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Assessment of readability of informed consent forms of gynecologic cancer clinical trials: A (Potential) barrier to enrollment?

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ABSTRACT

Objective: Limited English language proficiency (LEP) is associated with decreased clinical trial enrollment. Notably, the AMA and the NIH recommend that patient materials have a readability level commensurate to a sixth- through eighth-grade reading level. This study evaluated the readability of informed consent forms for gynecologic oncology clinical trials.

Methods: This was an IRB-exempt, retrospective, quantitative analysis of for gynecologic oncology clinical trials opened at Ohio State University, a National Cancer Institute (NCI)-designated institution, from 1/1/2017 through 12/31/2022. We analyzed patient informed consent documents from gynecologic oncology clinical trials. The researchers assessed the readability of these consent forms using standardized readability tests to determine their complexity and readability levels. Readability was assessed using Readability Studio Professional Edition software for five metrics.

Results: A total of 103 informed consent forms were reviewed, capturing trials for ovarian (n = 41, 39.8 %), endometrial (n = 21, 20.4 %), cervical (n = 14, 13.6 %), vulvar/vaginal cancers (n = 3, 2.9 %), as well as multi-disease site/basket trials (n = 24, 23.3 %). Most informed consent forms were from industry-sponsored studies (n = 45, 43.7 %) and NCI, NRG Oncology, and GOG Foundation (GOG) sponsored studies (n = 42, 40.8 %). The mean reading grade-level for all analyses was 13th grade, specifically 13 for ovarian cancer, 12.02 for endometrial, 12.9 for cervical, 12.8 for vulva/vaginal, and 13.0 for others (p = 0.26). There was no difference (p = 0.21) between NCI/NRG/GOG studies (13.3) and industry-sponsored trials (13.6).

Conclusions: In this study, we found that current informed consent forms do not meet current recommended readability standards for medical literature regardless of disease site or sponsor. This is an opportunity to reduce disparities and improve patient understanding and involvement in clinical trials.

1. Introduction

Clinical trials are foundational to the transformation of care for patients with cancer, including gynecologic malignancies. In addition to providing valuable information about the safety and efficacy of novel therapeutic options, clinical trials facilitate patient access to combinations of potentially active therapies, which may not be available or approved as standard of care. Accordingly, the National Comprehensive Cancer Network (NCCN) recommends clinical trial enrollment for all cancer patients, especially those intolerant or expected to have limited response to standard-of-care therapies (Clinical Trials, xxxx). Unfortunately, numerous barriers to clinical trial enrollment and equitable participation exist in real-world practice, including patient preference or performance status, geographic and financial burdens, and patient literacy (Medina, 2023; Reopell, 2023). In a recent study of over 2700 patients with gynecologic cancer by Jorge et al., those with limited English proficiency (LEP) were 3.4 times less likely to enroll in clinical trials (Jorge, 2023).

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Before clinical trial enrollment, patients must provide informed consent, acknowledging their understanding of the risks and benefits of the study and their rights and responsibilities (Gupta, 2013). However, informed consent forms are often written in complex language and may be lengthy, limiting understanding in those with LEP or limited health literacy. Obtaining informed consent for involvement in medical research presents a unique challenge as it necessitates a higher level of understanding compared to consent for standard medical care. Prior research has indicated that the language utilized in informed consent forms is not easily understood by most of the American population (Sugarman et al., 1999). The National Work Group on Literacy and Health suggests that approximately 25 % of American adults have rudimentary reading skills, with difficulty understanding medication instructions, a bus schedule, or directions on household products (Communicating with patients who have limited literacy skills. Report of the National Work Group on Literacy and Health. J. Fam. Pract., 1998). Accordingly, the American Medical Association (AMA) and the National Institutes of Health (NIH) recommend that patient materials have a readability level at the sixth- through eighth-grade reading level to represent the average reading age for adults in the United States (Centers for Disease Control and Prevention Web site, xxxx).

