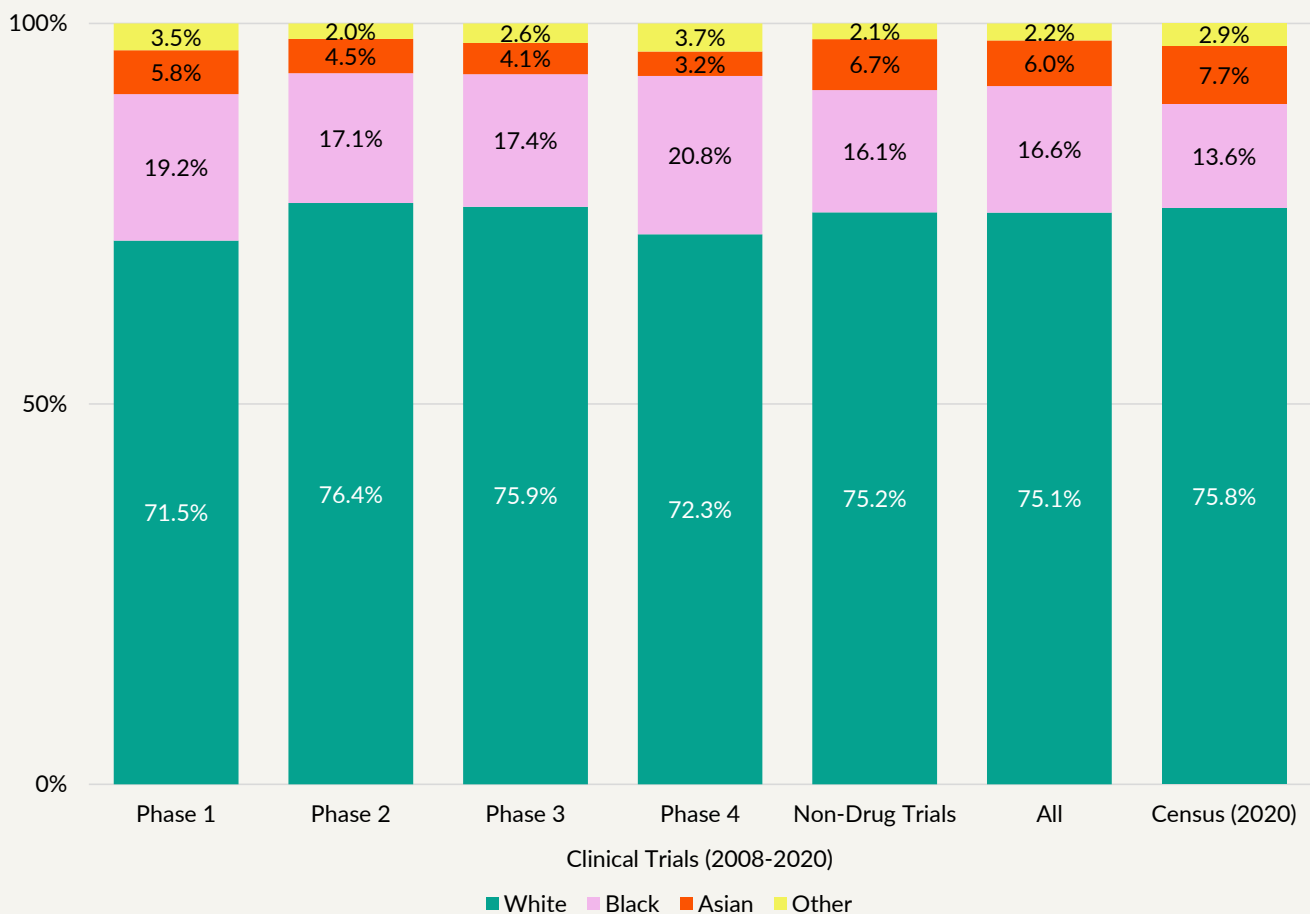
## Race

Finally, we report measures of racial mix in clinical trials and provide distributions that use demographics from the 2020 Census. As with sex and ethnicity, the Census is a broad guidepost that represents the general US population but is not necessarily the appropriate population mix for studies in all cases, as the demographic mix of a patient population often differs from that of the general population. For example, the CDC (2019) reports that 9.5 percent of non-Hispanic Black adults had heart disease in 2017 versus 11.5 percent of non-Hispanic Whites. This means that

a random sample of all patients with heart disease would have a higher proportion of non-Hispanic Whites than one would find in the Census, and a random sample of those with heart disease would deviate demographically from the Census.

