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Translated consent documents rarely used in non-industry sponsored studies

A dissertation submitted in partial satisfaction of the

requirements for the degree Master of Science

in Clinical Research

by

Maria Antonia Velez

2023

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ABSTRACT OF THE THESIS

Translated consent documents rarely used in non-industry sponsored studies

by

Maria Antonia Velez

Master of Science in Clinical Research

University of California, Los Angeles, 2023

Professor Marc A. Suchard, Chair

Patients from historically underrepresented racial and ethnic groups are enrolled in cancer clinical trials at disproportionately low rates in the United States 1-3. As these patients often have limited English proficiency⁴⁻⁷, we hypothesized that one barrier to their inclusion is the cost to investigators of translating consent documents. To test this hypothesis, we evaluated more than twelve-thousand consent events at a large Cancer Center and assessed whether patients requiring translated consent documents would sign consent documents less frequently in studies lacking industry sponsorship (for which the principal investigator pays translation costs) than for industry sponsored studies (for which this cost is covered by the sponsor). Here, we show that the proportion of consent events for patients with limited English proficiency in studies not sponsored by industry

was approximately half of that seen in industry sponsored studies. We also show that among those signing consent documents, the proportion of consent documents translated into the patient's primary language in studies without industry sponsorship was approximately half of that seen in industry sponsored studies. Our results suggest that the cost of consent document translation in trials not sponsored by industry is a potentially modifiable barrier to the inclusion of patients with limited English proficiency.

The dissertation of Maria Antonia Velez is approved.

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2023

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INTRODUCTION

Cancer clinical trials are the primary means of developing novel diagnostic and therapeutic strategies, and trial participation has been shown to improve patient outcomes 8,9. Patients from traditionally underrepresented racial and ethnic groups participate in clinical trials at disproportionately low rates 10-14. An increasing societal focus on diversity, equity, and inclusion has highlighted shortcomings in current clinical trial enrollment, offering opportunities to improve trial access in a broader population, with potentially greater generalizability of trial results 2,15. While barriers have been extensively studied, there has been limited progress toward achieving equity 1,2,7,10,12,16,17. Many impactful barriers, including low health literacy and mistrust of the healthcare system, are not easily addressed by individual clinical trial investigators 16,18. Investigator-related barriers to equitable clinical trial enrollment have been less thoroughly studied 18,19. While data supports the importance of having trial investigators and staff from a similar ethnic and racial background as potential trial participants, study investigators from traditionally underrepresented groups remain uncommon, whereas representation among study staff demonstrates significant regional variability 9,17,20,21.

The non-Hispanic White population in the United States has proportionally decreased, based in part on immigration from Asia and Latin America^{22,23}. The percentage of residents speaking a language other than English at home rose from 11% in 1980 to 22% by 2018, with rates above 70% among individuals identifying as Hispanic or Asian 23-25. Consequently, the relative importance of limited English proficiency, an established barrier to trial participation, has likely increased over time. Yet, factors contributing to the low participation of patients with limited English proficiency are understudied 7-9.

Ensuring that trial participants are appropriately informed regarding procedures and risks is a cornerstone of ethical research 26. Institutional Review Boards (IRBs) and the FDA mandate that presented consent documents are in a language understandable to the patient 27-29. Translation of consent documents is a formal and costly process requiring an official certificate of translation29-31. Translation can lead to enrollment delays, an important concern in cancer studies, in which patients' clinical condition often deteriorates over time 32. The impact of consent document translation on trial participation is difficult to study, as only limited data can be collected from patients who do not sign consent documents.

A large percentage of clinical trials are funded by industry33. As most involved companies are public, with a fiducial responsibility to maximize value for their shareholders, studies would be expected to be designed to achieve a strategic goal of the company. Most studies not sponsored by industry are funded by a grant from an industry partner or a philanthropic or governmental group33,34. In cases in which the grant is from an industry partner, the industry partner can provide study drug and/or additional financial support, although generally less funding than in industry sponsored studies (Figure 1) 35. In non-industry sponsored studies, the principal investigator generally operates on a fixed, per patient budget, whereas in industry sponsored studies, the study sponsor provides additional funds for consent translation beyond the negotiated per patient budget 36. Although an investigator can request funds for consent translation in the budget of a proposed grant, many grants have a budget cap, meaning that such a request would limit the funds that could be requested for other study activities 36. Were funds for translation costs included in a funded grant, those funds could often be directed to other study activities if consent document translation costs were below the budgeted amount.

Among several barriers to the participation of patients with limited English proficiency in clinical trials, we hypothesized that the additional cost of consent translation incurred by investigators on studies not sponsored by industry could discourage investigators from offering trial participation to patients for whom consent document translation is required 4,5,30. Although prohibited by regulations, an investigator who lacks sufficient funds may not offer consent documents to a patient who is not proficient in English (Figure 1), or the investigator could have the patient sign consent documents in a language for which documents are already available (generally English). Of these inappropriate approaches, the former would be nearly impossible to demonstrate, and the latter would be unlikely to be identified, as analyses to date have not evaluated the frequency of patients signing consent documents in a language in which the patient is not proficient.

To test our hypothesis that patients requiring consent document translation would sign consent documents less frequently in studies in which the investigator is responsible for the cost of translation (non-industry sponsored studies) compared to studies for which these costs can be passed on to industry, we assessed data from all consent events for studies conducted at the Jonsson Comprehensive Cancer Center over a six-year period to determine patients' primary language, English proficiency, and language of consent documents. We compared studies not sponsored by industry to those sponsored by industry to evaluate potential differences based on participant primary language and English proficiency.

METHODS

Study population:

After IRB approval, data were collected for all patients signing consent documents for studies conducted at the Cancer Center from January 1, 2013, to December 31, 2018, the data presented for the most recent Cancer Center competitive renewal period (five years plus one year of bridge funding). Data on consent events and investigator-reported patient demographics were extracted from the clinical trial database, OnCore (OnCore Enterprise Research, Advarra Inc, Columbia, MD) (Supplementary Methods). Patient characteristics, including primary language, need for a translator, insurance provider, and date of birth were obtained from the demographic section of the Epic (Epic Systems Corporation, Verona, WI) electronic health record. Using each patient's medical record number, patient data were matched to consent event data retrieved from OnCore. Study data was collected and managed using the Research Electronic Data Capture (REDCap) system, and protected health information was manipulated by a third party through the UCLA Department of Biostatistics 42,43.

Primary language and limited-English proficiency designations

Definitions for primary language can be found in the Supplementary Methods. Patients were considered to have limited English proficiency when the demographic section of the electronic health record indicated the need for an interpreter or when medical record review indicated need for an interpreter during any encounter within six months of study consent. Chart review was performed on a randomly selected sample of 200 consent events for patients with English as their primary language to evaluate whether there was an identifiable group requiring an interpreter six months before or after the consent date. Based on this analysis, adult patients with English as a primary language were considered proficient in English, while for pediatric patients, English

proficiency was evaluated regardless of the patient's primary language. Pediatric patients with limited English proficiency were those for whom the electronic health record indicated that the patient needed an interpreter or for whom the parents/guardians required an interpreter within 6 months of the consent date, as the parents/guardians sign the primary consent documents. When a pediatric patient had a primary language documented as English, but limited English proficiency was present (based on the parents/guardians), we considered the patient to have a primary language other than English and limited English proficiency.

Language of consent and sponsor assessment

All consent documents for patients with a primary language other than English were reviewed to determine whether the patient signed consent documents in their primary language. When this information was not available, all IRB-approved translated consent documents were reviewed. We considered patients to have signed consent documents in their primary language if IRB-approved consent documents were available at the time of consent or within 30 days after the consent event (Appendix).

As it could not be definitively determined whether a patient signed consent documents in a language different from their primary language for which they were also proficient, an additional analysis was performed in which we only identified consent events for which there were no translated consent documents at the time of consent or within 30 days after the consent event to identify patients who definitively signed English consent documents.

Study type and sponsor assessment

The Cancer Center labels studies as interventional when a clear pharmacologic, dietary, lifestyle intervention, procedural, or diagnostic intervention was performed on participants. All other

studies are labeled as observational. We did not have access to complete budget data, but the study sponsor was documented. Studies considered industry sponsored had a biopharmaceutical company serve as the funding sponsor. All other studies were considered non-industry sponsored. An additional analysis was performed, dividing studies based on whether there was no possibility of any funds for consent translation from industry (i.e. no industry partner or the only contribution of an industry partner was a study drug or device) versus studies in which funds for consent translation from industry could not be ruled out. Studies were also reviewed to assess whether they included a single solid or hematologic malignancy, multiple histologies or healthy patients.

Assessment of cost of consent document translation

For simplicity, we assumed that every study had the initial consent document translated at twenty cents per word, the median cost for translation paid by the Cancer Center studies during the evaluated period. (Supplementary Methods).

Statistical Analyses

Patient characteristics were summarized using frequency (%) and compared using Pearson Chi-square tests (Supplementary Methods). The median number of consent events between studies sponsored and not sponsored by industry were compared using the Wilcoxon Rank Sum test.