Limited LEP, poor healthcare literacy, and limited access to medical information are potentially modifiable barriers to clinical trial enrollment and participation disparities, particularly in underrepresented populations. The nuance between readability and literacy is also important in working to overcome these barriers. Medical readability refers to the clarity and simplicity of medical information, ensuring it can be easily understood by a broad audience, while medical literacy pertains to an individual's ability to comprehend, evaluate, and use medical information to make informed decisions about their health. Prior studies in non-gynecologic malignancies have demonstrated that the readability of clinical trial information, including informed consent forms, is above the literacy capabilities of the average American reader (Hillyer et al., 2020; Schumacher et al., 2017; Storino et al., 2016; Bothun et al., 2021). Therefore, as we work to increase diversity and equity in gynecologic oncology clinical trials, it is crucial to examine the current state of readability of informed consent forms. The objective of this study was to evaluate the readability of patient informed consent forms utilized for gynecologic oncology clinical trials.

2. Methods

2.1. Study design and data Collection

This study was considered IRB-exempt at The Ohio State University in Columbus, OH. All therapeutic interventional clinical trials opened within the Department of Gynecologic Oncology from 1/1/2017–12/31/2022 were considered for inclusion. Two study investigators (LMC, DOM) decided to utilize five years of clinical trial informed consent. Two investigators (WK, QK) obtained the patient informed consent documents, and those without available consent forms were excluded from the study. For studies with multiple available consent forms, the most recent version was obtained for analysis. The informed consent materials were obtained from institutional records and reformatted into Microsoft Word (Microsoft Corp., Redmond, WA, USA). Only English language consent forms were reviewed. These texts were edited to exclude hyperlinks, advertisements, or extraneous information. The texts were also revised to reflect the original paragraph or bullet formats presented on the websites.

2.2. Readability Assessment and Statistical analysis

Readability was assessed using Readability Studio Professional Edition software (Oleander Software Solutions Ltd., Maharashtra, India) in accordance with prior studies (Ibrahim et al., 2016; Seth et al., 2016; Weiss et al., 2016; Huang et al., 2015). Five standardized tests were utilized: the Automated Readability Index, Flesch Kincaid Grade Level, the Gunning Fog Index, the New Dale-Chall, and the Coleman-Liau Index. Further, three additional readability metrics were assessed: total words, percentage of complex sentences (greater than 22 words), and percentage of words greater than three syllables, which allowed for further analysis of the Flesch Reading Ease and for calculating the Fry Readability metric. These metrics are commonly used and well-validated measures of readability that report grade-level equivalents (Friedman and Hoffman-Goetz, 2006).

Details of the readability tests are displayed in Table 1. A primary analysis of all continuous readability data was performed to assess the individual readability statistics for all trials. Subsequently, the mean readability scores were compared according to the disease site (endometrial, cervical, ovarian, vulvar/vaginal, other) and trial sponsorship, including the National Cancer Institute (NCI), NIH, Gynecologic Oncology Group (GOG) or NRG Oncology, industry-sponsored or investigator-initiated trials (IIT) utilizing using an unpaired *t*-test. All descriptive and univariate statistics were performed via Readability Studio analysis, Excel, and MS Excel—software and GraphPad Prism version 10.0.0 for Windows, GraphPad Software, Boston, Massachusetts USA, https://www.graphpad.com.

3. Results

In total, of the 132 gynecologic cancer therapeutic clinical trials that enrolled patients by the Division of Gynecologic Oncology at The Ohio State University from 1/1/2017 through 12/31/2022, 103 were eligible for inclusion, and 29 were excluded due to no publicly accessible patient consent forms. Informed consent forms were reviewed from clinical trials in ovarian (n = 41, 39.8 %), endometrial (n = 21, 20.4 %), cervical (n = 14, 13.6 %), vulvar/vaginal cancers (n = 3, 2.9 %), and multi-disease site/basket trials (n = 24, 23.3 %). The majority of informed consent forms were from industry-sponsored studies (n = 45, 43.7 %%) followed by NCI, NRG Oncology, and GOG-sponsored trials (n = 42, 40.8 %), and the remainder were IIT (n = 13, 12.6 %).

Table 2 displays readability statistics for the informed consent forms

Table 1
Summary of readability tests.