Figure 17 reports the overall demographic mix for the clinical trials that reported information on the race of participants. The combined population of these studies was 75.1 percent White, 16.6 percent Black, 6.0 percent Asian, and 2.2 percent another reported race. This distribution is close to that reported in the 2020 Census and does not vary significantly across different phases of drug trials.

**Figure 17. Distribution of Race in Clinical Trials**



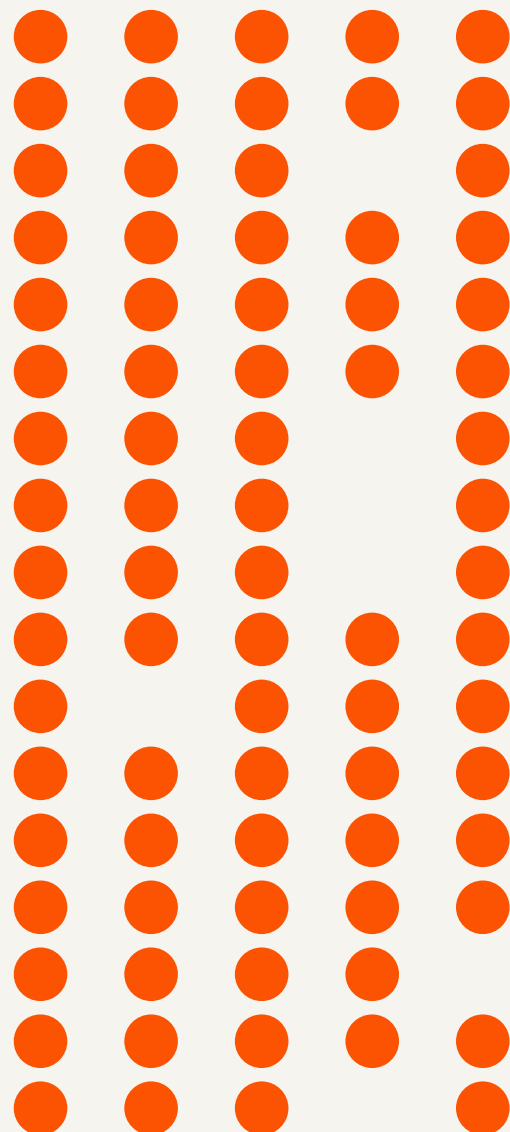
Source: Milken Institute (2023); AACT Database (2022); US Census Bureau (2020)

The balance of demographics across the pooled population of all studies does not necessarily indicate the demographic mix of any single study. As with sex and ethnic demographics, we again construct categories of studies based on a margin more than 10 percentage points outside of what would be expected, based on the 2020 Census. However, there are some additional complexities in constructing categories because of the presence of multiple possible responses to racial demographic questions, and because some groups have population shares small enough that a 10 percentage-point range around the 2020 Census levels would include zero. Further, understanding how racial composition varies across studies is difficult, as there are differences among the outcomes that are collected (if they are collected at all) from study to study. The FDA provides non-binding guidance on best practices for variable collection; see <https://www.fda.gov/regulatory-information/search-fda-guidance-documents/collection-race-and-ethnicity-data-clinical-trials>.

