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Challenges encountered during the process of obtaining informed consent in human subject research: A Scoping Review

Desafíos encontrados durante el proceso de obtención del consentimiento informado en la investigación con seres humanos: Una revisión del alcance

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SUMMARY

Introduction: *Informed consent is a procedure to encourage and invite participants by providing information when making research decisions. However, implementing informed consent is considered unfeasible and imposes constraints on the value of research inquiries. Obtaining informed consent is also seen as a potential bias in acquiring knowledge. In other words, research participants and researchers face many challenges in the process of informed consent. This comprehensive study aimed to map the challenges encountered while obtaining informed consent in human subject research.* **Methods:** *The electronic databases search using PubMed, MEDLINE (EBSCO), and ScienceDirect (Elsevier). Relevant studies were chosen using inclusion criteria, such as those published in 2014-2024 with "full text," English, human research subject, quantitative, qualitative, and mixed methods articles. JBI guidelines are a checklist used to assess eligibility. Data from studies described challenges encountered while obtaining informed consent in human subject research extracted and synthesized. Processes are supported by MeSH term, PCC worksheet, and convidence.org.* **Results:** *Twenty-one studies were identified to provide information about the challenges of obtaining informed consent in human subject research.* **Conclusion:** *This study categorizes three themes within eight subthemes related to challenges in obtaining informed consent: 1. Communication Issues, 2. Respondents' Issues, and 3. Ethical Considerations.*

Keywords: *Challenges, human subject, informed consent, research.*

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RESUMEN

Introducción: *El consentimiento informado es un procedimiento para animar e invitar al participante mediante la información a tomar decisiones en la investigación. Sin embargo, la aplicación del consentimiento informado se considera inviable e impone limitaciones al valor de las investigaciones. El proceso de obtención del consentimiento informado también se considera un sesgo potencial en la*

adquisición de conocimientos. En otras palabras, son muchos los retos a los que se enfrentan los participantes en la investigación y los investigadores en el proceso de obtención del consentimiento informado. El objetivo de este estudio es determinar los problemas que surgen durante el proceso de obtención del consentimiento informado en la investigación con seres humanos. **Métodos:** *Búsqueda en las bases de datos electrónicas PubMed, MEDLINE (EBSCO) y ScienceDirect (Elsevier). Los estudios pertinentes se eligieron utilizando criterios de inclusión, como publicados en 2014-2024 con «texto completo», en inglés, sujetos de investigación humanos, cuantitativos, cualitativos y artículos de métodos mixtos. Las directrices del JBI son la lista de comprobación utilizada para evaluar la elegibilidad. Se extrajeron y sintetizaron los datos de los estudios que describían los desafíos encontrados durante el proceso de obtención del consentimiento informado en la investigación con sujetos humanos. Procesos apoyados por el término MeSH, la hoja de trabajo PCC, convidence.org.* **Resultados:** *21 estudios fueron identificados para proporcionar información sobre los retos que plantea la obtención del consentimiento informado en la investigación con seres humanos.* **Conclusión:** *Este estudio categoriza tres temas dentro de ocho subtemas relacionados con las dificultades para obtener el consentimiento informado, a saber: 1. Problemas de comunicación, 2. Problemas de los encuestados, 3. Consideraciones éticas.*

Palabras clave: *Retos, sujeto humano, consentimiento informado, investigación.*

INTRODUCTION

Informed consent has been legally recognized since 1972. It includes explanations and effects connected to the procedure to be performed by the patient; the procedure requires permission from the patient as the research subject. Informed consent is when a healthcare provider educates a patient about a procedure or intervention's risks, benefits, and alternatives. The patient must be competent to make a voluntary decision about whether to undergo the procedure or intervention (1,2). Informed consent is both an ethical and legal obligation of medical practitioners. It preserves the individual's autonomy by telling them about the benefits, alternative methods, potential hazards, modes of operation, and reasons for planning (3). Informed consent not only fulfills moral requirements relating to individual human rights and individual responsibility for one's health, but it also preserves persons from being manipulated as objects of interest (4). Implicit in providing informed consent is assessing the patient's understanding, rendering an actual recommendation, and documenting the process. As a result, the study subject has the right to volunteer to provide informed consent without being coerced by anyone (5).

Society places a high priority on research involving human beings, and patient privacy is greatly valued. Important information about disease prevalence, risk factors, treatment outcomes, public health initiatives, functional skills, care patterns, expenditures, and healthcare service utilization is provided by existing research (6). The process will be successful if the objectives are carried out well: to respect and increase the patient's autonomy. Then, this research must also protect patients as research or human subjects from threatening dangers (7). Participants must receive an explanation of relevant information, such as conditions, objectives, risks, and potential benefits until alternatives are provided (5). However, participants usually need help understanding the subject information in the informed consent form. A study reported that informed consent had deficiencies in communicating the study, especially in explaining the risks (8). Preserving participants' independence and facilitating their decision-making ability is crucial. Nevertheless, considerable discussion remains regarding the methods for assessing and enhancing the informed consent procedure (9). Respecting potential participants' choice to decide whether or not to join in health research is essential to getting adequate informed consent (10). In fact, potential volunteers are given a lot of lengthy and detailed information, which might be confusing and cause anxiety (10). Even though the informed consent procedure in health research has been extensively studied, there still needs to be more understanding of the complexities of the procedure that impact marginalized people's capacity to make educated decisions about participating (10).

Getting informed consent can provide more challenges. In underdeveloped nations, participants may need help with study adherence, be unable to understand the hazards of clinical trials, be afraid of research procedures, or worry about them. The difficulties in gaining informed

consent might be more severe in developing nations when participants struggle with study adherence, are unable to weigh the risks of clinical trials, are afraid of research procedures, or worry about having less access to healthcare (11). It might be necessary for researchers, sponsors, and regulatory bodies to take deliberate action to address this issue, which could negatively impact research in underdeveloped nations that already struggle with inadequate infrastructure, resources, and illiteracy (11). In review research, Kadam addresses the challenges of the consent process and looks into creative ways to improve it (11). Further, it is claimed that individual educational limitations, demographic changes, and data technology advancements are the primary obstacles to acquiring informed consent. Educational limitations include research participant's literacy level and level of education, demographic changes including age and multiculturalism, data technology advancement's increased challenging ethical questions (12).

According to (13), several problems arise in the informed consent process, including language barriers, religious influence, incorrect expectations, individual perspectives, and the presence of vulnerable individuals. Although both papers present reasons concerning the difficulties associated with gaining informed consent, it is important to note that this research reviews articles that need more systematic steps. In contrast, systematic research demonstrated that obtaining informed consent could be more practical (14). Using "impractical" as the key search term, he found impracticality in obtaining informed consent forms. The impracticality involves an excessive burden in the procurement process for researchers, invalid results due to collecting the data right after the informed consent forms are signed, detrimental to participants as their privacy is infringed, and often irrelevant to the participants.

Based on the preceding discussion, implementing informed consent is vital on the one hand but also carries challenges on the other. Major challenges in obtaining informed consent forms have been said to be "impractical" as they introduce a potential bias in acquiring knowledge. In addition, from the participant's perspective, the term "impractical" refers to the fact that implementing informed consent would have negative consequences, such as compromising privacy and being insignificant. Therefore, researchers are responsible for creating a novel method to obtain informed consent and reduce potential harm to participants during the research process. A scoping review is required to identify further challenges in obtaining informed consent in human subject research. A scoping review will provide a broad understanding of the topic (15). Scoping reviews will identify and map the breadth of evidence available on a particular topic, field, concept, or issue, often irrespective of source (16). Scoping reviews define important terms and concepts and highlight important aspects of a concept, such as those pertaining to methodological research (16).

METHOD

A scoping review describes the available studies, provides an overview with a broad or detailed focus, and shows evidence if questions still need to be clarified or specific. This study used four ethical considerations such as transferability, reflexivity, validity, and transparency (17). Using "basic qualitative content analysis" (16), this process uses inductive and deductive reasoning. Inductive reasoning emerges themes and categorizes them from the data during extraction. Deductive reasoning generates concepts or variables from theory or previous studies. The steps of qualitative content analysis are as follows (18):

1) Developing the study's frame and operational definitions

Discovered the themes and subthemes in the theory or theories the researcher wants to find or validate. It also involved classifying those theories based on topics using a structured analysis matrix and the study's coding as a tool. Beyond that, the researchers need to read articles that include the established theories that intend to be investigated within the inclusion and exclusion criteria (Table 1). Furthermore, the researchers created an operational coding framework with definitions (Table 2)

2) Determining the unit of analysis and sampling materials to be analyzed.