Test	Variables assessed	Formula
Automated Readability Index	1. Word length (syllables) 2. Sentence length	$4.71\left(\frac{\text{characters}}{\text{words}}\right)+0.5\left(\frac{\text{words}}{\text{sentances}}\right)-21.43$
Flesch-Kincaid Grade Formula	1. Word complexity 2. Sentence length	$0.39\left(\frac{\text{total words}}{\text{total sentances}}\right)+11.8\left(\frac{\text{total syllables}}{\text{total words}}\right)-15.59$
Gunning Fog	1. Word complexity 2. Sentence length	$0.4[\left(\frac{\text{words}}{\text{sentences}}\right)+100\left(\frac{\text{complex words}}{\text{words}}\right)]$
New Dale-Chall	1. Word familiarity 2. Sentence length	$0.1579\left(\frac{\text{difficult words}}{\text{words}}\text{x}100\right)+0.0496\left(\frac{\text{words}}{\text{sentences}}\right)$
Coleman-Liau Index	1. Word length (characters) 2. Sentence length	$\text{CLI}=0.0588*\text{L}-0.396*\text{S}-15.8$
Flesch Reading Ease Formula	1. Word complexity 2. Sentence length	$206.83-1.015\left(\frac{\text{total words}}{\text{total sentences}}\right)+84.6\left(\frac{\text{total syllables}}{\text{total words}}\right)$
Fry Graph Readability Formula	1. Word complexity 2. Sentence length	Average number of words per sentence (y-axis) and syllables (x-axis) per hundred words

G, grade level: C, number of characters; S, number of sentences.

Table 2
Readability Metrics by Disease Site.

	Ovarian/ Fallopian tube/ Peritoneal (n = 41)	Endometrial (n = 21)	Cervical (n = 14)	Vulva/ vaginal (n = 3)	Other (n = 24)
Automated Readability index	13.8	13.8	13.3	13.2	13.8
Flesch-Kincaid	13.9	10.1	13.4	13.3	13.9
Gunning Fog	12.1	11.7	11.9	11.3	11.7
New Dale-Chall	13.2	12.4	13.2	12.8	12.6
Coleman-Liau Index	13.4	12.1	12.8	13.2	13.2
Average	13.28	12.02	12.92	12.76	13.04
Total words	8218.7	7190.2	8110.9	4338	7826.1
Difficult sentences with more than 22 words (percent of total)	119.3 (34.8 %)	100.1 (32.1 %)	113.1 (31.7 %)	63.3 (32.4 %)	117.4 (35.1 %)
Number of complex words with more than three syllables (percent of total)	14.50 %	15.10 %	15.00 %	15.10 %	14.90 %
Flesch Reading Ease (scale value)	45.5	45.4	48.8	47.3	45.8

Numeric values correlate to grade level with 16 correlating to last year of college.
Flesch reading ease formula values correlate to a scale representation of the literacy complexity analysis. The score is divided with 90–100 being very easy to read (6th grade level), 80–90 easy to read, 70–80 fairy easy, 60–70 understood by 7-9th grade students, 50–60 fairly difficult to read, 30–50 difficult to read and best understood by college students, 0–30 very difficult to read and representative of a college graduate level.

across the various disease sites. The overall mean reading level for gynecologic cancer clinical trial informed consent forms was 13, which correlated to a college first-year reading level. Further, the mean reading score of informed consent forms by disease site was 13.3 for ovarian cancer, 12.02 for endometrial cancer, 12.9 for cervical cancer, 12.8 for cervical cancer, and 13.0 for others. While endometrial cancer had a slightly lower average reading level of high-school seniors, this was not statistically significant compared to the other disease sites ($p = 0.26$). These averages were consistent amongst all five readability metrics, as seen in Fig. 1(A), which compares the disease sites and the correlated grade reading level. Notably, this analysis does not identify significant outliers among the disease sites, indicating consistent readability patterns across the various metrics.

In Fig. 1(B), we compare the readability levels of informed consent for the disease sites and their target readability standards. In this analysis, we established a baseline at zero to represent an acceptable reading level set at an eighth-grade reading comprehension level. This analysis shows consistently high readability levels in all disease sites, on average, at least four grades higher than the recommended reading level.

We then proceeded to analyze the complexity of informed consent forms in each disease-site. The mean consent form length for all gynecologic cancer clinical trial informed consent forms was 7136.8 words, with 33.2 % complex words and 14.9 % complex sentences. (Table 2)

Fig. 1. (A) Comparison of Readability Scores as depicted by grade level on the xaxis across all disease types using five readability metrics. (B) Differences between actual readability and target readability when compared to the recommended reading level of 8th grade (here represented by 0).