Logistic regression models with Generalized Estimating Equations, clustered by patient unique identifier to adjust for repeated measures, compared consent events for non-industry versus industry sponsored studies. As a sensitivity analysis, since patients clustered within each study may be more correlated than patients in other studies, the same Generalized Estimated Equation models were run specifying patients nested within each study as the repeated effect. Models were constructed in two consent event groupings: all consent events and the subset in which patients

signed consent documents in their primary language. The main explanatory variable was a language grouping variable (English primary versus primary other than English or limited English proficiency). Additional covariates were prospectively identified: age at consent, a single category for race and ethnicity in which Hispanic patients were coded as such regardless of race [i.e., Hispanic, Black, Asian or Pacific Islander, other (which included race or ethnicities in whose proportion in the evaluated population was less than 4.0%), non-Hispanic White], female versus male, interventional versus non-interventional, and the study's included histologies (single hematologic malignancy, solid malignancy, multiple histologies or healthy patients). For each set of models, we first constructed bivariable models and then multivariable models. Additional analyses were conducted to estimate the effect of the language grouping variable within subgroups based on the Department conducting the study and interventional studies. Consent events missing primary language were excluded from all analyses. Other methods for handling missing data are described in Supplementary Methods.

The McNemar's test compared the subset of patients who signed consent documents for both industry and non-industry sponsored studies to identify the probability of signing translated consent documents for a study based on whether or not the study had industry sponsorship (Appendix).

For all tests, a two-tailed P-Value <0.05 was considered statistically significant. Data were analyzed using SAS software, version 9.3 (SAS Institute) and JMP Pro 16.0 (SAS Institute Inc., Cary, NC, USA).

RESULTS

Study Population

Of 13,717 consent events between January 2013 and December 2018, those excluded from further analysis included 303 for which no medical record number was available, 1,212 at affiliated sites for which electronic health record access was not available, and 120 for which the primary language could not be identified. Most of the remaining 12,082 consent events were for patients with English as their primary language (n=11,340, 93.9%). Of the 742 consent events for patients with a primary language other than English, 481 (64.8%) included a patient meeting the definition for limited English proficiency (Figure 2).

Of 200 evaluated consent events evaluated as a control to ensure English proficiency among patients with English as a primary language, 58 were for children. Evidence of the need for an interpreter was not found in any of the consent events for adult patients, but there were four consent events for pediatric patients with English as their primary language for which need for an interpreter was documented, all based on limited English proficiency among the parents/guardians. Out of all 247 pediatric consent events in the study population, need for an interpreter was documented in seventeen consent events for patients with English as their primary language (6.9%). These seventeen patients were analyzed as having a primary language other than English and limited English proficiency.

As some patients signed consent documents for multiple studies, the 12,082 consent events occurred in 9,213 patients. Patients from racial and ethnic groups other than non-Hispanic White represented 26.7% of those signing consent documents. Yet, non-Hispanic White patients represented only 16.6% of patients with a primary language other than English (Figure 2, Extended

Data Table 1). Among members of racial and ethnic groups other than non-Hispanic White, 18.3% of those signing consent documents for studies had a primary language other than English, including nearly a quarter of Hispanic and Asian or Pacific Islander patients. The most common primary languages other than English were Spanish (40.8%, n=231) and Chinese (Mandarin, Cantonese, and simplified Chinese) (20.8%, n=118) (Extended Data Table 2). The median number of words in the initial English consent document was 7491.5 (range 598 to 20,382 words), with an estimated cost of \$1,498 for translation per initial consent document. Additional costs would be incurred to translate consent document at the time of protocol amendments, an amount that would vary by trial.

Consent events based on industry sponsorship

There were slightly fewer consent events for industry sponsored studies (n= 5,734) than non-industry sponsored studies (n= 6,348) (Extended Data Table 3). Of 758 studies for which patients signed consent documents, 34.4% (n=261) had any available IRB-approved translated consent documents. While most studies were sponsored by industry (n = 585), median number of consent events per study was less as compared to non-industry sponsored studies (5.0 versus 8.0, p<0.001). Yet, industry sponsored studies more frequently had translated consent documents available (51.4% versus 23.9%, p<0.001). The odds of a consent event for an industry sponsored study having any available translated consent documents were greater than for a non-industry sponsored study [odds ratio (OR) 3.20, 95% (confidence interval) 95% CI, 3.16 to 3.56, p<0.001] (data not shown).

Patients with a primary language other than English represented 8.1% of consent events in industry sponsored studies versus 4.4% in studies not sponsored by industry (p<0.001) (Figure 3). Patients

with limited English proficiency represented 5.5% of consent events in industry sponsored studies versus 2.8% in studies not sponsored by industry ($p<0.001$). Findings were similar when only interventional were analyzed (Extended Data Fig.1). The safety net insurer Medi-Cal was common among patients with a primary language other than English, but the proportion of patients with Medi-Cal as their payor was similar between studies with and without industry funding (Extended Data Fig.2).

Use of consent documents translated into the patient's primary language based on sponsor type

Patients with a primary language other than English signed consent documents in a language other than the patient's primary in 44.0% of consent events for industry sponsored studies versus 73.7% in studies not sponsored by industry ($p<0.001$). When analyzing patients with limited English proficiency, rates were 32.2% versus 67.2%, respectively ($p<0.001$) (Figure 4). When only evaluating studies in which there were no translated consent documents within 30 days of the date of consent, the corresponding results were 41.4% versus 71.2% for patients with a primary language other than English signing consent documents in English ($p<0.001$) and 30.3% versus 64.4% ($p<0.001$) in patients with limited English proficiency. Of 52 patients who signed consent documents for both industry and non-industry sponsored studies, ten signed all consent documents in their primary language, 24 signed all in a language different than primary and eighteen signed in their primary language for one study and a language different than primary for the other. Sixteen of these 18 patients signed consent document in a language different than primary for the non-industry sponsored study ($p=0.002$) (Figure 4C). Patients with a primary language other than English, including those with limited English proficiency, had a higher proportion of consent events in which the patient signed consent documents in a language different than their primary in studies not sponsored by industry across Departments (Extended Data Tables 4 and 5).

Differences in the proportion of consent events by sponsor type were largely driven by a difference in consent events in the patient's primary language. The proportion of consent events for patients with a primary language other than English who signed consent documents in the patient's primary language was 4.5% versus 1.2% ($p < 0.001$) in industry versus non-industry-sponsored studies, and 3.7% versus 0.9% ($p < 0.001$) for those with limited English proficiency (Figure 3). However, the proportion of consent events for patients with a primary language other than English who signed consent documents in a language different than primary was similar between industry and non-industry sponsored studies (3.6% versus 3.2%, $p = 0.44$) and patients with limited English proficiency (1.8% versus 1.9% ($p = 0.71$)).

Bivariable analyses of consent odds based on language and sponsor type

Among patients signing consent documents for Cancer Center studies, patients with a primary language other than English had lower odds of signing consent documents for non-industry sponsored studies compared to those whose primary language was English on bivariable analysis (OR, 0.50, 95% CI, 0.43 to 0.59, $p < 0.001$), as did patients with limited English proficiency (OR, 0.47, 95% CI, 0.38 to 0.57, $p < 0.001$) (Extended Data Table 6). When analyzing only consent events for which patients signed consent documents in their primary language, those with a primary language other than English (OR, 95% CI, 0.24, 0.18 to 0.31, $p < 0.001$), and limited English proficiency (OR, 0.23, 95% CI, 0.17 to 0.31, $p < 0.001$), had lower odds of signing consent documents for studies not sponsored by industry compared to patients with English as their primary language. Findings remained consistent when studies that could have received some industry support for consent translation were grouped with those that were sponsored by industry (Extended Data Table 7). Patients with a primary language other than English, including those

with limited English proficiency, had lower odds of signing consent documents for non-industry than for industry sponsored studies across Departments (Figure 5).

Multivariable analyses of consent odds based on language and sponsor type

A multivariable analysis was performed to evaluate whether associations were confounded by other factors. After adjusting for age at consent, gender, race, ethnicity, histology, and study type (observational versus interventional), patients with a primary language other than English (OR, 0.74, 95% CI, 0.63 to 0.94, $p=0.005$) and limited English proficiency (OR, 0.74, 95% CI, 0.58 to 0.95, $p=0.02$) had lower odds of signing consent documents for non-industry sponsored studies than patients with English as their primary language. Younger age, women and Asian and Pacific Islander and Hispanic (both compared to non-Hispanic White) patients also had lower odds of signing consent documents for non-industry sponsored studies. The odds of signing consent documents for observational studies was higher in studies not sponsored by industry (Table 1). When only patients who signed consent documents in their primary language were analyzed, the odds of signing consent documents for a non-industry sponsored study were considerably lower for patients with a primary language other than English (OR, 0.38, 95% CI, 0.27 to 0.52, $p<0.001$) and limited English proficiency (OR, 0.35, 95% CI, 0.25 to 0.50, $p<0.001$) compared to patients with English as their primary language. Results remained consistent when consent events were clustered by patients nested within each study (Extended Data Table 8).