The researcher chose what to analyze to achieve the study's objective after developing the framework based on the theory or theories to be tested and definitions of the key concept. Making this decision entails selecting the unit of analysis and the suitable subset of all data sources' populations or the sample of those units to be examined. As for the unit of analysis, it contains a complete text that is both large enough to be viewed as a whole and tiny enough to be remembered as a background for the meaning unit while the analysis is being conducted (Figure 1),

3) Getting a sense of the data.

In this phase, the researcher dug deeply into the gathered information. Next, they looked for the themes and subthemes classified in the previous step. The theme identification was from the data in each sampled piece of material. As a result, the researcher read the initial set of materials gathered to become familiar with the data and try to make sense of them. While reading a chosen article, the researcher gradually highlighted passages whose latent or manifest contents match, are close to, or are comparable to theory-based themes and/or sub-themes mentioned in the study's coding scheme.

4) Data coding and organizing.

The researchers made a reading summary form for every piece of material that had been read and recorded all the highlighted and coded passages in it. A few paragraphs of coded text from the text were shown in two new, designated columns. For reference reasons, one column provided the precise location of every coded passage in the content that has been read, and the other provided a general notion of the event's context.

5) Making connections, interpreting them, and drawing conclusions.

Next was creating meaning, concluding the scattered data, and looking deeper into the implications of the data, for example, by constructing a logical chain of evidence, contrasting and comparing text passages with theory-based themes and subthemes and the correlation between them at the levels of both manifest and latent content, and providing justifications in line with the contexts from which the data were gathered. Part of this step may involve identifying new themes or sub-themes from highlighted areas that don't fit into any designated category or sub-category. This process culminates in creating narratives using Compare Matrices of the meaning units in the themes (Appendix 2). The researcher then provided interpretations and understandings of the data displayed in the display and made connections to other sources, particularly to make latent content explicit and to make sense of the data in brief prose.

6) Verifying interpretation's plausibility and ensuring trustworthiness.

The researcher explained the study findings and provided details about the process that led to those findings, along with their limitations and strengths. Joanna Briggs Institute (JBI) critical appraisal supported this step. This appraisal aims to assess a study's methodological quality and determine the extent to which it has addressed the possibility of bias in its design, conduct, and analysis. The questions used in randomized control trials are 13, qualitative research is 10, case-control is 10, and cross-sectional is 8.

7) Making an appropriate outline for a detailed presentation.

Researchers presented the outline of coding schemes related to themes and sub-themes (Figure 2).

8) Thick description of the research history and findings.

This is a descriptive summary of the entire study. It embeds quotes where proof is required to support a topic, along with matrices containing the authors' details and year, country, objective/s, sample and its characteristics, material and methods, Joanna Briggs Institute (JBI) scores, and findings related to challenges encountered during the process of obtaining informed consent in human subjects that are provided in significant detail (Appendix 1).

RESULTS

Researchers started advanced searching on 13 February 2024. They used three databases: PubMed (23 articles), MedLine with EBSCO (16 articles), and Elsevier Direct (19 articles). In

Table 1. PCC worksheet to determine and develop keywords for the database

Population	Concept	Context
"Research subjects" OR human subjects OR research subject OR subject, research OR subjects, research OR human subjects OR human subjects). OR	"Consent forms" OR consent form OR (consent form OR informed consent documents OR consent documents, informed OR document, informed consent OR informed consent forms).	"Research" OR research OR (research activities OR activities, research OR activity, research, OR research activity).

Table 2. Inclusion and exclusion criteria

Inclusion Criteria	Exclusion Criteria
Articles published in 2014-2024 Articles with "full text" Articles in English Articles with human research subject Articles used quantitative and qualitative methods	Articles with a literature review method Article about obtaining informed consent but not related to the challenges Books and documents

addition, researchers conducted hand searching (14 articles). On 16 April 2024, after reviewing the title, abstract, and full text, 21 articles were included in our topic.

According to the theme development using content analysis, as explained before, three themes support the research questions: communication issues, respondent issues, and ethical considerations issues. The results of the article mapping tables based on the research questions have shown that all articles have answered the research questions. Three themes out of eight sub-themes supporting the research questions have been obtained. The first theme consists of two sub-themes supported by nine reference articles. The second theme consists of four sub-themes supported by nineteen reference articles. The third theme consisted of two sub-themes supported by nine articles.

Theme 1: Communication Issues

There are various challenges to obtain informed consent, including communication issues. Nine studies supported this theme and have two sub-themes: information issues and language barriers. There are many challenges in information issues such as unexplained informed consent, incomplete information, risks/effects and further information/other studies that are reasons for participants not to register for research, the need for spaced or larger text in informed consent, complexity in research procedures, consent materials, too much and too little information, statements in informed consent that are lacking and informed consent that are too long (19-24). Moreover, language barriers are also a challenge that causes participants to refuse to enroll in research. Language barriers might occur between participants' daily language and the language used in informed consent. Three studies support this sub-theme (25-27).

Theme 2: Respondents' Issues

Respondents' issues, including lack of knowledge, unwillingness, individual' situational, and individual perspective, were also reported as challenges in obtaining informed consent. A total of 14 studies supported the respondents'

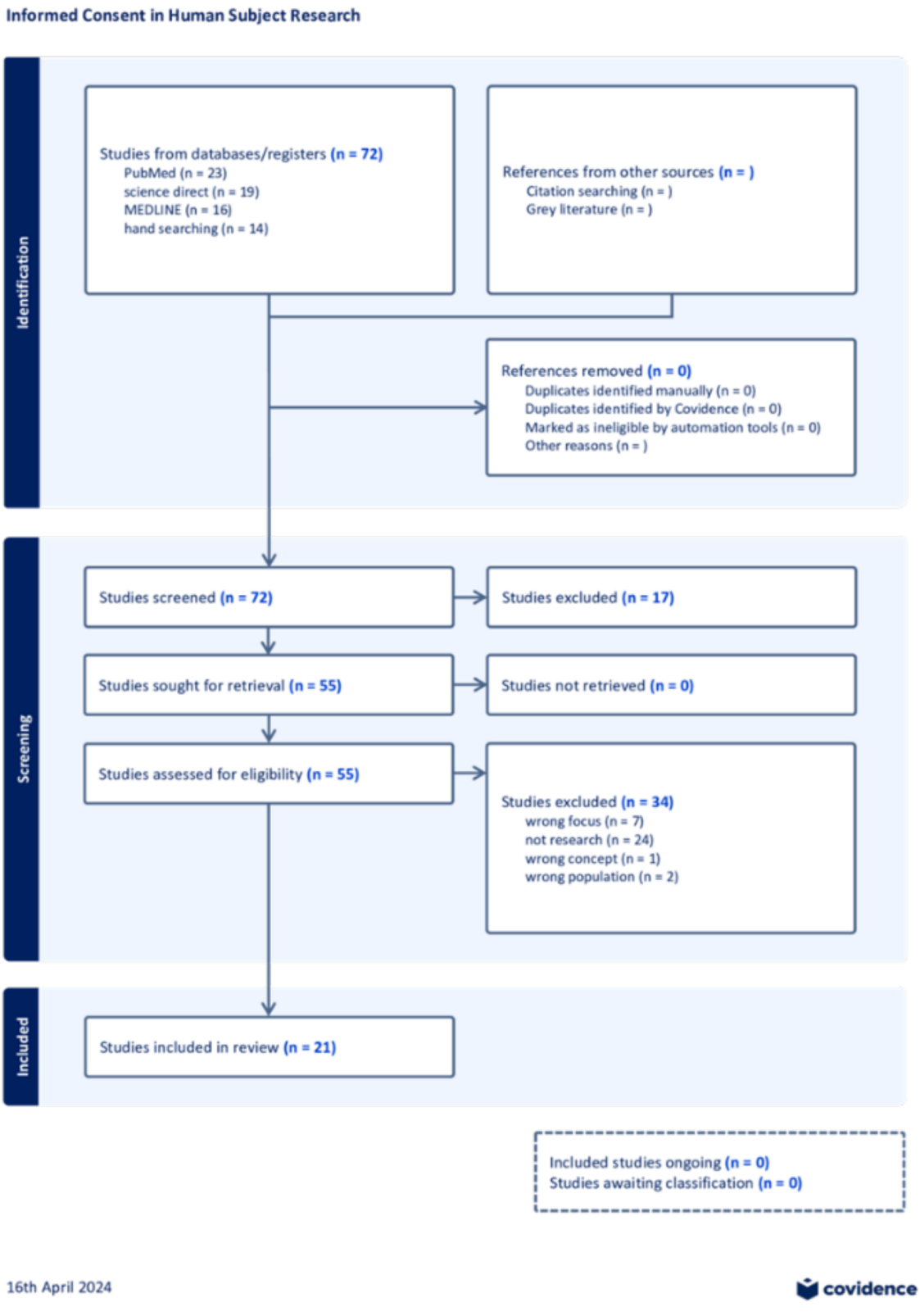

Figure 1. PRISMA ScR.