When further delineated by each disease site, the mean length of the consent forms was significantly greater for ovarian (n = 8218.7), endometrial (n = 7190), cervical cancer (n = 8110), and other (n = 7820) compared to vulvar and vaginal cancer (n = 4338) ($p = 0.02$). The percentage of words considered complex (those containing more than three syllables) were overall similar, with 14.5 % in ovarian cancer, 15.1 % in endometrial cancer, 15.0 % in cervical cancer, 15.1 % in vulva/vaginal cancer, and 14.9 % in other trials. The representation of complex words was not statistically significant between the disease types ($p = 0.45$). The percentage of sentences considered complex (those with more than 22 words) in ovarian cancer was 34.8 %, in endometrial cancer 32.1 %, in cervical cancer 31.7 %, in vulva/vaginal cancer 32.4 % and in other trials 35.1 %. The representation of complex words was not statistically significant between the disease types ($p = 0.59$). We also report each disease site's Flesch Reading Ease score, a scale representing the literacy complexity analysis. The cervical cancer and vulva/vaginal cancer had slightly higher scores of 48.8 and 47.3, respectively, representing college-level reading ability and bordered on statistically significant when compared to the ovarian cancer score of 45.5, endometrial cancer 45.4 and other sites of 45.8 ($p = 0.07$). These metrics of literary complexity were further graphed onto a Fry Readability Graph, as seen in Fig. 3 (A).

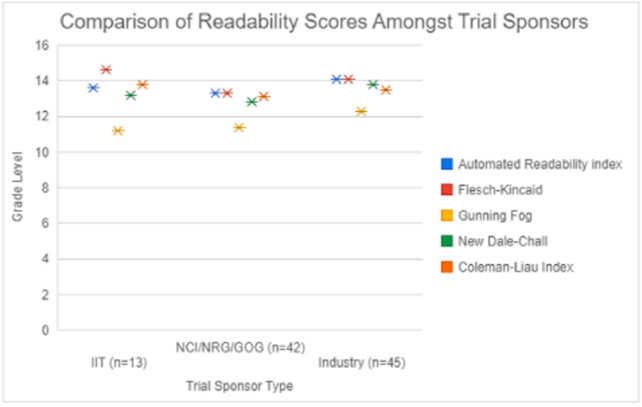
When readability metrics were compared based on sponsor, (Table 3) the average reading grade level of IIT trials was 13.3 (college sophomore), 12.8 for NCI/NRG/GOG trials (first-year college students), and 13.6 for industry-sponsored trials (college sophomore) ($p = 0.21$). These averages also represented minimal outliers in the five metrics, as seen in Fig. 2(A). Fig. 2(B) further compares readability to the acceptable reading level of 8th grade, which is zero on the y-axis. Across all sponsors, the informed consent documents were at least four grades higher in their readability than the recommended reading level.

Additional complexity analyses were performed based on the trial

Table 3
Readability metrics by clinical trial sponsor type.

	IIT (n = 13)	NCI/NRG/GOG (n = 42)	Industry (n = 45)
Automated Readability index	13.6	13.3	14.1
Flesch-Kincaid	14.6	13.3	14.1
Gunning Fog	11.2	11.4	12.3
New Dale-Chall	13.2	12.8	13.8
Coleman-Liau Index	13.8	13.1	13.5
Average	13.28	12.78	13.56
Total words	5498.1	6601.6	9312.7
Difficult sentences with more than 22 words (percent of total)	81.6 (33.83 %)	92.8 (32.05 %)	138 (32.40 %)
Number of complex words with more than three syllables (percent of total)	16.07 %	14.52 %	14.91 %
Flesch Reading Ease (scale value)	44.9	48.4	43.8

IIT, Investigator-initiated trials; NCI, National Cancer Institute; NRG Oncology, Gynecologic Oncology Group (GOG).
Numeric values correlate to grade level with 16 correlating to last year of college.
Flesch reading ease formula values correlate to a scale representation of the literacy complexity analysis. The score is divided with 90–100 being very easy to read (6th grade level), 80–90 easy to read, 70–80 fairy easy, 60–70 understood by 7-9th grade students, 50–60 fairly difficult to read, 30–50 difficult to read and best understood by college students, 0–30 very difficult to read and representative of a college graduate level.