Taking these data complexities into account, we construct categories based on the percentage of a study's population that is White. The 2020 Census reports the general population to be approximately 76 percent White, so we report percentages of studies that are more than 86 percent White and percentages of studies that are less than 66 percent White. Likewise, we report studies that are 100 percent or 0 percent White. A study designed to examine two, but not all, racial demographic groups could, in theory, fall into any of the above categories. This means that the measures of racial demographic mix that follow are less accurate than the measures of sex and ethnic mix due to the ability of the race demographic variable to take on more than two possible outcomes.

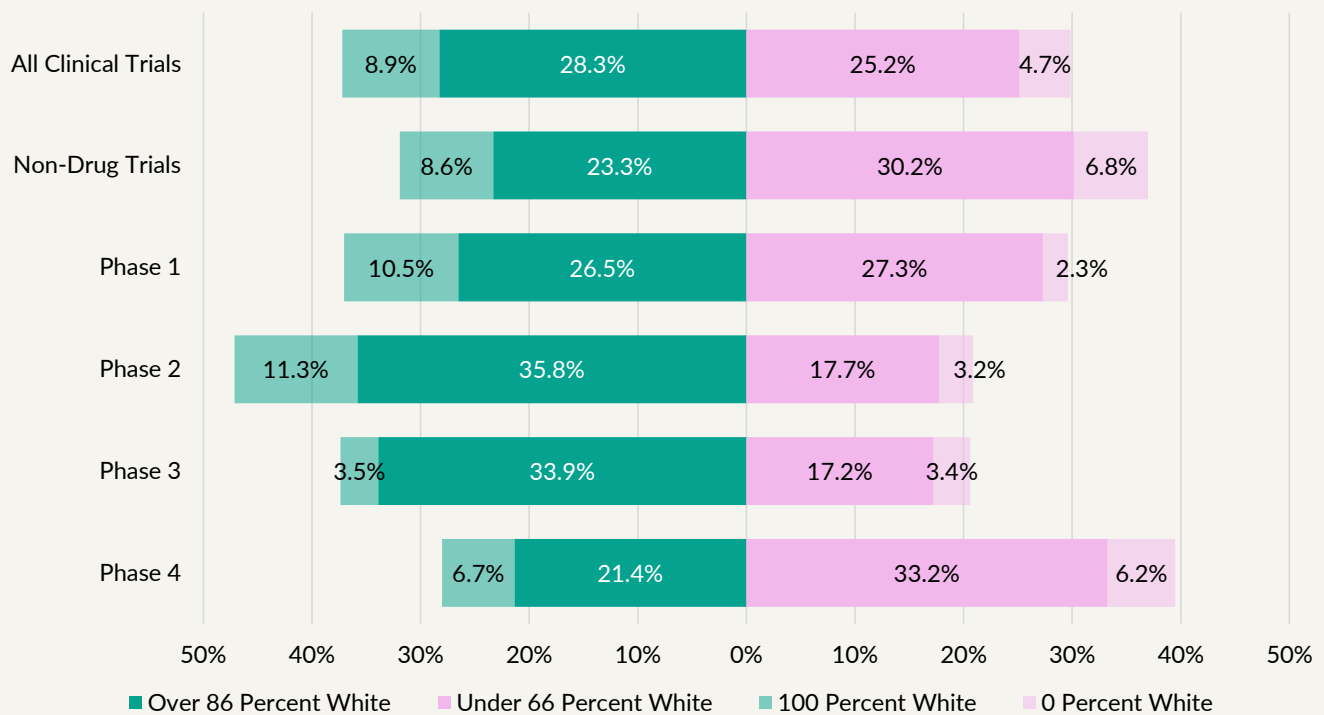
Figure 18 reports the prevalence of the categories defined above. In general, studies that are more than 86 percent White (28.3 percent of clinical

Understanding how racial composition varies across studies is difficult, as there are differences among the outcomes that are collected (if they are collected at all) from study to study.