DISCUSSION

We found that the proportion of consent events for patients with a primary language other than English was lower in non-industry versus industry sponsored studies. For non-industry sponsored studies, patients with a primary language other than English frequently signed consent documents

in in a language different than their primary. Findings persisted when analyses were restricted to patients with limited English proficiency.

Studies to date assessing the impact of financial costs to investigators of consent document translation as a potential impediment are lacking. Standard economic theory argues that increasing the expense faced by an individual for an activity discourages the individual from engaging in that activity 37. Our concern that the cost to the investigator of consent document translation would discourage enrollment of patients requiring translated consent documents drove us to test the hypothesis that patients requiring translated consent documents would be less likely to sign consent documents for studies not sponsored by industry. While a retrospective study cannot prove causation, the consistent associations across analyses support the hypothesis that patients requiring translated consent documents were selectively missing from studies not sponsored by industry. These observations were unlikely to be driven by differential enrollment by sponsor type, as the odds of having any translated consent documents available for non-industry sponsored studies was substantially lower despite a greater median number of consent events per study when compared to industry sponsored studies. These observations are also unlikely to be driven by differences in the patient population by sponsor type, as when the same patient signed consent documents for both an industry and non-industry sponsored study, nearly all patients who signed consent documents in discrepant languages signed in a language different from their primary for the non-industry sponsored study.

Our investigation was driven by an awareness of insufficient participation of patients from traditionally underrepresented groups on clinical trials. So, our approach focused on potential barriers to participation posed by language. An approach that increases consent events for non-

industry sponsored studies among patients with a primary language other than English to the level seen in industry sponsored studies would be expected to lead to a modest but real increase in representation of patients on Cancer Center studies from ethnic or racial groups other than non-Hispanic White. Although our analysis focused on cancer studies, investigators studying other diseases face similar pressures. Whether our findings extend beyond oncology studies should be investigated.

Our results also raise concern about the quality of information conveyed to patients with limited English proficiency. The NIH Policy and Guidelines on the Inclusion of Women and Minorities clearly indicates that cost of inclusion of participants with limited English proficiency in clinical research should not hinder their participation 38. However, no additional resources are typically provided to investigators to cover the cost of consent translation on studies not sponsored by industry, which are typically funded through federal grants or cooperative groups 30,39. As such, a potential readily modifiable barrier to the participation of patients with a primary language other than English would be to increase the availability of funds for the translation of consent documents to be used by investigators on non-industry sponsored studies. This approach may also increase the quality of information presented to patients with limited English proficiency.

Strengths of the current dataset include a large number of consenting events based on six years of heavily curated data at a high-enrolling Cancer Center, the high number of translated consent documents, and the large number of patients signing consent documents for studies not sponsored by industry. Additionally, inclusion of all consent events for which the appropriate data was available increases confidence in our results and reduces potential biases. The primary weakness of our analysis is its single institution nature. Sensitivities regarding patient health information,

study-related data, and differences in regulatory structures make cross-center studies difficult. The general consistency across Departments suggests that the observed findings are widespread. However, data from additional Cancer Centers would enhance confidence in our findings. National Cancer Institute designated Cancer Centers serve unique populations by design 40, and while Southern California has greater racial and ethnic diversity than some areas of the Country 41, increasing non-Hispanic White populations are not limited to this region.

Significant findings for Asian and Pacific Islander race and Hispanic ethnicity in our multivariable analysis suggest that our models may not have optimally separated the effects of race and ethnicity from language. As other racial groups were not underrepresented in non-industry sponsored studies, it is possible that the effect of language in the multivariable analysis may have persisted for Asian and Pacific Islander and Hispanic patients based on perceived limited English proficiency. This will be an important topic for future research. Another limitation is the retrospective nature of our study and reliance on electronic health record data. There is the possibility that data may not be documented accurately, and we were not able to independently verify language proficiency.

As our analysis was designed to compare consent events by presence or absence of industry sponsorship, all data included were from patients signing consent documents for Cancer Center studies. We were unable to assess important barriers, including patient-related barriers, preventing patients from consenting to any Cancer Center study. Clearly, the cost of consent translation was not the only factor discouraging translation of consent documents among patients who did sign consent documents. Even on industry sponsored studies, a substantial proportion of patients with limited English proficiency signed consent documents in a language different than their primary.

Other barriers, such as delays associated with consent document translation and lack of training for research staff on appropriate consent practices for patients with limited English proficiency, may have played important roles. As such, additional impediments should be explored to inform possible future interventions.

CONCLUSION

Our findings suggest that an important barrier for patients with limited English proficiency to participate in cancer studies may be the cost that consent translation presents to investigators, particularly in studies not sponsored by industry. This work identifies a potentially modifiable barrier to enrolling these patients on studies, which is of particular importance in an increasingly multicultural and multilingual population.

TABLES AND FIGURES

Variable	Multivariable Analysis for patients with a primary language other than English signing consent documents			Multivariable Analysis for patients with a primary language other than English signing consent documents in patient's primary language			Multivariable Analysis for patients with limited English proficiency signing consent documents			Multivariable Analysis for patients with limited English proficiency signing consent documents in patient's primary language		
	OR	95% CI	P Value	OR	95% CI	P Value	OR	95% CI	P Value	OR	95% CI	P Value
Age												
Age at consent (per year)	0.97	0.97-0.98	<0.001	0.98	0.97-0.98	<0.001	0.97	0.97-0.98	<0.001	0.97	0.97-0.98	<0.001
Language												
English Primary		Reference			Reference			Reference			Reference	
Primary Other than English*	0.74	0.63-0.94	0.005	0.38	0.27-0.52	<0.001	-	-	-	-	-	-
Limited English Proficiency**	-	-	-	-	-	-	0.74	0.58-0.95	0.02	0.35	0.25-0.50	<0.001
Race and Ethnicity												
Non-Hispanic White		Reference			Reference			Reference			Reference	
Asian or Pacific Islander	0.64	0.54-0.75	<0.001	0.66	0.56-0.79	<0.001	0.65	0.55-0.77	<0.001	0.66	0.55-0.79	<0.001
Black	1.00	0.80-1.26	0.97	1.02	0.81-1.29	0.85	1.06	0.80-1.27	0.97	1.02	0.81-1.28	0.86
Hispanic	0.75	0.63-0.89	<0.001	0.76	0.64-0.92	0.003	0.73	0.62-0.88	<0.001	0.76	0.63-0.90	0.002
Other	1.15	0.87-1.54	0.32	1.16	0.87-1.56	0.30	1.15	0.86-1.53	0.34	1.2	0.87-1.56	0.30
Unknown	3.38	2.86-4.01	<0.001	3.40	2.86-4.04	<0.001	3.43	2.89-4.06	<0.001	3.43	2.88-4.02	<0.001
Study Type												
Interventional		Reference			Reference			Reference			Reference	
Observational	36.2	28.3-46.4	<0.001	35.1	27.3-44.9	<0.001	35.7	27.7-37.3	<.0001	34.9	27.2-44.8	<.0001
Gender												
Male		Reference			Reference			Reference			Reference	
Female	0.38	0.35-0.42	<0.001	0.37	0.33-0.42	<0.001	0.38	0.35-0.42	<.0001	0.37	0.34-0.41	<0.001
Histology												
Single Solid Malignancy		Reference			Reference			Reference			Reference	

Healthy	1.78	1.35-2.35	<0.001	1.87	1.41-2.48	<0.001	1.86	1.37-2.52	<.0001	1.88	1.41-2.50	<0.001
Multiple Histology	0.38	0.34-0.42	<0.001	0.38	0.34-0.42	<0.001	0.36	0.33-0.40	<.0001	0.38	0.34-0.42	<0.001
Single Heme Malignancy	0.06	0.04-0.08	<0.001	0.06	0.04-0.09	<0.001	0.06	0.04-0.09	<.0001	0.06	0.04-0.09	<0.001

Table 1. Multivariable analysis for odds ratio for the association between various factors and signing consent documents into a non-industry sponsored study.