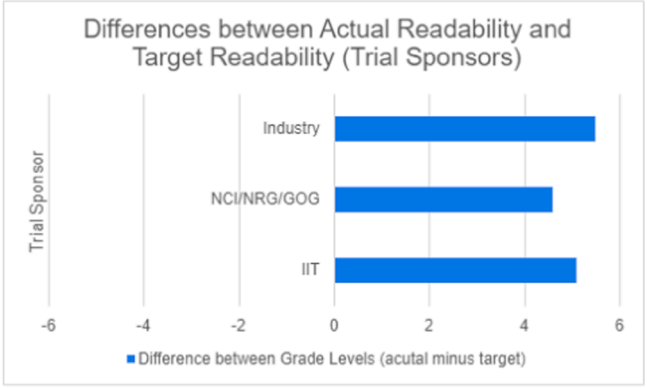


Fig. 2. (A) Comparison of Readability Scores as depicted by grade level on the xaxis across all clinical trial sponsors using five readability metrics. (B) Differences between actual readability and target readability when compared to the recommended reading level of 8th grade (here represented by 0). Any data that lies to the left of the set zero point would represent consent written at a reading level lower than eighth grade and any data that lies to the right correlates to a higher reading level than the target of eighth grade.

sponsor. (Table 3) The IIT-sponsored trials had an average length of 5,498 words, 33.8 % difficult sentences, and 16.1 % complex words. Trials sponsored by the National Cancer Institute, NIH, Gynecologic Oncology Group, or NRG were, on average, 6601 words in length, with 14.5 % complex words and 32.1 % difficult sentences. Finally, those studies sponsored by industry had an average length of 9312, with 14.9 % complex words and 32.4 % difficult sentences. Using the Flesch Reading Ease score, IIT-sponsored trials scored 44.9, compared to NCI/NRG/GOG trials scoring 48.4, and industry-sponsored trials scoring 43.8. Trials sponsored by NCI/NRG/GOG trials had a statistically significantly increased complexity score ($p = 0.02$). The various readability scores and the markers of consent ease (word count, complex words, and difficult sentences) were also compared with an unpaired *t*-test between investigator-initiated and NRG/GOG/NCI with a p-value of 0.89. The comparison between investigator-initiated and industry sponsor was 0.66, and between NRG/GOG/NCI and industry-sponsored was 0.21. These metrics of literary complexity were further graphed onto a Fry Readability Graph, as seen in Fig. 3 (B).

4. Discussion

Ensuring the readability of clinical trial consent documents is essential to promoting informed decision-making among study participants. Clear and understandable language in consent forms is crucial to ensuring that patients are fully aware of the risks and benefits of the clinical trials and their rights as study participants. Low health literacy and complex medical terminology can be significant barriers to understanding, leading to potential participant confusion, noncompliance, and lack of participation. As such, it is the responsibility of the researchers and sponsors to prioritize the readability of consent forms, including the use of plain language and appropriate formatting. A concerning revelation emerged in our review encompassing over 100 therapeutic clinical trials aimed at women with gynecologic cancer. None of the consent forms associated with these trials met the recommended readability standards for the average American patient, specifically those set at the 6th to 8th-grade reading level as recommended by the American Medical Association. Remarkably, our analysis revealed that the average reading level in these consent forms was equivalent to that of a college freshman, a substantial barrier that must be addressed. Furthermore, it is important to note that our investigation uncovered no discernible difference in readability based on disease site or clinical trial sponsor. This underscores the universality of the issue, emphasizing the need for a comprehensive and globally applicable solution to address the readability challenge in informed materials.

Our analysis, which compares the actual readability of informed consent forms to the target readability standards, clearly highlights a substantial gap between the inherent complexity of these materials and the desired accessibility for a broader readership. The consistent and reproducible readability patterns observed across all metrics, with reading levels consistently exceeding the 11th grade, demonstrate that this issue is prevalent in our field. The disparity in our efforts to provide accessible reading materials for patients becomes even more apparent when considering elderly patients, as highlighted in the findings of Lopez-Parra et al. (López-Parra M, Zamora-Carmona F, Sianes-Gallén M, López-González E, Gil-Rey D, Costa-Ventura H, Borrás-Sánchez M, Rayo-Posadas G, Arizu-Puigvert M, Vives-Vilagut R. Patient Information and Informed Consent for Research in the Elderly: Lessons Learned from a Randomized Controlled Trial. Healthcare (Basel) [online]., 2022). Their research revealed that patients aged 65 and older exhibit higher levels of poor comprehension, particularly in the context of medical information. Given that a substantial portion of gynecologic malignancy patients fall within this age group, it underscores another potential component of barriers to trial enrollment.