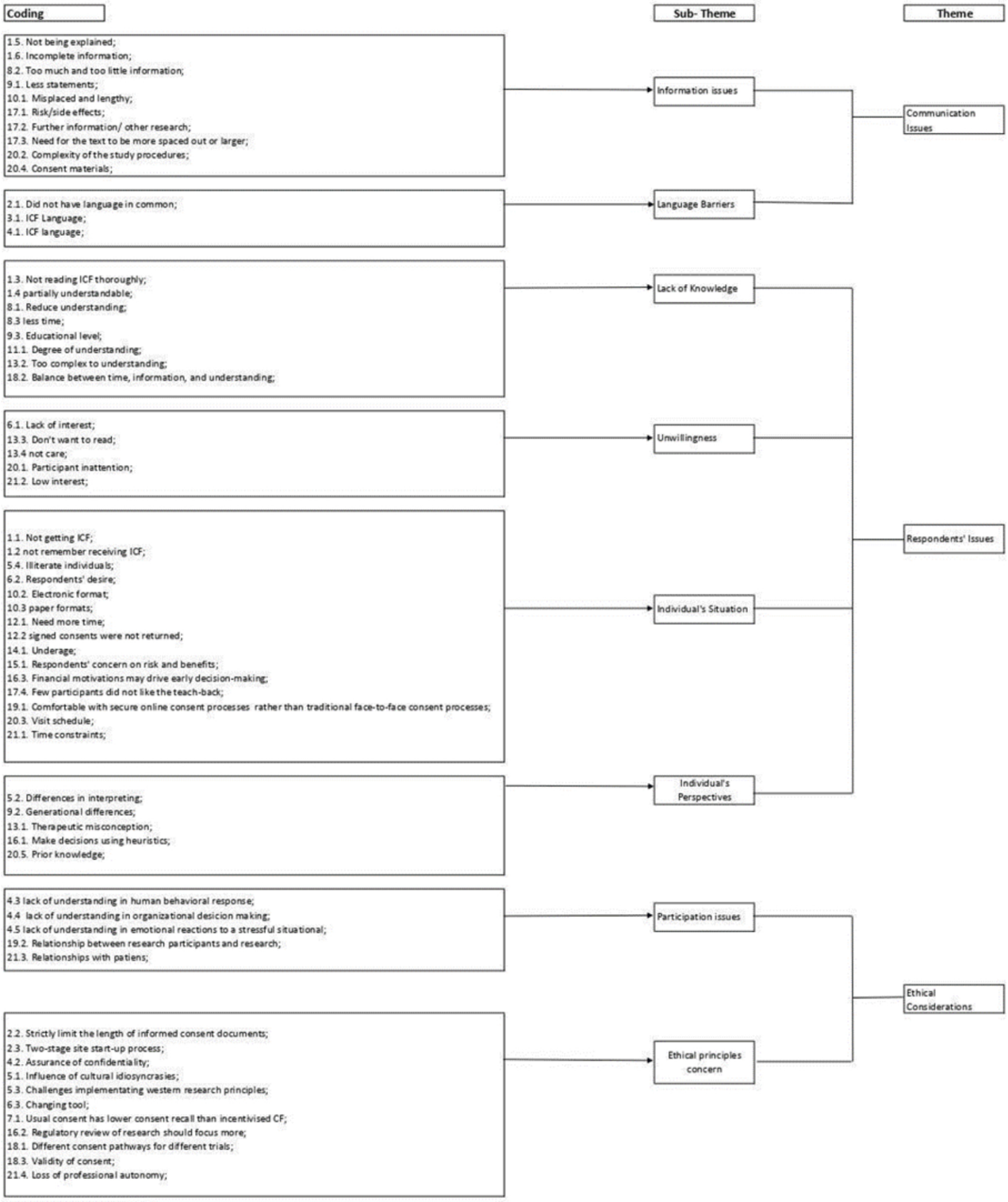

Figure 2. Themes, Sub-themes, and Codings.

issues. Contributing factors that appear in the lack of knowledge were the complexity of IC (28), educational level (21), not reading ICF thoroughly (19), degree of understanding (19, 20), and less time (20). To obtain informed consent, participants must be willing. Factors related to the unwillingness of the participants are lack of interest (29,30) and inattention, such as not wanting to read and not caring (24,28). In addition, individual's situational such as memory limitations (19), illiterate individuals (31), respondents' desire for methods of informed consent such as electronic or paper format, and teach-back (22,23,33), time constraints (30,33), underage (34), financial motivations (35), visit schedule (24), signed consents were not returned (33), respondents' concern about risk and benefits (21). It should also be considered when obtaining an IC. Five studies discuss an individual's perspective influenced by generational differences (21), prior knowledge (24), differences in interpreting (31), making decisions using heuristics (35), and therapeutic misconception (28).

Theme 3: Ethical Considerations Issues

Ethical considerations issues consisted of two sub-themes, i.e., participation issues and concerns about ethical principles. Participation issues can be concluded that challenges in obtaining informed consent are inseparable from the participants' trust in researchers. The relationship between research participants and researchers plays an important role in shaping preferences regarding the consent process (32). Another coding is a lack of understanding of human behavioral response, organizational decision-making, and emotional reactions to a stressful situational (27). The sub-theme of ethical principles concern explains that, in obtaining informed consent, a researcher must pay close attention to the informed consent document given to participants. Simplified informed consent and rules described in detail will help participants determine participation in research because each participant needs a guarantee of confidentiality so that their information data will not be misused in research (27). Ethical considerations issues in obtaining informed consent were also challenges, such as culturally sensitive approaches, participants' concerns about losing autonomy when choosing to participate in research, and the consent pathway used can vary depending on the trial being conducted, so these various things become obstacles for researchers in obtaining informed consent (30,31). The usual consent has lower consent recall than incentivized consent forms, and eight studies support this sub-theme (25,27,29-31,35-37).

DISCUSSION

This study focuses on the challenges of obtaining informed consent in human research. Based on the findings, this discussion elucidates important areas concerning respondents' communication issues and ethical considerations. In this study, communication issues consist of information and language barriers. It explains that every recipient of informed consent must understand communication with informed consent because it is how researchers convey all research-related information to respondents. This is supported by the concept that informed consent can only be achieved through effective communication between the researchers and the participants (38). Issues such as incomplete information, too much information, and too little misplaced, lengthy, and complex can make the participants unable to understand easily. Communication can be effective when the information is simplified and clear. In addition, language barriers in influencing obtaining informed consent are supported by previous research were several institutions also use interpreters to translate while obtaining informed consent for respondents who cannot speak English (22). Some of the respondents also don't have a common language with each other, even regarding the ICF, so the language in ICF must be easy to understand and clear (39). It is also discusses the impacts on the respondents, which, as the respondents cannot understand the aim and roles clearly, can affect the relationship between research participants and the researchers and the relationship with the patients. Moreover, miscommunication due to language barriers can affect misunderstandings in informed consent if the participants can't understand the idea of informed consent (40).

Lack of knowledge of respondents' issues related to IC complexity can be seen in the amount and chosen words. A study in congruence states that shorter and easier-to-understand consent forms do not adversely affect the quality of informed consent. Longer consent forms do not lead to better understanding, and concise forms do not increase satisfaction (41). Moreover, the degree of understanding is correlated to educational level. Studies supporting this statement show that those with low education have more difficulty understanding the voluntariness of studies, placebos, randomization, and freedom of withdrawal (5). Therefore, the delivery of the information of IC needs to be adjusted based on educational level (42). Besides, some participants claimed they needed more time to understand the IC. A similar finding was obtained indicating several reasons, such as the acute phase of the patient's condition, limited time to express important and necessary information, language barriers, and the patient's understanding of the information described (40). Lack of time is a challenge detrimental to IC quality and practice (40). Participants take notice of the risks and benefits of the research before signing the informed consent. Respondents sometimes have trouble understanding and have many questions about risks and benefits. Therefore, researchers need to prepare and learn how to convey the risks and benefits that respondents will experience (43). Participants' trust in professionals such as doctors should also be considered while obtaining IC or real researchers to obtain signed consent. A study states that the mediator or informant doesn't fully understand the procedure and recognizes that only professionals can convey consent information properly (43). In regard to individual situational it was shown that in less developed countries, misunderstandings are experienced more frequently, especially by respondents with low income, illiterate, and less exposed to the research (11). Besides, disease severity, age, and cognitive disability affect a respondent's decision-making. Respondents' willingness to receive the IC is influenced by the amount of information contained in the IC. A qualitative study revealed that the amount of information about gaps and risks that will occur increases the concern to participate (26). Although giving longer IC to respondents, it couldn't increase understanding and willingness (26). Research on pediatric zones revealed that decision-making needs to involve parental consent (44). Concern about possible discomforts, such as pain or embarrassment, and pro-social goals are powerful motivators encouraging teenagers to participate in research. To ensure that younger teenagers' consent is as authentic as possible, researchers assessing their consent should consider their vulnerability to advice from reliable sources (44). To reduce bias in an individual's perspective, researchers need to adjust the way of delivering informed consent information, such as media and simplified language, to increase the understanding and memory of participants (11).