*Patients with a primary language other than English compared to patients with English as their primary language. ** Patients with limited English proficiency compared to patients with English as their primary language. Abbreviations, OR; odds ratio, CI; confidence Interval

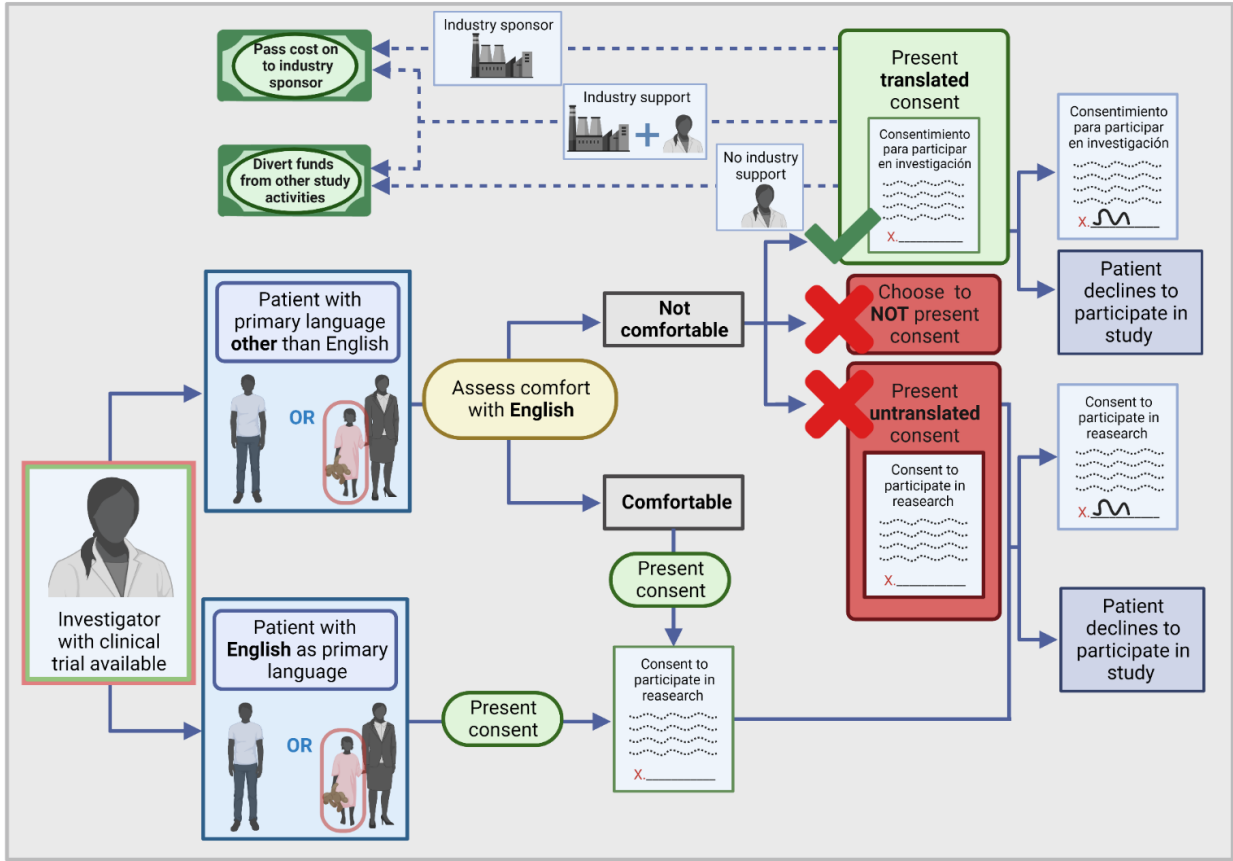


Figure 1. Consent process and cost allocation of consent document translation.

An investigator meeting an eligible patient for a clinical trial should assess the patient’s (or parent/guardian’s) comfort with signing an English consent document. If patient (or parent/guardian) is not comfortable with signing a consent document in English, the investigator should translate the consent documents. Depending on the study funder, this cost can be either completely passed on to the industry sponsor, potentially covered by the industry sponsor or covered completely by the investigator.

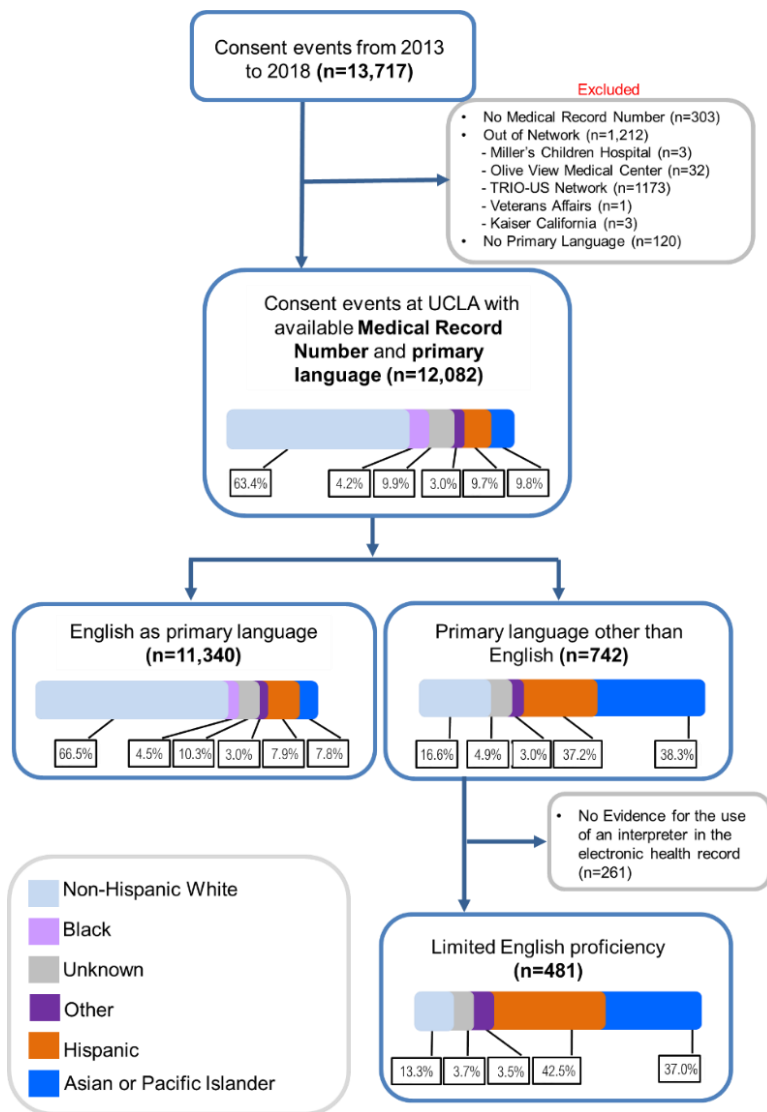


Figure 2. Consent events included in the study.

Consent event data for patients who consented into Cancer Center studies from 2013 to 2018 were included in our analysis if they had a medical record number in our electronic health system as well as a documented primary language (n=12,082). Patients were considered to have English as their primary language (English Primary, n=11,340) or to have a primary language other than English (n=742). Patients with a primary language other than English were considered to have limited English proficiency if there was evidence for the use of an interpreter in the electronic health record. The racial/ethnic distribution of patients is depicted.

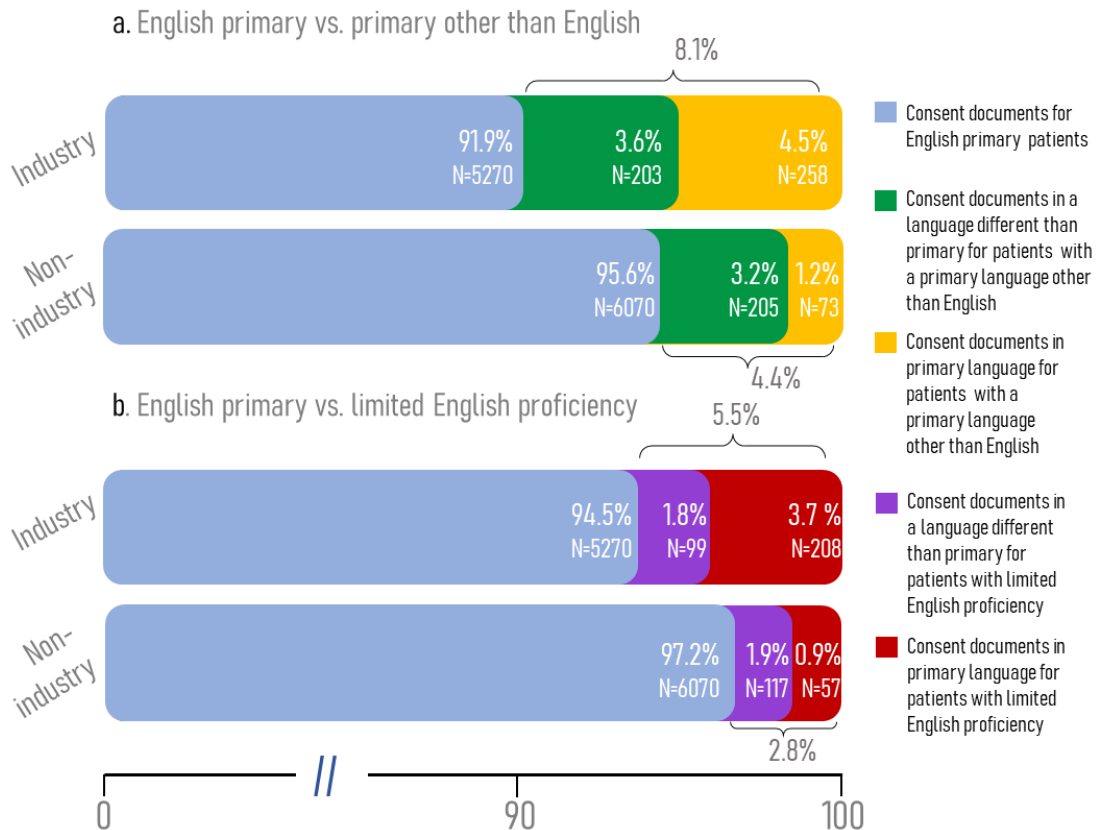


Figure 3. Comparison of the proportion of consent events based on primary language and English proficiency in industry versus non-industry sponsored studies.