The goal of inclusivity in clinical trials similarly extended to non-English speaking patients. We know from the literature that structural barriers (e.g., lack of clinical trials in regions with a high density of

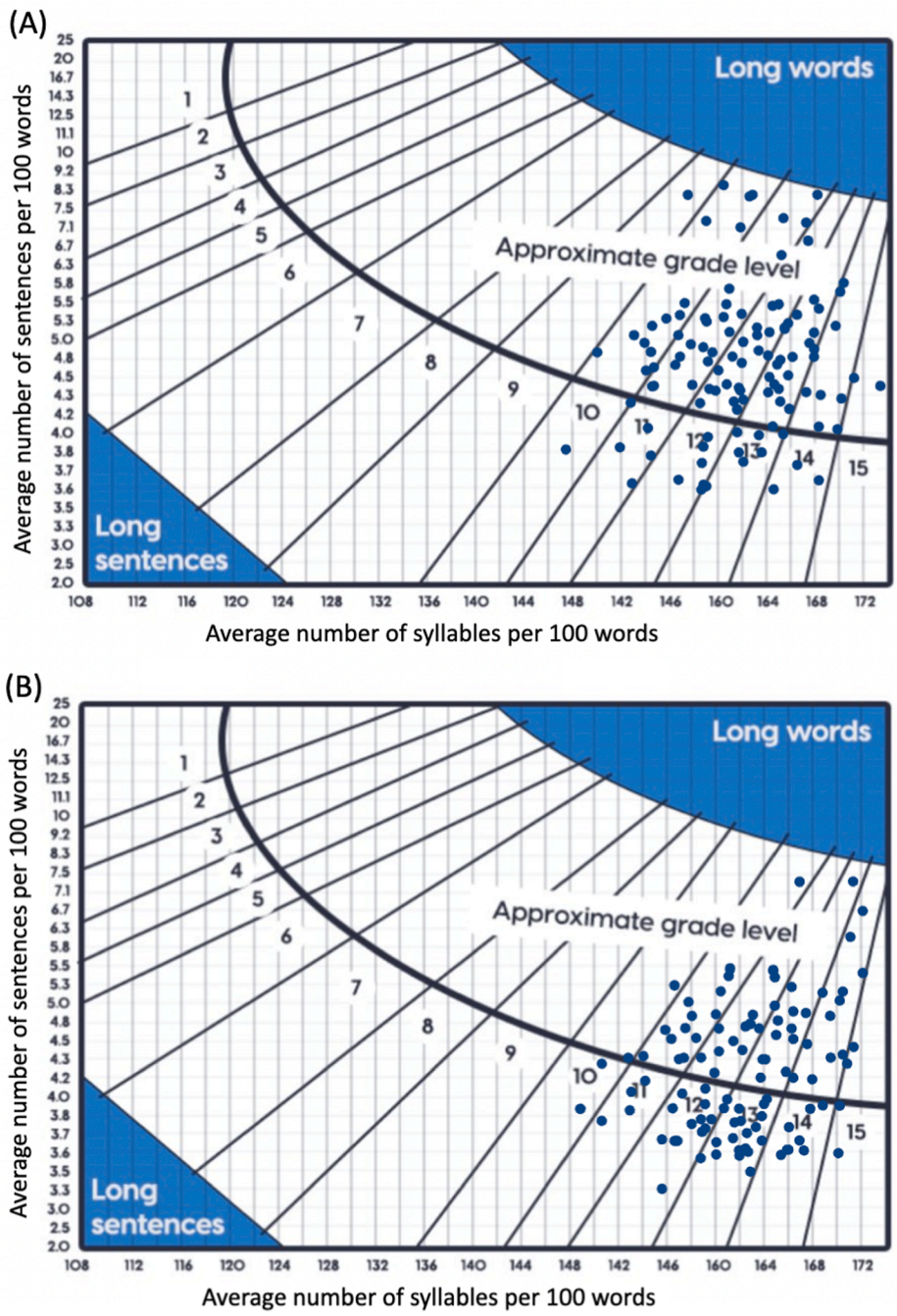


Fig. 3. (A) Fry Readability Graph for disease types. (B) Fry Readability Graph for sponsor type. Allows for grade reading level to be approximated by plotting the average number of sentences (y-axis) and syllables (x-axis) per hundred words.