Issues of ethical consideration can further occur when obtaining informed consent. Participation problems are inseparable from the participants' trust in the research. Researchers must be involved in their ability to gain participants' trust because confidentiality plays an important role in research involvement related to the consent process (27). This study explains that informed consent guarantees the rights and welfare of participants involved in a study. Researchers must provide all the information needed by participants clearly because it will affect patient involvement (45). After participants are given time to read and understand information about the nature, purpose, and consequences of the research, they have the right to decide on their involvement without any element of coercion (46). Simplified informed consent and detailed rules greatly influence the participation of participants who need assurance of confidentiality so that their data information is not disseminated. This is a challenge in obtaining informed consent on ethical issues. These results are consistent with studies that explain that assessing understanding and regulatory requirements is an important component of ethical principles (43). Our results suggest that preferences for the consent process are significantly shaped by how research participants and researchers are perceived to interact (32,47), provide support for the issue of the relationship between the participant/patient and the researcher who states that oncology clinical researchers note conflicts of interest occur during patient enrollment. Still, that relationship is also highly important in advising patients about whether to participate in the trial.

CONCLUSIONS

Informed consent is a tool to ask participants for consent to participate in research. However, in the process of obtaining informed consent, there are various challenges. This study categorizes three themes within eight related challenges while obtaining informed consent: communication issues, respondents' issues, and ethical considerations. In overcoming the challenges faced while obtaining informed consent, researchers must prepare strategies to attract attention, provide understanding, and consider the researcher's and participants' ethics.

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Appendix 1 Matrices Table

No	Authors details and Year	Country	Objectives	Sample and its Characteristics	Material and Methods	Findings	JBI
1	Agozzino et al., 2019	Italy	We investigated whether they signed the consent form and whether they read and understood the information about the surgical intervention. We also investigated whether verbal communication between patients and physicians affected patient decision-making.	The study comprised adult postoperative patients admitted for general surgery and provided written consent to take part. Interviews were conducted by one of four suitably qualified physicians. They are all experts in the field of public health. The hospital and the surgical team were separate entities from epidemiology and hospital organization. Each patient was interviewed privately, and confidentiality was guaranteed for their responses.	Cross-sectional Study. The questionnaire was divided into four sections. Section 1: Descriptive characteristics of the study participants (n = 6 questions). Section 2: Information on the written IC form's delivery, signing, reading and comprehensibility (n = 6 questions). Section 3: Additional information (acquired orally) on explaining the consent and the effect of the written and oral information (n = 11 questions). Section 4: Information on the surgery outcome and post-surgical period (n = 4 questions).	Most respondents (84.5%) personally received a written IC form, or they reported that they delegated it to a parent or a relative; 1.6% declared that they did not get it, and the others (13.9%) did not recall receiving it. All patients who received the IC form signed it personally or through a relative or parent, but only 51.8% reported reading it thoroughly. Among those who read the IC, 90.9% judged it clear and 9.1% deemed it partially understandable. No one considered it incomprehensible. Approximately half of patients received the written IC form a day before surgery (at the earliest), while 41.1% received it within some hours or immediately before surgery. Forty-five percent of patients receiving the written forms were given them by the surgeon who performed the procedure (Table 2). Not all patients had written consent to explain to them; it was explained orally only to 65.6%; however, 93.9% of patients received further oral information; among these, 68.6% considered this information incomplete, and only 31.4% considered it complete. The information was provided progressively during pre-operative examinations (66.7%) and was understandable according to most (97.1%) recipients.	8/8
2	Denning et al., 2015	Africa, Asia, Europe, North America or South America/ Mexico, Australia	To enhance study participants in informed consent. A unique opportunity to investigate the impact of the length and complexity of informed consent forms on participant understanding and satisfaction among geographically varied participants is offered	154 locations participated in the substudy by gaining permission for at least one participant to engage in START, out of the 221 sites that registered to participate in START and 157 sites that opened to the substudy. Of the 64 START locations that were unavailable to the substudy, 23 could open due to a financing group policy decision at the policy level. 41 sites that were left out of the Informed Consent Substudy, about one-third (n = 14)	Cross Sectional Study. Participants in START Informed Consent and Substudy gave responses to questions regarding their satisfaction comprehension and voluntariness of the informed consent process. The questionnaire had 26 items addressing the participant's experience with the consent process, and assessing the participant's understanding	They did not have a language in common with another participating site (such as the single site in Nigeria, where the patient base speaks Hausa). The regulations strictly limit the length of informed consent documents to less than the length of the researchers' concise consent template. The START study's two-stage site start-up process (beginning enrolment at 101 pilot sites, then adding 120 new sites to complete the trial) was also a limiting factor as many of the sites that had not been part of the pilot did not want	7/8

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No	Authors details and Year	Country	Objectives	Sample and its Characteristics	Material and Methods	Findings	JBI
			by the Strategic Timing of Antiretroviral Therapy (START) project.	did not take part because they did not share a language (e.g., the only site in Nigeria, where the patient base speaks Hausa) with another participating site.	of the information in the consent. The example questions are about the mechanism of randomization and the possible risks and benefits of participating.	the delay in enrolment that may have occurred with participation in substudies.	
3	Denning et al., 2015	United States	To assess whether the amount of information provided about legal protections could affect an individual's willingness to participate in the study and their concerns about discrimination and difficulty in deciding whether to join the study.	Using Qualtrics Research Services to recruit US residents aged 18 years or older, with quotas set to ensure that gender, age, race/ethnicity, educational attainment, and household income mirrored the general US population. The sample (n = 1,195) had a mean age of 45.9 (SD = 17.9) years, and 40% had a high school education. Participants were 51.3% female and 36.7% non-Hispanic White.	Randomised Controlled Trial. This research team used a literature study to develop an interdisciplinary survey. A hypothetical scenario asking participants to anticipate being requested to participate in a genetic research study and a brief excerpt of informed consent text regarding GINA were read to them near the beginning of the survey to fulfill study objectives.	- When making an actual decision about participation in a research study, the informed consent document language may have more or less impact on willingness to participate because individuals are also weighing other potential risks and benefits of the study. - On the other hand, we cannot presume clinicians and researchers know this information nor expect informed consent documents to list every possible specific risk of a study or clinical procedure, especially if some are likely to be very rare or unknown or if disclosure would require listing every omission in an anti-discrimination law. Too much detail about the limits of GINA's coverage could overwhelm individuals and heighten fears of discrimination when those risks may be quite low depending on the clinical or research testing being considered	12/13
4	Quigley et al., 2019	United States	To improve an understanding of the ethical challenges of field researchers with place-based communities in environmental studies/sciences and environmental health.	Approximately two thousand researchers were surveyed, but only those employed in place-based communities were eligible to participate. Interact with research participants from cultural groups in the US and foreign research institutions. In subjects such as conservation biology, ecology, sustainability sciences, environmental health, geography, natural resources, ecology, environmental studies, and related sciences, 75% of respondents said they were researchers and worked in environmental fields. Public health and community development were the primary fields of employment	Cross Sectional Study. This survey was put up electronically using the University Qualtrics Survey tool. Respondents were sent a link to complete the survey, consisting of all 45 questions. Question One of the surveys requires each responder to fill out an informed consent form. The "Four Principle Approach" to bioethics served as the framework for the survey questions, which we further refined by applying them to the protection of place-based communities and cultural groups.	-Provides researchers' recommendations for ensuring community training on informed consent logistics, with knowledge of confidentiality requirements and data access rules; ensures adequate knowledge of the informed consent document using native languages; and utilizes cultural norms to secure appropriate consent. Use Native-speaking translators and local languages, report results both in English and local languages, provide a consent copy to participants, do mapping exercises with names, and use visual images, mapping, and photographs to give voice to the community's own stories. It would be best if you were particularly cognizant of a place's context and/or her	8/8