A. Blue indicates the proportion of consent events for patients with English as their primary language. The bracketed areas indicate the proportion of consent events for patients with a primary language other than English in industry sponsored studies (top bar) versus non-industry sponsored studies (bottom bar) (8.1% versus 4.4%, $p < 0.001$). Green indicates the proportion of consent events for patients with a primary language other than English signing consent documents in a language different than their primary in industry sponsored studies (top bar) compared to non-industry sponsored studies (bottom bar) (3.6% versus 3.2%, $p = 0.44$). Yellow indicates the proportion of consent events for patients with a primary language other than English signing

consent documents in their primary language in industry sponsored studies (top bar) compared to non-industry sponsored studies (bottom bar) (4.5% versus 1.2%, $p < 0.001$). **B.** Blue indicates the proportion of consent events for patients with English as their primary language. The bracketed areas indicate the proportion of consent events for patients with limited English proficiency in industry sponsored studies (top bar) versus non-industry sponsored studies (bottom bar) (5.5% versus 2.8%, $p < 0.001$). Purple indicates the proportion of consent events for patients with limited English proficiency signing consent documents in a language different than their primary in industry sponsored studies (top bar) compared to non-industry sponsored studies (bottom bar) (1.8% versus 1.9%, $p = 0.71$). Red indicates the proportion of consent events for patients limited English proficiency signing consent documents in their primary language in industry sponsored studies (top bar) compared to non-industry sponsored studies (bottom bar) (3.7% versus 0.9% $p < 0.001$).

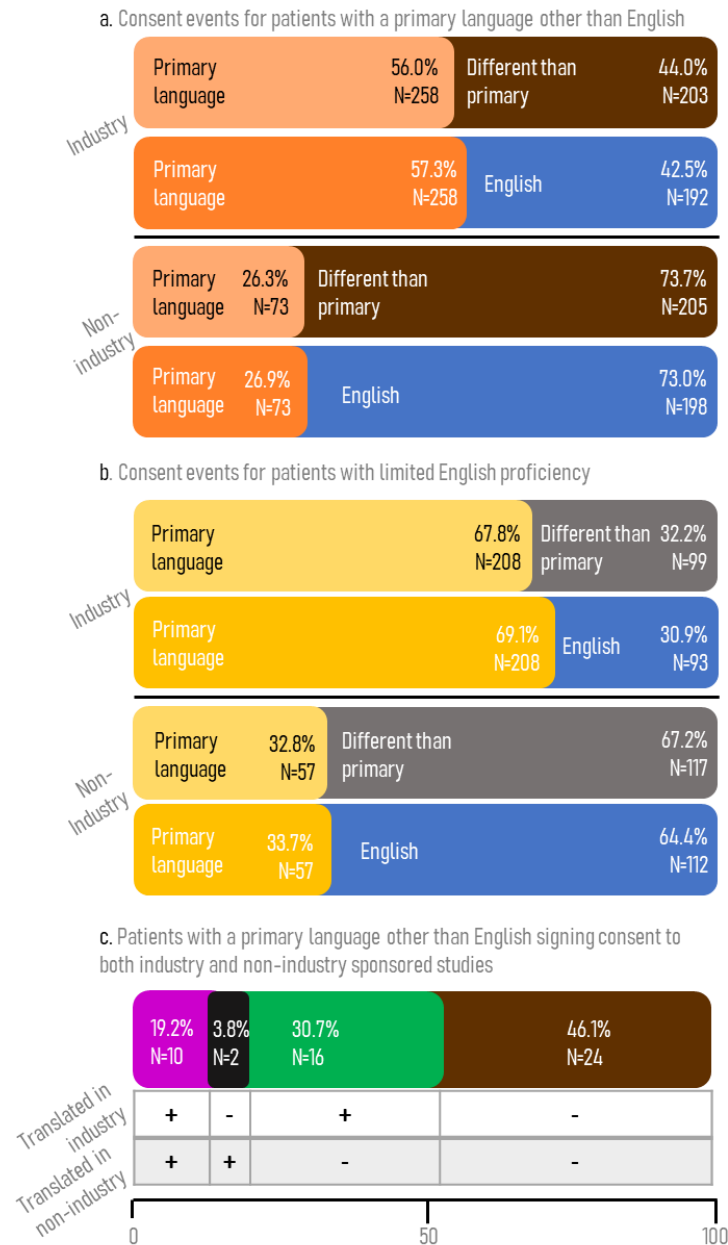


Figure 4. Comparison of the proportion of consent events by language.

A. The proportion of consent events for which patients with a primary language other than English signed consent documents in their primary language in industry (top bar) versus non-industry sponsored studies (bottom bar) (light orange, 56.0% versus 26.3%, $p < 0.001$; dark orange, 57.3% versus 26.9%, $p < 0.001$). Brown indicates the proportion of consent events for which patients

signed consent documents in a language different than primary in industry (top bar) versus non-industry sponsored studies (bottom bar) (44.0% versus 73.7%, $p < 0.001$). Blue indicates the proportion of consent events for which patients signed consent documents in English in industry (top bar) versus non-industry sponsored studies (bottom bar) (42.5% versus 73.0%, $p < 0.001$) **B.** The proportion of consent events for which patients with limited English proficiency signed consent documents in their primary language in industry (top bar) versus non-industry sponsored studies (bottom bar) (light yellow, 67.8% versus 32.8%, $p < 0.001$; dark yellow, 69.1% versus 33.7%, $p < 0.001$). Grey indicates the proportion of consent events for which patients signed consent documents in a language different than primary in industry (top bar) versus non-industry sponsored studies (bottom bar) (32.2% versus 67.2%, $p < 0.001$). Blue indicates the proportion of consent events for which patients signed consent documents in English in industry (top bar) versus non-industry sponsored studies (bottom bar) (30.0% versus 64.4%, $p < 0.001$). **C.** Among patients with a primary language other than English signing consent documents for both an industry and a non-industry sponsored study, ten (green) signed consent documents in their primary language for both and 24 signed consent documents in a language different than primary for both. Of the eighteen patients who signed consent documents in discrepant languages, sixteen (fuchsia) signed in their primary language in the industry sponsored study versus two (black) in the non-industry sponsored studies ($p = 0.002$).

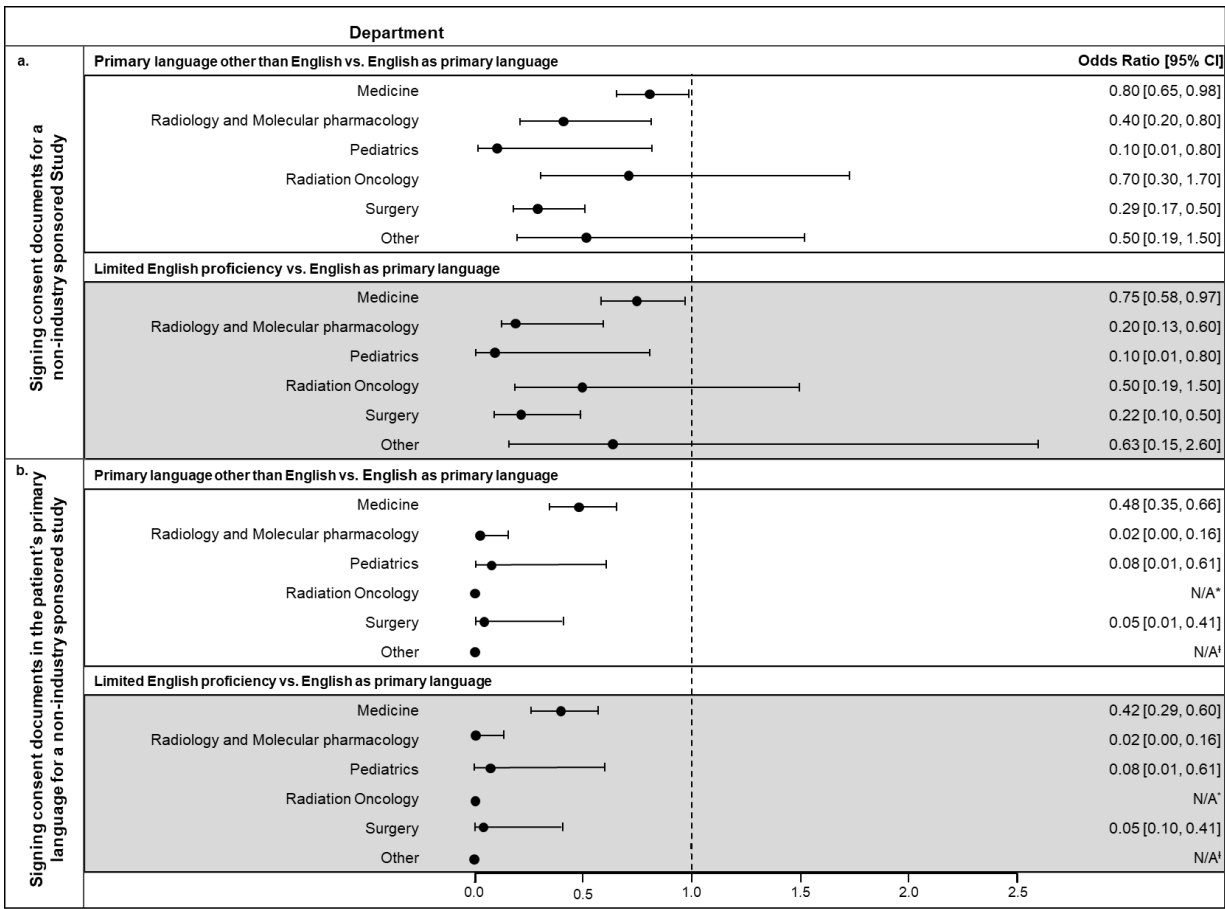


Figure 5. Odds Ratios for patients with a primary language other than English and with limited English proficiency of signing consent documents in non-industry sponsored studies compared to patients with English as their primary language across the different Departments.