**Figure 18. Prevalence of Clinical Trials That Deviate from the Census**



*Note: The category thresholds are based on a 10 percentage-point deviation from the demographic mix found in the 2020 Census and do not necessarily represent underlying disease prevalence by demographic.*

*Source: Milken Institute (2023); AACT Database (2022)*

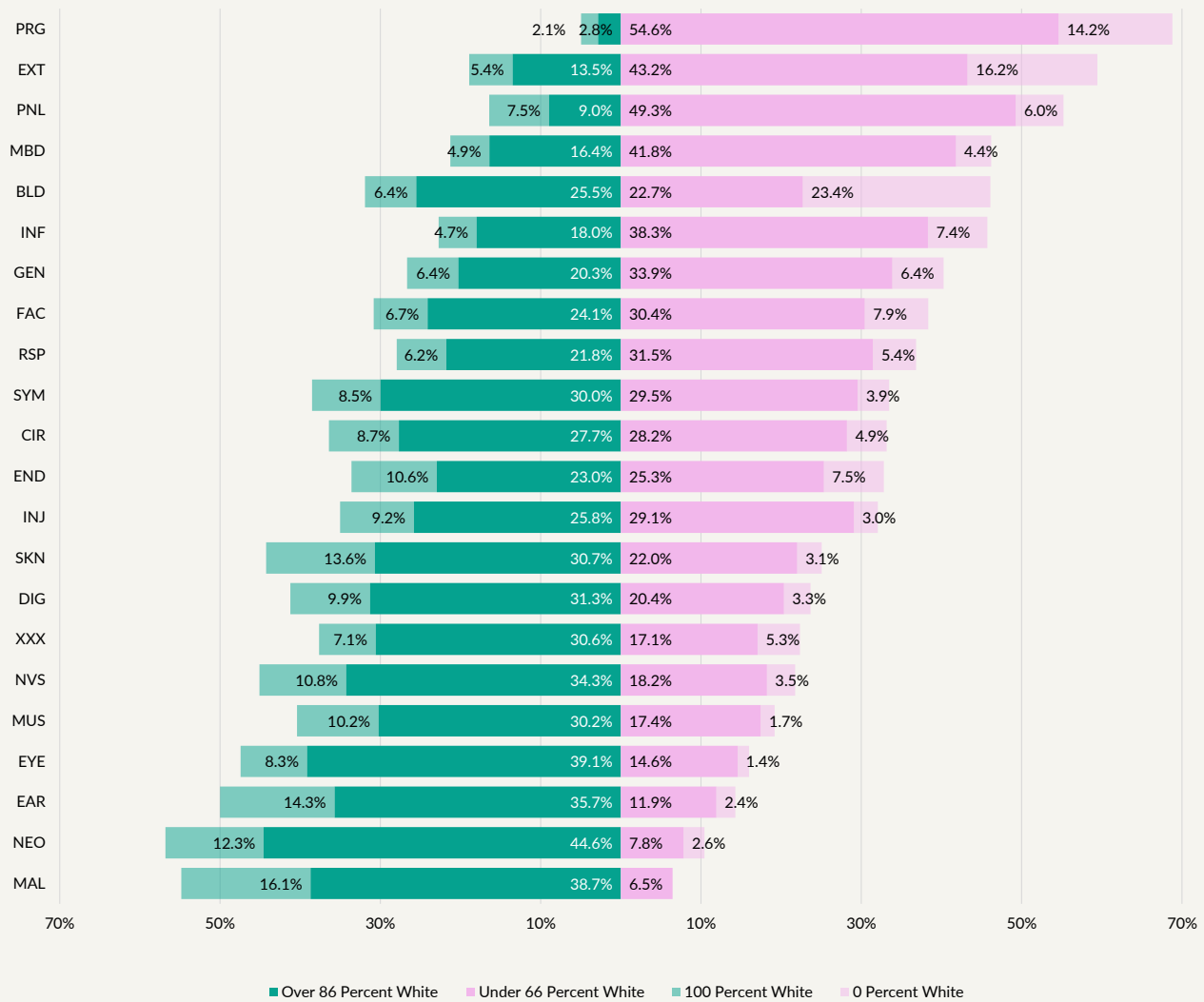
trials that report race) are slightly more common than studies less than 66 percent White (25.2 percent of trials that report race). Studies that are 100 percent White are uniformly more common than 0 percent White studies, regardless of whether a study is a drug trial, and, if it is a drug trial, regardless of phase.