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No	Authors details and Year	Country	Objectives	Sample and its Characteristics	Material and Methods	Findings	JBI
				the remaining respondents.		social structural arrangements to really understand human behavioral response, organizational decision-making, or emotional reactions to a stressful situation. By working with elders in the consent process, a respondent remarked that their research team was informed about language barriers with different participants and how to allow the community to say when/who/how it was appropriate to work with individual community members. With some participants, we spent time meeting with them, getting to know them and B6:D6them know us, and when they were comfortable with participating in the study.	
5	Killawi et al., 2014	Qatar	To delineate procedures related to recruiting, obtaining informed consent, and compensating health research participants in Qatar's extremely high-density multicultural setting.	A total of 153 individuals were approached, and 84 were enrolled. The latter showed a diverse age range (18 to 75 years), varied language representation (Arabic (n = 24), English (n = 20), Hindi (n = 20), and Urdu (n = 20), and balanced gender distribution (women (n = 43) and men (n = 41).	Qualitative Research. The project instruments included a recruitment script, an interview guide, and a single sheet containing both information about the research and a waiver of written informed consent.	1. Influence of cultural idiosyncrasies on the level of disclosure and the informed consent process in clinical care. 2. Differences in interpreting ethical research principles 3. Challenges implementing Western research principles, particularly informed consent 4. Difficulty in obtaining informed consent from illiterate individuals	7/8
6	McCarty et al., 2015	United States	To evaluate long-term recall of elements of informed consent.	One hundred twenty-two men enrolling in the PMRP biobank were approached to participate in the consenting study; 71 (58%) agreed that 35 were randomized to the CBT and 36 to traditional consent.	Randomised Controlled Trial. The questionnaire comprised 24 statements on knowledge of the components of informed consent and 14 statements asking individuals to rate their degree of understanding on a 5-point scale. There was also a query regarding how much of the $20 used to cover enrolment-related costs would affect their choice to take part. Using Wilcoxon and Fisher's methods, comparisons were made between the computer-based and traditional methods and between the present and historical cohorts' precise examinations.	Most of the 52 men who participated in the biobank but declined participation in the consent study cited the reason as "not interested." Two people declined participation in the consent study because they did not want to be randomized to the kiosk; they preferred the face-to-face consent process. Two people withdrew from the computer-based consenting arm after they had started and changed to traditional consent; one changed his mind about being willing to use the computer, and one was unable to hear even when using headphones. They were not followed further for the consenting study. The men randomized to the computer-based consenting reported that the program was easy to use.	12/13

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No	Authors details and Year		Objectives	Sample and its Characteristics	Material and Methods	Findings	JBI
7	Festinger et al., 2015	United States	This study examines a combined incentivized consent and CF procedure that simplifies the cognitive task and increases motivation to learn consent information.	Of the 254 clients approached, 104 (41%) indicated interest and consented to participate. Before the consent procedure, participants were randomly assigned to the ICF (n=52) or CAU condition (n=52)	Cross-Sectional Study. The 15-item consent quiz assessed all principal topics covered in the host study's consent form, including the study purpose, procedures, remuneration, human rights protections (e.g., confidentiality), and recourse in the event of harm (e.g., whom to contact with additional questions or concerns).	Quiz scores in the two conditions did not differ at the first administration (p=0.39, d=0.2); however, ICF scores were significantly higher at each subsequent administration (second: p=0.003, Cohen's d=0.6; third: p<0.0001, d=1.4; fourth: p<0.0001, d=1.6; fifth: p<0.0001, d=1.8); The ICF/Incentive Consent Form procedure increased consent recall from 72% to 83%, compared with the CAU/ consent as usual condition in which recall decreased from 69% to 59%. This supports the statistical and clinical utility of a combined remedial and motivational consent procedure for enhancing the recall of study information and human research protections	8/8
8	Roessler et al., 2015	United States	To report on an effort to study the development and usefulness of an extensive, broad-use, opt-in biorepository for genomic research, focusing on three ethical issues: providing appropriate understanding, recruiting in ways that do not comprise autonomous decisions, and assessing costs versus benefits. A second goal of this project was to learn more about factors that influence a subject's decision to contribute a sample to biorepository a	Research Volunteers. From the initial population of 6,498, 1,047 (16%) individuals responded, and 230 (4%) eventually enrolled—ambulatory care patients. An additional 250 subjects were recruited in two ambulatory care settings to study the impact of clinic workflow on recruiting times and rates.	Cross-sectional study. The understanding was validated using a 14-question quiz (first 30 subjects) structured (remaining 450 semi-interview subjects). Understanding was judged on a 5-point scale (1 = "doesn't make any sense at all" and 5 = "makes perfect sense"). The SC thoroughly explained any items rated less than five before subjects were enrolled.	- As biomedical research has become more complex, relying on long, complex consent forms has been shown to While too much information may be confusing, too little information could leave key questions unaddressed, putting researchers and review committees in the difficult position of weighing the importance of information, particularly presumed required regulatory language, against understanding. - As a result, even if adding words reduces understanding, IRBs must do so to meet HIPAA requirements. As an example, to meet HIPAA requirements, a newly established UMH Biorepository, which modeled its consent process and documents on the MICHR BioLibrary project, felt compelled to move away from our validated checklist IC to a longer (200 words longer) reorganized IC, which has not been validated (University of Michigan Medical School, n.d.). This change gives reassurance of compliance but not understanding, placing compliance above human protection They took the time to understand what	8/8

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No	Authors details and Year	Country	Objectives	Sample and its Characteristics	Material and Methods	Findings	JBI
						we were asking and to make an informed decision about participation. When we approached them during clinic visits, they had less time and took less time to make decisions. For some, a general commitment to help others was enough to justify enrolment.	
9	Koonrungsesomboo n et al., 2015	Thailand	To evaluate the applicability of the principles and informed consent form (ICF) template proposed by the Strategic Initiative for Developing Capacity in Ethical Review (SIDCER) in a clinical pharmacokinetic study by comparing the volunteers' understanding of the enhanced ICF (developed based on the SIDCER methodology) and the conventional ICF (which was previously approved by local Ethics Committee and used in the clinical study).	Volunteers (age > 18) who can read and write Thai were recruited from universities, colleges, cafeterias, hospitals, and markets in Chiang Mai, Thailand.	Randomized controlled trial. This study was an open-label, randomized-controlled study of the two different ICF interventions (1:1), i.e., the enhanced ICF and the conventional ICF, using a post-test questionnaire as an assessment tool. The post-test questionnaire (in Thai) consisted of 21 short case studies were each case study was designed to illustrate a common practical situation of one element required, followed by a question with three possible answers.	Interestingly, two items were in the conventional ICF, but the proportions of the participants correctly answered between the two groups did not show a statistically significant difference. This could be due to a practicable drawback of the evaluation tool: a close-ended question with multiple answer choices gave an individual a chance to provide the correct answer inadvertently were sufficiently presented in both ICFs but the enhanced ICF group achieved a higher score. - Although there was a trend for baby boomers in the enhanced ICF group to do better, it was not statistically significant enough to conclude that the improved ICF was more effective in this generation than the conventional ICF (83.3% vs. 63.6%, p = 0.105). A possible reason for this result is the small number of subjects in the baby boomer generation in comparison to the other generations -Regarding the educational level, although the result indicates that the enhanced ICF increased the proportion of the participants with optimal understanding in the participants with educational levels 1 and 2, there was little effect in the participants with educational level 3 whose understanding level was high in both groups. This is consistent with the lines of evidence demonstrating that the educational level is a major determinant of research subjects' comprehension. In research practice, subjects generally come from various backgrounds with different educational levels; thus, the SIDCER ICF could be of value.	12/13