*OR could not be calculated as no consent documents were translated into patient’s primary language. [†] OR could not be calculated because there were no patients with a primary language other than English or limited English proficiency who signed consent documents in their primary language in industry sponsored studies. Abbreviations; OR, Odds Ratio, CI; confidence Interval.

A. Top panel (white): Odds of consent events for patients with a primary language other than English signing consent documents in non-industry sponsored studies compared to patients with English as their primary language across different Departments.

Bottom panel (gray): Odds of consent events for patients with limited English proficiency signing consent documents in non-industry sponsored studies compared to patients with English as their primary language across different Departments.

B. Top panel (white): Odds of consent events for patients with a primary language other than English signing consent documents in their primary language in non-industry sponsored studies compared to patients with English as their primary language across different Departments.

Bottom panel (gray): Odds of consent events for patients with limited English proficiency signing consent documents in their primary language in non-industry sponsored studies compared to patients with English as their primary language across different Departments.

APPENDICES

Supplementary Methods

Study Population

Patient demographic characteristics such as race, ethnicity and gender were investigator-reported as these were collected by research coordinators at the time of consent for clinical trial participation and recorded in the electronic trial repository, Oncore. Language data was obtained by clerical staff at the time the patient had the initial encounter with the medical system.

Primary language and limited English proficiency designations

Adult patients with a listed primary language other than English in the demographics section of the electronic health record were designated as a patient with a primary language other than English, and those with English listed as their primary language were designated as patients with

English as their primary language. While patients with a primary language listed as “unknown” were excluded from our analysis, those with a primary language of “other” were included. If there was evidence of need for an interpreter in the demographic section of the electronic health record or the utilization of an interpreter within six months was documented for a patient with a primary language of “other”, they were considered to have limited English proficiency. Whether or not there was evidence of limited English proficiency, patients with a primary language listed as “other” were considered to have a primary language other than English.

Language of consent documents

We could not be definitively determined whether a patient signed consent documents in a language different from their primary language for which they were also proficient (e.g., a primary Farsi speaker who was also comfortable in Korean on a study for which a Korean consent was available), and we could only assess if the patient signed consent documents in their primary language (yes versus no).

The additional 30 days for translation of consent documents were permitted in the definition of consent documents in the patient’s primary language to account for the “short form” consent method. A short consent form consisting of a translated standardized document accompanied by verbally translated study-specific information is permitted when obtaining consent from subjects with a primary language other than English was not anticipated. As is generally true, the studied Cancer Center subsequently requires signature of translated written consent documents. Many institutions, including the studied Cancer Center, generally discourage the use of the short form because of concerns regarding the quality of information conveyed. There is also concern related to potential procedural errors that could be problematic at the time of regulatory audit.

The formal process of obtaining consent from a patient for a study has to be in the presence of one of the investigators or sub-investigators of the study at the studied Cancer Center.

Assessment of cost of consent documents

Consent documents were defined as including: 1) a study-specific informed consent document describing the purpose of the study, details regarding study procedures, expected duration, and risks associated with participation, 2) a confidentiality statement for which study specific data can be added to a non-study-specific template and 3) a document stating the research subject's rights, which is not study-specific. For the purpose of assessing cost, only the document which was entirely study-specific was considered.

Statistical analysis

Analyses on Patient Population

Pearson Chi-square tests were used to compare gender and race/ethnicity of patients with a primary language other than English and limited English proficiency to patients whose primary language was English. Patients with "unknown" race or ethnicity were excluded from these analyses.

Analyses on Consent Event groups and subgroups

All analyses performed on consent events groups and subgroups were conducted using a logistic regression model with Generalized Estimated Equation method to adjust for repeated. The endpoint for every analysis was consent events in non-industry versus industry sponsored studies.

Analysis of the probability of signing a consent document in a language different than primary in industry versus non-industry sponsored studies

For the analysis evaluating the language of signed consent documents in patients who signed consent documents for both industry and non-industry sponsored studies, if there were multiple consent events per sponsor type (industry or non-industry) we considered the patient to have signed consent documents in a language different than primary for that sponsor type if at least one consent event in that sponsor type was signed in a language different than primary.

Consent Events groups and subgroups

Overall Consent Event Group: included all consent events in which the primary language of the study participant was known (including “other”). Note: all groups and subgroups are bolded for ease of identification. The Overall Consent Event Group was further divided into subgroups and sub-subgroups based on the groupings listed below.

Proficiency Evaluable Subgroup: included all consent events for patients with English as a primary language or limited English proficiency (excluded consent events for patients with a primary language other than English who were not designated as limited English proficiency).

Primary Consent Language Evaluable Subgroup: included all consent events in which patients signed consent documents in their primary language (excluded patients who signed consent documents in a language other than their primary language, including exclusion of those with language coded as “other” for whom chart review could not identify the primary language on a study for which non-English consent documents were available).

Interventional Study Subgroup: included all consent events for interventional studies.

Primary Other than English Subgroup: included all consent events for participants with a primary language other than English. This was further subdivided into:

- **Medi-Cal Evaluable sub-subgroup:** included patients with data available on chart review to determine whether Medi-Cal was the payor.
- **Consent Language Evaluable sub-subgroup:** included patients for which we could determine if they signed a consent document in their primary language or in a language different than primary.
 - o A subgroup of this sub-subgroup included the “**Evaluable for signing consent in English**” sub-subgroup which included patients for which we could determine if they signed a consent document in their primary language or in English.

Limited English Proficiency Subgroup: Included all consent events for patients with limited English Proficiency. This was further subdivided into:

- **Consent Language Evaluable sub-subgroup:** included patients for which we could determine if they signed a consent document in their primary language or in a language different than primary.
 - o A subgroup of this sub-subgroup included the “**Evaluable for signing consent in English**” sub-subgroup which included patients for which we could determine if they signed a consent document in their primary language or in English.

Consent in language different than primary subgroup: included all consent events in which patients signed consent documents in a language different than primary. Patients with “other” as

their primary language when their language of consent was unknown were excluded if there were non-English consent documents available for the study.

Department Subgroups: divided all consent event into mutually exclusive groups based on department conducting the study (Medicine, Radiology and Molecular Pharmacology, Pediatrics, Radiation Oncology, Surgery, Other).

Primary and Secondary Analyses

The primary analysis evaluated the odds of patients with limited English proficiency signing consent documents in their primary language in non-industry versus industry sponsored studies, conducted in the Proficiency Evaluable Sub-subgroup of the Primary Consent Language Evaluable Subgroup. All variables of interest were included in the multivariable model, regardless of statistical significance on bivariable analyses.

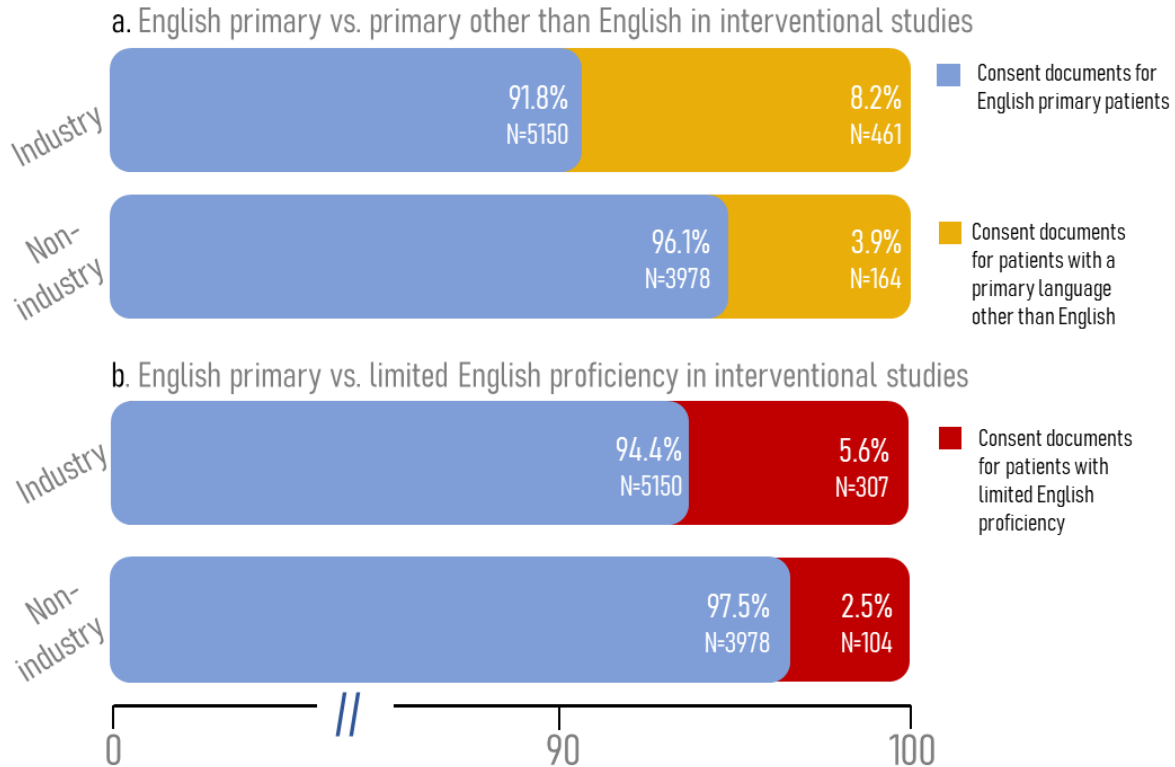
The secondary analyses evaluated the probability of patients with a primary language other than English signing consent documents (in the Overall Consent Event Group) or signing consent documents in their primary language (in the Primary Consent Language Evaluable Subgroup) in non-industry versus industry sponsored studies. It also evaluated the probability of patients with limited English proficiency signing consent documents (in the Proficiency Evaluable Subgroup) in a non-industry sponsored study versus industry sponsored study.