There is a lot of variation in demographic balance across disease classification. Studies of pregnancy, childbirth, and the puerperium (PRG) and of external causes of morbidity (EXT) are far more likely to be under 66 percent White. In contrast, studies of congenital malformations, deformations, and chromosomal abnormalities (MAL) and studies of neoplasms (NEO) are far more likely to be over

86 percent White. In general, there is sizable variation in the racial demographic mix, with most disease classifications having more than 40 percent of studies outside 10 percentage points of the mix found in the 2020 Census; deviations are commonly observed in both directions (see Figure 19). Again, we cannot determine the extent to which this is due to disease classifications having within them a wide variety of illnesses with differing patient populations or to what extent this is due to differences in study recruitment.



**Figure 19. Prevalence of Clinical Trials That Deviate from the Census by Disease**



*Note: The category thresholds are based on a 10 percentage-point deviation from the demographic mix found in the 2020 Census and do not necessarily represent underlying disease prevalence by demographic.*

*Source: Milken Institute (2023); AACT Database (2022)*

# Limitations

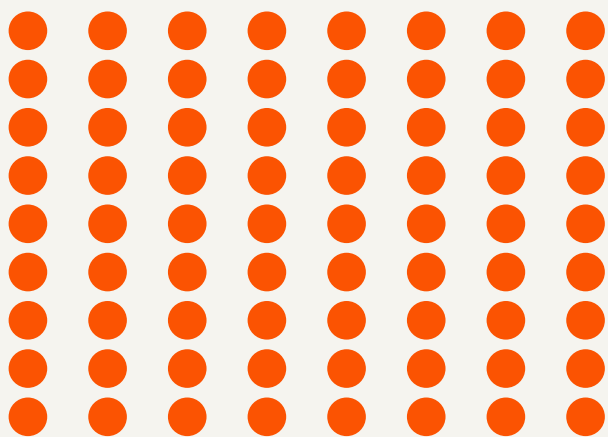


This report is based on the data reported on ClinicalTrials.gov. Although we can describe those data, we are not privy to the complete process from the researchers' collection of data to the eventual (possible) uploading of results. If a study

does not upload results, or uploads results but does not report a specific demographic, that does not necessarily mean that the demographic was never collected, just that it is not part of the ClinicalTrials.gov public registry. For example, there

are instances where no results were uploaded to ClinicalTrials.gov (meaning that no demographic information was publicly available via the website), but where an article based on the clinical trial was published in a scholarly journal that included the relevant demographic information. See, for example, Cigrang et al. 2011, Jasinski et al. 2018, and Tuscano et al. 2019. We are not claiming that these studies were required to upload their results to ClinicalTrials.gov, just that the relevant demographics were collected (as evidenced by their publication elsewhere) but not uploaded to the public registry.

This report is strictly descriptive. The cause of any reporting gaps or demographic imbalances described in the above sections and potential policy solutions for closing these gaps or managing imbalances are not contained herein. For example, this report cannot discern whether a sex imbalance in a set of studies is due to random sampling over sex-imbalanced underlying patient populations, an imbalance in active external recruitment activities, an imbalance in which patient chooses to go to the doctor and is recruited on-site for convenience, or an imbalance in the likelihood of one sex versus another agreeing to participate (Alsan and Wanamaker 2018). Rather, this report describes the state of demographics in clinical trials in the US based on the features of the ClinicalTrials.gov data.



# Conclusion

There are several notable patterns with respect to demographics in studies reported to ClinicalTrials.gov. The first is that the rate of reporting results (which is necessary for demographic information to become public) is generally low. Even when results are reported, the included demographics vary: Sex is reported almost universally, but ethnicity and race are reported much less frequently. When race is reported, there is notable variability from study to study in the possible outcomes that the variable can take on.