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No	Authors details and Year	Country	Objectives	Sample and its Characteristics	Material and Methods	Findings	JBI
10	Rothwell et al., 2014	United States	To explore the appropriateness of an electronic informed consent model within an RCT	Participants recruited for the parent RCT project were randomly selected and randomized to either an electronic consent group (n = 32) or a simplified paper-based consent group (n = 30). To explore the appropriateness of an electronic informed consent model within a RCT.	Randomized controlled trial.The The survey used in this study was based on a survey that measured subjective understanding of informed consent within the clinical trials	Another finding from this research that may influence the informed consent process was the participants' qualitative responses during the interviews. They reported that some information discussed during the electronic informed consent process appeared misplaced and lengthy. This suggests that it might be most effective to have some elements of the consent process in electronic format and others in paper format of a research study.	12/13
11	Paris et al., 2015	France	Toevaluate the comprehension of participants of an improved informed (ICD). consent document	Between April 2009 and March 2013, 481 patients were seen in the six centers. The Grenoble Centre had 338 patients, Saint-Etienne 57, Lyon 44, Toulouse 21, Créteil 13, and Clermont Ferrand 7.	Randomized controlled trial. Using questionnaire	-The participant's degree of understanding needs improvement; ICDs are not easy to read, and the readability of French ICDs was much lower than the provided text school-level texts. It was not improved following IRB reviews; American IRBS often provide text for informed consent forms that fall short of their own readability standards, and high schools provide text. Readability was also low in other languages, such as Spanish or German.	12/13
12	Aliyu and Mahmud, 2016	Canada	This study evaluates postal recruitment and informed consent obtainment for research involving a rare disease to feasibility, response assesses rate, timeliness, and cost in the context of the disease and setting where physical access to research volunteers for recruitment may be challenging.	A list of narcolepsy cases from the two provincial sleep centers, one at the Psych and Sleep Disorder Center of the Health SciencesCenter and the other at Misericordia Hospital, both located in Winnipeg, Manitoba	A retrospective case-control study. Cases were defined based on confirmation of clinical diagnosis of narcolepsy within the study period. A range of identified information, including personal identifiers, symptoms of narcolepsy, diagnostic laboratory tests, and their outcomes, was needed.	All those who provided consent agreed to the range of confidential information to be extracted. The time from the invitation to the receipt of the signed consent forms in the mail varies from a minimum of 18 days to a maximum of 93 days. The median time for consent obtainment was 39 days with an interquartile range (IQR) of 45 days (Fig. 2). In two cases, the consent forms were re-mailed because the initial documents they received were lost. These cases were identified because their signed consents were not returned, and they had to be contacted by phone to ascertain the status of their consent documents. The estimated cost in Canadian Dollars was based on the components used from the initial invitation to consent obtainment, which included 31 postal stamps, 26 small-size envelopes, 5 large-size envelopes, and 41 printed pages for the	9/10

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No	Authors details and Year	Country	Objectives	Sample and its Characteristics	Material and Methods	Findings	JBI
						Another finding from this research that 41 printed pages for the first invitation; 125 postal stamps, 45 small envelopes, 45 large envelopes and 90 printed pages used for the second invitation. It took an average of 5 to 7 min to print an invitation letter, seal, label, append, stamp, and drop it in the office mailbox. The estimated costs of the ingredients units involved were provided along with corresponding costs per consent in Table 1. Most of the cost was accounted for by staff salary and to a lesser extent, the postal stamp.	
13	Ittenbach et al., 2015	United States	This study aimed to assess the self-reported reading and understanding of informed consent documents in a Phase 1 clinical trial among a sample of adults with low incomes.	A total of 11 respondents reported household incomes of less than US$25,000 per year, averaged 29.0 (SD 10.61) years of age; four = (36%) were male and seven (64%) were female. All 11 (100%) self-reported their race as Black. Nine (82%) reported a high school education, one (9%) a General Equivalency Degree (GED), and one (9%) a 2-year college education. Concerning reading ability, seven (64%) had a reading level of seventh to eighth grade and four (36%) read at the 12th-grade (high school) level	The current study was embedded within a larger Phase 1 randomized immunization study on Escherichia (E.) coli as a supplemental ethics sub-study. Using questionnaire	Hypothesis 1: This may be a version of the therapeutic misconception, in which the physician or researcher is regarded as a trustworthy professional who would not undertake anything that would harm them; hence, it would seem rational and easier to trust a trustworthy professional than to exert the effort to read a consent form critically. Hypothesis 2: Subjects may find the consent material too complex to understand and save face by pretending they read it. Hypothesis 3: Subjects may be so accustomed to signing presumed "boilerplate" that they don't want to read that they treat consent forms much the way they treat agreements pertaining to software they purchase online and download. Hypothesis 4: Subjects may simply not care.	8/8
14	Grady et al., 2014	United States	To better understand the perspectives of adolescent research participants and their parents about assent and parental permission	Recruited a purposive sample of adolescents participating in a wide range of clinical research and representing a variety of illnesses as well as healthy volunteers at the NIH and Seattle Children's Hospital who were 13-17 years of age, had enrolled in the previous six months in a research study for any disorder	Qualitative research. The interviews primarily used close-ended questions, with a few open-ended questions for which respondents were asked to explain or clarify what they were asked to answer. Instrument development is described in detail elsewhere.	A small but disconcerting subset of our teen cohort was dissatisfied with the process, felt pressure to enroll, and/or said it would have been difficult or impossible to refuse. These teens may be the most in need of support and protection. Somewhat unexpectedly, there were no differences by age or severity of illness in perceived pressure	10/10

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No	Authors details and Year	Country	Objectives	Sample and its Characteristics	Material and Methods	Findings	JBI
				or as healthy controls, spoke English or Spanish, were physically and cognitively able to be interviewed, were willing to be interviewed, and had a parent or guardian also willing to be interviewed.		Aor difficulty refusing. There was, however, a trend for female teens to report more pressure and more difficulty saying no than their male counterparts, and parents would have tried harder to convince female teens to unroll.	
15	Karbwang et al., 2018	India, Indonesia, Malaysia, Philippine s, Sri Lanka, Taiwan, and Thailand	To determine the perspectives of research participants about the type and extent of information they need when they are invited to participate in biomedical research.	Individuals participate at various centers (clinical research units or comparable settings) in 7 Asia-Pacific countries.	Multi-center, cross-sectional, descriptive survey. The study materials use a Likert-scale questionnaire.	The top three items that were of most concern to the respondents in this study were related to the concepts of risks and benefits (i.e., major foreseeable risk, direct benefit, and common adverse effects of the intervention).	7/8
16	Kraft et al., 2020	United States	Enrolled parents should evaluate and decide whether to enrol their children in research before or after receiving the consent form.	106 parents were approached and permitted their contact information to be shared with the study team. A total of 88 parents (67 enrolees, 21 decliners) completed the survey (83% participation rate); 79 of 88 reporting gender (instead of sex, as biological sex was not relevant to survey) information were women (91%), 66 participants (75%) were non-Hispanic White, and 63 participants (72%) had annual household.	Cross-sectional study. This study uses an online survey.	A total of 106 parents were approached, and their contact information was permitted to be shared with the study team. Fifty-nine parents (67%) responded that they decided whether to enrol in the weight management study before receiving the consent form. Only 17 of 69 parents (25%) who remembered receiving the consent form responded that it taught them new information.	7/8
17	Jamerson & Shuster, 2023	United States	To determine if an audio-assisted presentation of informed consent with or without teach-back would improve the willingness to consider participation in a clinical trial	The population is African American and biracial in Durham, NC. The sample included 71 participants	Randomized controlled trial. Online Survey and phone for semi-structured interview	Providing audio-assisted informed consent to facilitate communication increased the willingness to participate in a clinical trial.	10/13
18	Celine Y. Chhoa, Alexandra Sawyer, Susan Ayers, Angela Pushpa-Rajah, and Lelia Duley, 2017	UK	To explore clinicians' views and experiences of offering two consent pathways for recruitment to a randomized trial of	Invitations to be interviewed were sent to 20 clinicians, and 17 clinicians from 7 hospitals responded: 5 consultant neonatologists, three neonatal or pediatric registrars, five neonatal nurses, and four midwives	Qualitative research. The interview schedule (Additional file 1) consisted of open-ended questions to explore clinicians' views and experiences of inviting women	The two-stage pathway for consent developed for use in the Cord Pilot Trial when birth was imminent was acceptable to clinicians for comparable low-risk studies, although some concerns were raised about the practicalities of obtaining	9/10

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No	Authors details and Year	Country	Objectives	Sample and its Characteristics	Material and Methods	Findings	JBI
			timing of cord clamping at very preterm birth		in the trial. Interviews were conducted in a private hospital room or by telephone and lasted approximately 20-30 minutes.	Aor difficulty refusing. There was, horal assent	
19	Kelly et al., 2015	UK	To establish the views of research volunteers on the consent process, to explore their views on the consent process in different research scenarios, and to inform debate on emerging models of consent participation in research. for	Of the 4 284 subjects invited to participate, 2308 completed the online consent questionnaire (54% response rate), with a mean age of 55, age range = 18-87 years (89% female, 11% male)	Cross-sectional study. On joining the registry, volunteers are invited to complete online or postal health questionnaires, come to St. Thomas's Hospital for a clinical study visit, and donate blood for DNA and biochemical markers.	Most volunteers preferred to be informed of the identity of the main researcher of a study in which they are participating, which is contrary to current practice. Over 80% were willing to complete the consent process online instead of face-to-face. Respondents did not view their DNA differently from their medical information regarding the consent process.	8/8
20	Suver et al., 2020	United States	To identify opportunities to improve how IC is obtained in AD research, we examined the IC process from the perspectives of study coordinators at two Alzheimer's Disease Research Centers (ADRC)	The study coordinators were primarily female (n½ 10), two-thirds White (n 1/4 9), one-quarter African American (n½ 4), almost all under 40 years old (n²¼ 11), almost two-thirds under 30 (n¼ 8), and most had at least one year experience as a study coordinator for the ADRC studies (n ¼ 10)	Qualitative research. ICF: We reviewed each center's IC form for content and readability levels	Coordinators reported overall satisfaction with the IC process. However, many reported needing help maintaining participant attention, explaining complex procedures and addressing medical misinformation.	9/10
21	Mazurenko et al., 2022	United States	To describe and evaluate implementing a primarily electronic provider recruitment strategy based on the 7R framework.	Eligible PCPS included physicians, nurse practitioners, and physician assistants from general internal medicine or family medicine practices that provide primary care services to adult patients with chronic pain.	Randomized controlled trial. The research coordinator maintained a detailed spreadsheet of each communication between relevant stakeholders to quantify recruitment effectiveness.	We recruited 45 of 63 eligible PCPs practicing at ten primary care clinic locations over 55 days. On average, It took 17 business days to recruit a PCP (range 0-48) and required three attempts (range 1-7). Email communication	10/13