Handling Missing Data:

Consent events for patients in which primary language was unknown were excluded from all analyses. A complete case analysis was run in all of the multivariable models where an

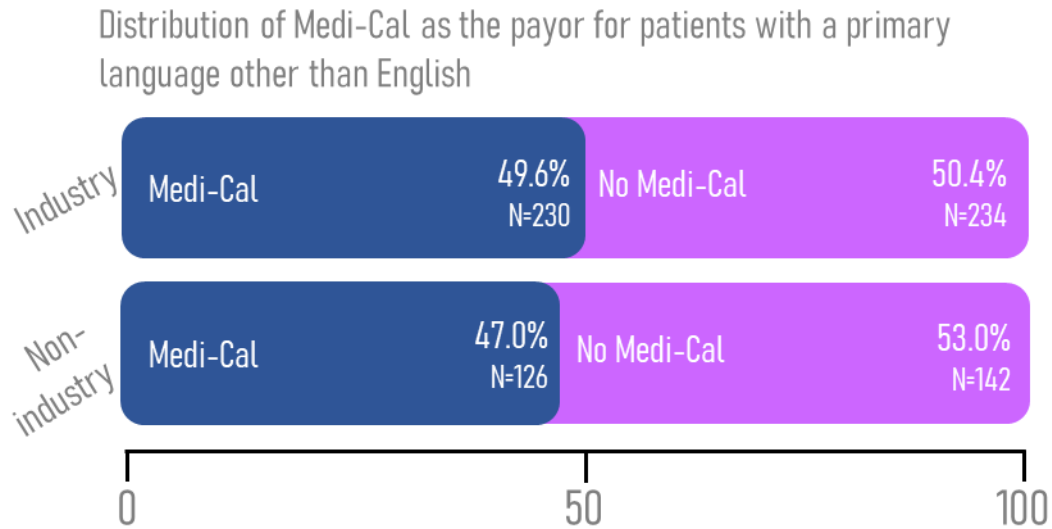
“unknown” category was included for the following variables: Race/ethnicity and gender. However, for consent events for which patients had a primary language of “other” and the language of consent was “unknown” were excluded from any analysis evaluating consent events in the patient’s primary language or in a language different than primary.

EXTENDED DATA FIGURES AND TABLES



Extended Data Figure 1. Comparison of the proportion of consent events based on primary language and English proficiency in interventional industry versus non-industry sponsored studies.

A. Blue indicates the proportion of consent events for patients with English as their primary language. Yellow indicates the proportion of consent events for patients with a primary language other than English in industry sponsored studies (top bar) versus non-industry sponsored studies (bottom bar) (8.2% versus 3.9%, $p < 0.001$). **B.** Blue indicates the proportion of consent events for patients with English as their primary language. Red indicates the proportion of consent events for patients with limited English proficiency in industry sponsored studies (top bar) versus non-industry sponsored studies (bottom bar) (5.6% versus 2.5%, $p < 0.001$).



Extended Data Figure 2. Medi-Cal as the payor for patients with a primary language other than English in industry and non-industry sponsored studies.

The proportion of consent events for patients with Medi-Cal as the payor in industry sponsored studies was 49.6% (top bar, blue), and the proportion of patients in non-industry sponsored studies was 47.0% (bottom bar, blue) (49.6% vs 47.0%, $p=0.50$). The proportion of consent events for patients without Medi-Cal coverage was 50.4% in industry sponsored studies (Top bar, lavender) and 53.0% in non-industry sponsored studies (bottom bar, lavender).

Characteristic, n (%)	Total n=9213	English Primary n=8636 (94%)	Primary Other than English n=577(6%)	P Value [§]	Limited English Proficiency n=376 (4%)	P Value*
Gender[†]						
Female	3513 (38.1)	3255 (37.7)	260 (45.1)	<0.001 [¶]	175 (46.5)	<0.001 ^{††}
Male	5686 (61.7)	5368 (62.2)	316 (54.8)		201 (53.4)	
Race and Ethnicity[†]				<0.001 ^{††}		<0.001 ^{¶¶}
Asian or Pacific Islander	901 (9.8)	680 (7.8)	221 (38.3)	<0.001	139 (37.0)	<0.001
Black	389 (4.2)	389 (4.5)	0	<0.001	0	<0.001
Other**	279 (3.0)	262 (3.0)	17 (3.0)	0.74	13 (3.5)	0.80
Hispanic	902 (9.7)	687 (7.9)	215 (37.2)	<0.001	160 (42.5)	<0.001
Non-Hispanic White	5840 (63.4)	5744 (66.5)	96 (16.6)	<0.001	50 (13.3)	<0.001

Extended Data Table 1. Characteristics of patients who signed consent documents to Cancer Center studies.

[§] Comparison between patients with primary language other than English and English primary language.* Comparison between patients with limited English proficiency and patients with English as primary language.[†] Unknown Total: 14 (0.2%).[¶] Comparison of the proportion of female and male patients between patients with a primary language other than and patients with English as primary language.^{††} Comparison of the proportion of female and male patients between patients limited English proficiency and patients with English as primary language.[†] Unknown Total: 902 (9.7%).^{††} Comparison for overall difference between racial and ethnic groups among patients with primary language other than English and patients with English as primary language (English Primary).^{¶¶} Comparison for overall difference between racial and ethnic groups among patients with limited English proficiency and patients with English as primary language. ** Other: American Indian; 16 (5.7%), Multiracial; 28 (10.0%), Other; 235

(84.3%). Abbreviations: n, number. Racial and ethnic groups representing less than 4.0% of the study population were included as “other”.

Language	Number of patients	Percent
Spanish	231	40.8%
Chinese	118	20.8%
Korean	63	11.1%
Farsi, Persian	33	5.8%
Armenian	30	5.3%
Russian	20	3.5%
Vietnamese	19	3.4%
Japanese	12	2.1%
Arabic	8	1.4%
Other	6	1.1%
Tagalog	6	1.1%
Hindi	<5	<0.4%
Hungarian	<5	<0.4%
Lithuanian	<5	<0.4%
Thai	<5	<0.4%
Afar	<5	<0.4%
Burmese	<5	<0.4%
Cambodian	<5	<0.4%
Danish	<5	<0.4%
Ethiopian	<5	<0.4%
French	<5	<0.4%
Greek	<5	<0.4%
Hebrew	<5	<0.4%
Indonesian	<5	<0.4%
Italian	<5	<0.4%
Laotian	<5	<0.4%
Ukrainian	<5	<0.4%

Extended Data Table 2. Primary languages spoken by patients with a primary language other than English.

	Non-Industry Sponsored Study	Industry Sponsored Study	P Value
Studies, N (%)	173 (22.9)	585 (77.1)	
Studies that had at least one translated consent document, N (%)	39 (14.9)	222 (85.1)	
Consent events, N (%)	6344 (52.5)	5738 (47.5)	
Median number of consent events per study (range)	8.0 (1-791)	5.0 (1-206)	<0.001
Consent events for studies that translated at least one consent, N (%)	1513 (23.9)	2951 (51.4)	<0.001
Median number of consent events for studies that translated at least one consent document (range)	9.5 (1-510)	8.0 (1-206)	0.57
Consent events for studies that did not translate any consent, N (%)	4831 (76.2)	2787 (23.4)	<0.001
Median number of consent events for studies that did not translated at least one consent (range)	8.0 (1-791)	4.0 (1-93)	<0.001
Number of Interventional studies, N (%)	143 (19.8)	577(80.2)	
Median number of consent events for interventional studies (range)	8.0 (1-585)	5.0 (1-206)	<0.001

Extended Data Table 3. Characteristics and distribution of consent events in non-industry and industry sponsored studies.