The second pattern is that, while the overall average demographic distribution across all reported study participants is close to the general population's demographic distribution as reported by the 2020 Census, this population average hides considerable variation from study to study and does not capture differences in disease burden across populations. Most trials have a study population that is more than 10 percentage points different from the general population, as reported by the 2020 Census. For many classes of studies, the imbalance is sizable both in favor of and against a single demographic.

In some cases, a demographic imbalance may be an artifact of randomly drawing from an imbalanced underlying population: To the extent that a demographic is over-represented in a population with a specific ailment relative to the general population, we would expect them to be over-represented in the population of studies focusing on that ailment. As noted earlier, for example, men experience hearing loss at twice the rate of women, and we would expect a study randomly selected from people experiencing hearing loss to include more men than women. However, we also cannot rule out other sources of demographic imbalance, such as differences in the desire to participate in

the health-care sector, differences based on spatial demographic clustering relative to the location of studies, and demographic differences in access to health-care services.

One important contribution of this report is simply to set a baseline for how complete the demographic data from ClinicalTrials.gov are. The Final Rule of the FDAAA is only universally applicable for ACTs initiated as of January 18, 2017. Given the long time-lags that can exist between study initiation, completion, and uploading of final results, we would expect that future years will see higher rates of reporting as a larger proportion of clinical trials falls under the mandatory reporting requirements. Future replications of these analyses will be able to show to what extent reporting has or has not improved relative to this baseline.

This report also serves as a guidepost for future research. Clinical trial demographic mix does not match the general population, but for many diseases the exact demographic mix of the patient population and the extent to which it diverges from the general population are not well documented. To the extent that future work can fill in this missing piece of information, study-specific recruiting practices can be improved or, if they already generate a representative sample, used as a template for others.

# Appendix. Clinical Classifications Software for ICD-10-CM

<b>ICD-10-CM Diagnosis Chapter</b>	<b>3-Character Abbreviation</b>
Diseases of the Blood and Blood-Forming Organs and Certain Disorders Involving the Immune Mechanism	BLD
Diseases of the Circulatory System	CIR
Diseases of the Digestive System	DIG
Diseases of the Ear and Mastoid Process	EAR
Endocrine, Nutritional, and Metabolic Diseases	END
External Causes of Morbidity	EXT
Diseases of the Eye and Adnexa	EYE
Factors Influencing Health Status and Contact with Health Services	FAC
Diseases of the Genitourinary System	GEN
Certain Infectious and Parasitic Diseases	INF
Injury, Poisoning, and Certain Other Consequences of External Causes	INJ
Congenital Malformations, Deformations, and Chromosomal Abnormalities	MAL
Mental, Behavioral, and Neurodevelopmental Disorders	MBD
Diseases of the Musculoskeletal System and Connective Tissue	MUS
Neoplasms	NEO
Diseases of the Nervous System	NVS
Certain Conditions Originating in the Perinatal Period	PNL
Pregnancy, Childbirth, and the Puerperium	PRG
Diseases of the Respiratory System	RSP
Diseases of the Skin and Subcutaneous Tissue	SKN
Symptoms, Signs, and Abnormal Clinical and Laboratory Findings, Not Elsewhere Classified	SYM
Unacceptable principal diagnosis (inpatient data) or first-listed diagnosis (outpatient data)	XXX

Source: Agency for Healthcare Research and Quality, <https://hcup-us.ahrq.gov/toolssoftware/ccsr/dxccsr.jsp> (2023)

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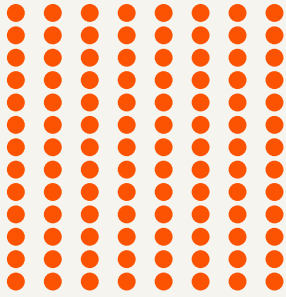
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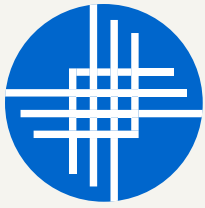


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