Appendix 2 Compare Matrices

No	Title	Authors' details and Year	"What challenges are encountered while obtaining informed consent in human subject research?"	Coding
1	Does written informed consent adequately inform surgical patients? A cross sectional study	Agozzino et al., 2019	Most respondents (84.5%) personally received a written IC form, or they reported that they delegated it to a parent or a relative; 1.6% declared that they did not get it, and the others (13.9%) did not recall receiving it. All patients who received the IC form signed it personally or through a relative or parent, but only 51.8% reported reading it thoroughly. Among those who read the IC, 90.9% judged it clear, and 9.1% deemed it partially understandable. No one considered it incomprehensible. Approximately half of patients received the written IC form a day before surgery (at the earliest), while 41.1% received it within some hours or immediately before surgery. Forty-five percent of patients receiving the written forms were given them by the surgeon who performed the procedure (Table 2). Not all patients had the written consent for explained to them; it was explained orally only to 65.6%; however, 93.9% of patients received further oral information; among these, 68.6% judged this information to be incomplete, and only 31.4% considered it complete. The information was provided progressively during pre-operative examinations (66.7%) and was understandable according to most (97.1%) recipients.	1.1 not getting ICF; 1.2 not remember receiving ICF; 1.3 not reading ICF thoroughly; 1.4 partially understandable; 1.5 not being explained; 1.6 incomplete information
2	Reported consent proce-sses and demographics: a substudy of the INSIGHT Strategic Timing of Antiretroviral Treatment (START) trial.	Denning et al., 2015	They did not have a language in common with another participating site (such as the single site in Nigeria, where the patient base speaks Hausa). The regulations strictly limit the length of informed consent documents to less than the length of the researchers' concise consent template. The START study's two-stage site start-up process (beginning enrolment at 101 pilot sites, then adding 120 new sites to complete the trial) was also a limiting factor as many of the sites that had not been part of the pilot did not want the delay in enrolment that may have occurred with participation in substudies.	2.1 did not have a language in common; 2.2 strictly limited the length of informed consent documents; 2.3 two-stage site start-up process
3	The goldilocks co-nundrum: Disclosing discrimination risks in informed consent	Prince et al., 2022	- When making an actual decision about participation in a research study, the informed consent document language may have more or less impact on willingness to participate because individuals are also weighing other potential risks and benefits of the study. - On the other hand, we cannot presume clinicians and researchers know this information nor expect informed consent documents to every possible specific risk of a study or clinical procedure, especially if some are likely to be very rare or unknown or if disclosure would require listing every omission in an anti-discrimination law. Too much detail about the limits of GINA's coverage could overwhelm individuals and heighten fears of discrimination when those risks may be quite low depending on the clinical or research testing being considered	3.1 ICF language
4	Survey on Using Ethical Principles in Environmental Field Research with Place-Based Communities	Quigley et al., 2019	- Provides researchers' recommendations for ensuring community training on informed consent logistics, with knowledge of confidentiality requirements and data access rules; to ensure adequate knowledge of the informed consent document by using native languages and to utilize cultural norms to secure appropriate consent using Native-speaking translators and local languages, report results both in English and local languages, provide a consent copy to participant, do mapping exercise with names, use visual images, mapping and photographs to give voice to the community's own stories. - Without being particularly cognizant of a place's context and/or social structural arrangements, you cannot really understand human behavioral response, organizational decision-making, or emotional reactions to a stressful situation. By working with elders in the consent process, a respondent remarked that their research team was informed about language barriers with different participants and how to allow the community to say when/who/how it was appropriate to work with individual community members. With some	4.1 ICF language; 4.2 assurance of confidentiality; 4.3 lack of understanding in human behavioral response; 4.4 lack of knowledge in organizational decision-making; 4.5 lack of understanding in emotional reactions to a stressful situational

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			participants, we spent time meeting with them, getting to know them andthem know us, and when they were comfortable participating in the study.	
5	Procedures of recruiting, obtaining informed consent, and compensating research participants in Qatar: findings from a qualitative investigation	Killawi et al., 2014	1. Influence of cultural idiosyncrasies on the level of disclosure and the informed consent process in clinical care. 2. Differences in interpreting ethical research principles 3. Challenges implementing Western research principles, particularly informed consent 4. Difficulty of obtaining informed consent from illiterate individuals	5.1 influence of cultural idiosyncrasies; 5.2. differences in interpreting; 5.3. challenges implementing Western research principles; 5.4. illiterate individuals
6	Long-Term Recall of Elements of Informed Consent: A Pilot Study Comparing Traditional and Computer-Based Consenting	McCarty et al.,2015	The majority of the 52 men who participated in the biobank but declined participation in the consent study, cited the reason as "not interested." Two people declined participation in the consent study because they did not want to be randomized to the kiosk; they preferred the face-to-face consent process. Two people withdrew from the Computer-based consenting arm after they had started and changed to traditional consent; one changed his mind about being willing to use the computer, and one was unable to hear even with the use of headphones. They were not followed further for the consenting study. The men who were randomized to the computer-based consenting reported that the program was easy to use.	6.1 lack of interest; 6.2 respondents' desire; 6.3 changing tools
7	Achieving new levels of recall in consent to research by combining remedial and motivational techniques	Festinger et al., 2015	Quiz scores in the two conditions did not differ at the first administration (p=0.39, d=0.2); however, ICF scores were significantly higher at each subsequent administration (second: p=0.003, Cohen's d=0.6; third: p<0.0001, d=1.4; fourth: p<0.0001, d=1.6; fifth: p<0.0001, d=1.8); The ICF/Incentive Consent Form procedure increased consent recall from 72% to 83%, compared with the CAU/consent as usual condition in which recall decreased from 69% to 59%. This supports the statistical and clinical utility of a combined remedial and motivational consent procedure for enhancing recall of study information and human research protections	7.1 usual consent has lower consent recall than incentivized CF
8	The MICHR Genomic DNA BioLibrary: An Empirical Study of the Ethics of Biorepository Development	Roessler 2015	- As biomedical research has become more complex, relying on long, complex consent forms has been shown to B2:E23 While too much information may be confusing, too little information could leave key questions unaddressed, putting researchers and review committees in the difficult position of weighing the importance of information, particularly presumed required regulatory language, against understanding. - As a result, even if adding words reduces understanding, IRBs are compelled to do so to meet HIPAA requirements. As an example, to meet HIPAA requirements, a newly established UMH Biorepository, which modeled its consent process and documents on the MICHR BioLibrary project, felt compelled to move away from our validated checklist IC to a longer (200 words longer) reorganized IC, which not been validated (University of Michigan Medical School, n.d.). This change gives reassurance of compliance but not understanding, placing compliance above human protection They took the time to understand what we were asking and to make an informed decision about participation. When we approached them during clinic visits, they had less time and took less time to make decisions. For some, a general commitment to helping others was enough to justify enrollment.	8.1 reduce understanding; 8.2 too much and too little information; 8.3 less time