Department/Division	Proportion (%)	95% CI	P Value
Medicine			<0.001
Industry Sponsored Study	39.8	35.0 - 44.7	
Non-Industry Sponsored Study	64.1	54.1 - 72.3	
Radiology and Molecular Pharmacology			<0.001
Industry Sponsored Study	60.0	26.2 - 87.8	
Non-Industry Sponsored Study	98.4	91.2 - 99.9	
Pediatrics			NA ¹
Industry Sponsored Study	0.0	0.0 – 84.1	
Non-Industry Sponsored Study	25.9	11.1 – 46.3	
Radiation Oncology			NA [‡]
Industry Sponsored Study	100.0	63.0 - 100	
Non-Industry Sponsored Study	100.0	79.4 - 100	
Surgical specialties			0.05
Industry Sponsored Study	82.6	6.1.2 – 95.5	
Non-Industry Sponsored Study	97.3	85.8 – 99.9	
Other			NA*
Industry Sponsored Study	100	54.0 - 100	
Non-Industry Sponsored Study	44.4	13.7 – 78.8	

Extended Data Table 4. Proportion of consent events in which patients with a primary language other than English signed consent documents in a language different than primary in industry sponsored and non-industry sponsored studies across Departments.

¹P Value could not be generated because there were no patients who signed consent documents in a language different than primary in industry sponsored studies. [‡] P Value could not be generated because there were no consent documents translated. * P Value could not be generated because there were no patients who signed consent documents in a language different than primary in industry sponsored studies.

Department/Division	Proportion (%)	95% CI	P Value
Medicine			<0.001
Industry Sponsored Study	27.7	22.2 – 32.8	
Non-Industry Sponsored Study	59.5	47.8 – 70.4	
Radiology and Molecular Pharmacology			0.01
Industry Sponsored Study	55.6	21.2 – 86.3	
Non-Industry Sponsored Study	97.4	86.1 – 99.9	
Pediatrics			NA [†]
Industry Sponsored Study	0.0	0.0 - 84.2	
Non-Industry Sponsored Study	25.9	11.1 – 46.3	
Radiation Oncology			NA [‡]
Industry Sponsored Study	100.0	54.0 - 100	
Non-Industry Sponsored Study	100.0	66.3 - 100	
Surgical specialties			0.08
Industry Sponsored Study	69.2	38.5 – 90.3	
Non-Industry Sponsored Study	93.7	69.7 – 99.8	
Other			NA [*]
Industry Sponsored Study	100.0	29.2 - 100	
Non-Industry Sponsored Study	40.0	5.3 - 85.3	

Extended Data Table 5. Proportion of consent events in which patients with limited English proficiency signed consent documents in a language different than primary in industry sponsored and non-industry sponsored studies across Departments.

[†]P Value could not be generated because there were no patients who signed consent documents in a language different than primary in industry sponsored studies.[‡]P Value could not be generated because there were no consent documents translated.* P Value could not be generated because there were no patients who signed consent documents in a language different than primary in industry sponsored studies.

Variable	Bivariable Analysis for signing consent documents			Bivariable Analysis for signing consent documents in patient's primary language		
	OR	95% CI	P Value	OR	95% CI	P Value
Age						
Age at consent (per year)	0.99	0.98-0.99	<0.001	0.99	0.98-0.99	<0.001
Language						
English Primary		Reference			Reference	
Primary Other than English*	0.50	0.43-0.59	<0.001	0.24	0.18-0.31	<0.001
Limited English Proficiency**	0.47	0.38-0.57	<0.001	0.23	0.17-0.31	<0.001
Race and Ethnicity						
Non-Hispanic White		Reference			Reference	
Asian or Pacific Islander	0.61	0.53-0.69	<0.001	0.61	0.53-0.70	<0.001
Black	1.22	0.92-1.36	0.25	1.13	0.93-1.37	0.22
Hispanic	0.81	0.71-0.92	0.002	0.79	0.69-0.90	<0.001
Other	1.44	1.13-1.83	0.004	1.44	1.13-1.85	0.004
Unknown	3.34	2.89-3.94	<0.001	3.36	2.84-3.97	<0.001
Study Type						
Interventional		Reference			Reference	
Observational	32.4	25.1-41.8	<0.001	32.4	25.1-41.8	<0.001
Gender						
Male		Reference			Reference	
Female	0.37	0.34-0.40	<0.001	0.36	0.33-0.39	<0.001
Histology						
Single Solid Malignancy		Reference			Reference	
Healthy	1.62	1.23-2.14	<0.001	1.70	1.28-2.26	<0.001
Multiple Histology	0.46	0.42-0.50	<0.001	0.45	0.41-0.49	<0.001
Single Heme Malignancy	0.07	0.05-0.09	<0.001	0.07	0.05-0.09	<0.001

Extended Data Table 6. Bivariable analysis odds ratio for the association between various factors and signing consent into a non-industry sponsored study.

*Patients with a primary language other than English compared to patients with English as their primary language.** Patients with limited English proficiency compared to patients with English as their primary language. Abbreviations, OR; odds ratio, CI; confidence Interval.

Language	OR	95% CI	P Value
English Primary		Reference	
Primary Other than English*	0.615	0.52-0.72	<0.001
Limited English Proficiency**	0.64	0.53-0.79	<0.001

Extended Data Table 7. Bivariable analysis for odds ratio for the association language and signing consent documents into a non-industry sponsored study with studies for which we could not definitively determine that they did not obtain industry funding coded as industry sponsored studies.

*Patients with a primary language other than English compared to patients with English as their primary language.** Patients with limited English proficiency compared to patients with English as their primary language. Abbreviations, OR; odds ratio, CI; confidence Interval.

Variable	Multivariable Analysis for patients with a primary language other than English signing consent documents			Multivariable Analysis for patients with a primary language other than English signing consent documents in patient's primary language			Multivariable Analysis for patients with limited English proficiency signing consent documents			Multivariable Analysis for patients with limited English proficiency signing consent documents in patient's primary language		
	OR	95% CI	P Value	OR	95% CI	P Value	OR	95% CI	P Value	OR	95% CI	P Value
Age												
Age at consent (per year)	0.97	0.97-0.98	<0.001	0.98	0.97-0.98	<0.001	0.97	0.97-0.98	<0.001	0.98	0.97-0.98	<0.001
Language												
English Primary		Reference			Reference			Reference			Reference	
Primary Other than English*	0.79	0.65-0.96	0.019	0.40	0.29-0.54	<0.001	-	-	-	-	-	-
Limited English Proficiency**	-	-	-	-	-	-	0.78	0.61-0.99	0.04	0.36	0.27-0.52	<0.001
Race and Ethnicity												
Non-Hispanic White		Reference			Reference			Reference			Reference	
Asian or Pacific Islander	0.55	0.48-0.66	<0.001	0.58	0.49-0.69	<0.001	0.63	0.53-0.73	<0.001	0.58	0.55-0.79	<0.001
Black	0.95	0.76-1.28	0.6	0.95	0.76-1.18	0.64	1.05	0.84-1.30	0.66	0.95	0.76-1.18	0.64
Hispanic	0.67	0.58-0.78	<0.001	0.69	0.58-0.81	<0.001	0.75	0.64-0.88	<0.001	0.68	0.57-0.81	<0.001
Other	0.99	0.77-1.28	0.92	1.00	0.77-1.23	0.99	1.13	0.87-1.45	0.36	1.00	0.77-1.29	0.97
Unknown	1.23	0.86-1.41	0.31	1.12	0.89-1.40	0.032	3.31	2.78-3.94	<0.001	1.12	0.89-1.40	<0.001
Study Type												
Interventional		Reference			Reference			Reference			Reference	
Observational	30.3	24.8-37.2	<0.001	29.2	23.8-35.9	<0.001	31.3	25.6-28.8	<.0001	29.2	23..2-35.8	<.0001
Gender												
Male		Reference			Reference			Reference			Reference	
Female	0.36	0.33-0.39	<0.001	0.36	0.32-0.39	<0.001	0.38	0.35-0.42	<.0001	0.35	0.32-0.39	<0.001
Histology												
Single Solid Malignancy		Reference			Reference			Reference			Reference	
Healthy	1.73	1.30-2.3	<0.001	1.82	1.36-2.43	<0.001	1.78	1.37-2.52	<.0001	1.83	1.41-2.40	<0.001

Multiple Histology	0.33	0.30-0.37	<0.001	0.33	0.29-0.36	<0.001	0.35	0.32-0.39	<.0001	0.33	0.30-0.36	<0.001
Single Heme Malignancy	0.06	0.04-0.09	<0.001	0.06	0.04-0.09	<0.001	0.06	0.04-0.09	<.0001	0.06	0.04-0.09	<0.001

Extended Data Table 8. Multivariable analysis for odds ratio for the association between various factors and signing consent into a non-industry sponsored study nested by study.

*Patients with a primary language other than English compared to patients with English as their primary language. ** Patients with limited English proficiency compared to patients with English as their primary language. Abbreviations, OR; odds ratio, CI; confidence Interval.

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