minority patients) and clinical factors (e.g., narrow eligibility criteria that disproportionally affects underrepresented populations) have resulted in lower clinical trial enrollment in other cancer types of racial and ethnic minority groups with evidence this contributes to poorer survival in these groups (Temkin et al., 2018; Del Carmen and Rice, 2018; Elshami et al., 2022). Within this context, consent readability within the context of limited English proficiency is likely a further barrier to overcome. Jorge et al. evaluated the accrual of patients with LEP in gynecologic oncology clinical trials in an NCI-designated Comprehensive Cancer Center and found a $>$ 3-fold lower accrual for patients with LEP (Jorge et al., 2023). The authors highlight issues, including the absence of translated informed consent forms, the increased time required to obtain consent for LEP patients, and the exclusion of LEP patients based on clinical trial eligibility criteria, as significant barriers to accrual. While our analysis did not directly address the intricacies of translated consent forms, we believe that improving the accessibility of clinical trials, including enhancing the readability of consent documents, may improve enrollment. Moreover, addressing these aspects can contribute to a comprehensive approach to mitigating health and oncology-related disparities pervasive in gynecologic cancer patients (Collins et al., 2014).

Clinical trial consent is a critical communication tool between researchers and study participants. The consent process ensures that participants understand the study's purpose, procedures, potential risks and benefits, their rights as participants, and alternative therapies. However, research has shown that consent forms are often written in complex language and medical terminology, which can be difficult for participants with limited literacy levels to understand. While our review of

consent forms cannot fully assess the impact of the dialogue between the patient and the research team, our data supports that there is a gap between expected and actual readability metrics in informed consent documents.

Our analysis showed that the readability of consent forms, regardless of the sponsor, average at a college-level reading ability, with over 30 % of sentences classified as complex. There is room for improvement in changing our consent to reflect the average patient and encourage an improved understanding of their medical decisions. Other prospective interventional trials have explored alternatives to relying solely on traditional printed consent forms or patient information, as highlighted by the research conducted by Bernard et al. (Bernard et al., 2022). In their study, the incorporation of interactive multimedia education platforms results in a significant improvement in patient comprehension at the outset of fertility treatments. Remarkably, patients who continued to access these multimedia resources throughout their treatment demonstrated sustained and enhanced comprehension levels by the treatment's conclusion. This encouraging outcome was corroborated by Tucker et al. and Chelela et al., who introduced multimedia-enhanced counseling for patients undergoing endometrial cancer staging surgery and Latina patients with breast cancer on understanding clinical trials, respectively (Tucker et al., 2022; Chalela et al., 2018). Due to this approach, their research revealed higher levels of patient satisfaction and comprehension.

Furthermore, Buckley et al. conducted a feasibility study that examined the implementation of electronic informed consents (Buckley et al., 2023). Their findings indicated that this shift towards electronic consent did not increase the technological burden on participants and maintained the essential elements of participant agency. As highlighted in our analysis, these studies collectively illustrate a promising strategy for addressing the readability issues identified in clinical trial consents. While embracing interactive multimedia and electronic approaches can enhance patient understanding and engagement, as a future direction more research must be completed with a focus on specific interventions for informed consent forms and measurable outcomes of patient understanding and comprehension to ensure patients are truly informed when deciding to participate in trials.

Our study has several important limitations that are inherent to the study design. The available data within the dataset limited the analysis, and we performed our analysis utilizing trials opened at a single tertiary care NCI-designated institution. Further, we did not directly analyze these consent forms using patient literacy analysis or perspective. Therefore, we are extrapolating grade level and acceptable literacy from academic readability metrics. Lastly, regardless of the readability statistics, our study did not directly address patient comprehension of these consent forms to specifically evaluate usable health literacy data. Lastly, our analysis only studied English-language consent forms. Despite these limitations, several important strengths warrant mention. This analysis is the first study in gynecologic oncology to perform a readability analysis of informed consent forms. It provides analysis for action for the first time that our clinical trials, irrespective of sponsor or disease site, are not meeting a crucial national metric, which offers a critical area for future collaboration and initiative.

In this analysis of patient-facing informed consent forms for gynecologic cancer clinical trials, we identified that the median reading level far exceeded appropriate metrics for expected literacy and understanding, regardless of disease site or sponsor. Researchers and sponsors should prioritize the readability of consent forms to ensure proper comprehension is achieved for all. It is our collective duty to improve equity and accessibility in clinical trials and to ensure that our patients' decisions are genuinely "informed." .

Author Disclosure

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WKK, QH, MH, RV and LMC report no conflicts.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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