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9	Improved participants' understanding in a healthy volunteer study using the SIDCER informed consent form: a randomized-controlled study	Koonrungsesomboon et al., 2015	- Interestingly, there were two items in the conventional ICF, but the proportions of the participants who correctly answered between the two groups did not show a statistically significant difference. This could be due to a practicable drawback of the evaluation tool: a close-ended question with multiple answer choices gave an individual a chance to provide the correct answer inadvertently were sufficiently presented in both ICFs but the enhanced ICF group was able to achieve a higher score. - Although there was a trend for baby boomers in the enhanced ICF group to do better, it was not statistically significantly enough to conclude that the enhanced ICF was more effective in this generation than the conventional ICF (83.3 % vs. 63.6 %, p = 0.105). A possible reason for this result is the small number of subjects in the baby boomers generation in comparison to the other generations - With regards to the educational level, although the result indicates that the enhanced ICF increased the proportion of the participants with optimal understanding in the participants with educational levels 1 and 2, there was little effect in the participants with educational level 3 whose understanding level was high in both groups. This is consistent with the lines of evidence demonstrating that the educational level is a major determinant to research subjects' comprehension. In research practice, research subjects generally come from various backgrounds with different educational levels; thus, the SIDCER ICF could be of value.	9.1 less statements; 9.2 generational differences ;9.3 educational level
10	A Randomized Controlled Trial of an Electronic Informed Consent Process	Rothwell et al., 2014	Another finding from this research that may influence the informed consent process was the participants' qualitative responses during the interviews. They reported that some information discussed during the electronic informed consent process appeared misplaced and lengthy. This suggests that it might be most effective to have some elements of the consent process in electronic format and others in paper format	10.1 Misplaced and lengthy; 10.2 Electronic formats; 10.3 paper formats
11	Improved informed consent documents for biomedical research do not increase patients' understanding but reduce enrolment: a study in real settings	Paris et al., 2015	The participant's degree of understanding remains unsatisfactory, ICDs are not easy to read, the readability of French ICDs was much lower than that of highly provided text school-level texts and was not improved following IRB reviews; American IRBs often provide text for informed consent forms that fall short of their readability standards, high school provide text, and readability was also low in other languages such as Spanish or German	11.1 degree of understanding
12	Postal recruitment and consent obtainment from index cases of narcolepsy	Aliyu and Mahmu, 2016 Ittenbach et al., 2015	All those who provided consent agreed to the range of confidential information to be extracted. The time from the invitation to the receipt of the signed consent forms in the mail varies from a minimum of 18 days to a maximum of 93 days. The median time for consent obtainment was 39 days with an interquartile range (IQR) of 45 days. The consent forms were re-mailed in two cases because the initial documents they received were lost. These cases were identified because their signed consents were not returned, and they had to be contacted by phone to ascertain the status of their consent documents. The estimated cost in Canadian Dollars was based on the components used from the initial invitation to consent obtainment which included 31 postal stamps, 26 small size envelopes, 5 large size envelopes and 41 printed pages for the first invitation; 125 postal stamps, 45 small envelopes, 45 large envelopes and 90 printed pages used for the second invitation. It took an average of 5 to 7 min to print an invitation letter, seal, label, append, stamp, and drop it in the office mailbox. The estimated costs of the ingredients units involved were provided along with	12.1 needs more time; 12.2 signed consents were not returned

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			corresponding costs per consent in Table 1. Most of the cost was accounted for by staff salary and to a lesser extent, the postal stamp.	
13	Readability and Unders-tanding of Informed Consent Among Participants With Low Incomes: A Preliminary Report	Ittenbach et al., 2015	Hypothesis 1: This may be a version of the therapeutic misconception, in which the physician or researcher is regarded as a trustworthy related professional who would not undertake anything that would harm them; hence, it would seem rational and easier to simply trust a trustworthy professional than to exert the effort to read a consent form critically. Hypothesis 2: Subjects may find the consent material too complex to understand and save face by pretending they read it. Hypothesis 3: Subjects may be so accustomed to signing presumed "boilerplate" that they don't want to read that they treat consent forms much the way they treat agreements pertaining to software they purchase online and download. Hypothesis 4: Subjects may simply not care	13.1 Therapeutic misconception; 13.2 too complex to understanding; 13.3 don't want to read; 13.4 not care
14	Assent in Research: The Voices of Adolescents	Grady et al., 2014	A small but disconcerting subset of our teen cohort was dissatisfied with the process, felt pressure to enroll, and/or said it would have been difficult or impossible to refuse. These teens may be the most in need of support and protection. Somewhat unexpectedly, there were no differences by age or severity of illness in perceived pressure or difficulty refusing. There was, however, a trend for female teens to report more pressure and more difficulty saying no than their male counterparts, and parents would have tried harder to convince female teens to enroll	14.1 dissatisfied; 14.2 elt pressure to enroll; 14.3 impossible to refuse to enroll; 14.4 no differences by age; 14.5 harder to convince female teens to enroll.
15	What information and the extent of information research participants need in informed consent forms: a multi-country survey	Karbwang et al., 2018	The top three items that were of most concern to the respondents in this study were related to the concepts of risks and benefits (i.e., major foreseeable risk, direct benefit, and common adverse effects of the intervention)	15.1 Respondents' concern on risk and benefits
16	Assessing Parent Decisions About Child Participation in a Behavioral Health In-tervention Study and Utility of Informed Consent Forms.	Kraft et al., 2020	How to improve research decision-making: (1) some individuals may make decisions using heuristics rather than deliberative weighing of the details involved in a trial, (2) regulatory review of research should focus more on early engagement with prospective participants, and (3) financial motivations may drive early decision-making for some individuals	16.1. make decisions using heuristics; 16.2. regulatory review of research should focus more; 16.3. financial motivations may drive early decision-making
17	Evaluation of Informed Consent with Teach-Back and Audio Assistance to Improve Willingness to Participate in a Clinical Trial Among Underrepresented Minorities: A Randomized Pilot Trial	Shuster, 2023	- When asked the reasons for not being willing to enroll, the most frequent reasons cited were risks/side effects and further information/other research would be needed and the impact of the study and study drug on their quality of life - When commenting on the presentation of the summary, some individuals commented on the need for the text to be more spaced out or larger - Another group of comments centered on technological features of hearing the audio. Example comments related to the technology were "The voice is too robotic"; "I like the ability to speed up the audio"; "The audio voice was monotone and it took longer due to extra pauses"; and "The audio helped me with the summary. It helps me to organize and understand the document. - For the few participants who did not like the teach-back, the comments were that "it didn't feel like it made me understand better," "it feels awkward because it felt like I am being quizzed, like a pop quiz"	17.1. risks/side effects; 17.2 information/ other research; 17.3. need for the text to be more spaced out or larger; 17.3. few participants did not like the teach-back

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18	Clinicians' views and experiences of offering two alternative consent pathways for participation in a preterm intrapartum trial: a qualitative study	Celine Y. Chhoa,Alexandra Sawyer,Su-san Ayers, Angela Push-pa -Rajah, and Lelia Duley (2017).	Six major themes were identified in clinicians' experiences of offering the two consent pathways: (1) team approach to offering participation; (2) consent form as a record; (3) consent and involvement as a continual process; (4) different consent pathways for different trials; (5) balance between time, information, and understanding; and (6) validity of consent. Differences were explored between the professions; however, as there were no overall differences between professional groups (i.e. doctor, nurse, midwife) regarding the content of the themes, the results are presented for the whole sample.	18.1. different consent pathways for different trials; 18.2 balance between time, information and understanding; 18.3 validity of consent;
19	Evaluating the Consent Preferences of UK Research Volunteers for Genetic and Clinical Studies	Kelly et al., 2015	In some scenarios, research participants reported that they would be comfortable with not signing a new consent form for future research uses of their data and DNA, and are comfortable with secure, online consent processes rather than traditional face-to-face consent processes. Our findings indicate that the perceived relationship between research participants and researchers plays an important role in shaping preferences regarding consent process and suggest that traditional consent processes do not capture this relationship. We argue that the development of new formats of consent should be informed by empirical re-Search on volunteers' perceptions and preferences regarding the consent process	19.1. comfortable with secure online consent processes rather than traditional face-to-face consent pro- cesses; 19.2. relationship between research participants and researchers
20	Informed Consent in Two Alzheimer's Disease Research Centers: Insights From Research Coordinators	Suver et al., 2020	1. Participant inattention, including the duration of the IC process and boredom 2. Complexity of the study procedures, visit schedule, and consent materials 3. Prior knowledge, including confusion about the scientific process, misinformation, and therapeutic misconception	20.1. participant inattention; 20.2. complexity of the study procedures; 20.3. visit schedule; 20.4. consent materials; 20.5. prior knowledge
21	Evaluation of electronic recruitment efforts of primary care providers as research subjects	Mazurenko et al., 2022	Recruiting individual healthcare providers, such as physicians, nurse practitioners, and other medical professionals, as subjects in research studies is often challenging. Healthcare providers report numerous barriers to participation, including time constraints, low interest in research topics, concerns about relationships with patients, loss of professional autonomy, and reluctance to modify existing clinical workflows. Due to the co-occurring COVID-19 pandemic resulting in high workload and stress among eligible PCPs, we could not gather feedback from eligible PCPs on how they perceived our predominantly electronic recruitment strategy. Relatedly, we did not conduct a baseline assessment of several 7R framework strategies, such as PCPs perception of the research team's reputation for conducting rigorous research, which may have shed more light on the effectiveness of our recruitment efforts.	21.1. time constraints; 21.2. low interest; 21.3. relationships with patients; 21.4. loss of professional autonomy; 21.5. reluctance to modify existing clinical workflows