IJCOM 2022 July;2(1):40-7

Issues About Digital Informed Consent in Clinical Research

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Abstract

Introduction: *Informed consent* is a concrete form of moral and ethical values that urgently needs to be emphasized, especially in research that requires the role of humans as subjects and is commonly associated with experimental research. Informed consent itself consists of two forms of print and digital, along with the times many parties began to examine how the role of informed consent, the advantages and disadvantages between print and digital, the application of good digital informed consent, and how information about research should be conveyed to the research subject so that it is easy to understand and in accordance with moral and ethical standards. The purpose of this article is to address issues related to digital informed consent in clinical research.
Methods: We conducted a search on the SpingerLink database in March 2022 to see various publications in the last 2 years related to electronic informed consent using keywords: digital, informed consent, research.
Results: Total 4 articles as source of literature review. Recent research shows the tendency of research subjects to choose digital informed consent because content is easier to personalize, makes it easier to understand content that is only needed by the subject, and the ease of adding digital content in certain forms of media such as audio, and video into digital formats. From the researcher's side will increase the active participation and number of study subjects, making it easier for long-term interaction, especially follow-up research. There are 4 types of informed consent based on utilization for research and 5 informed consent processes that must be carried out in clinical research, which is attempted using language that is easily understood by the research subject and dynamic for further research.
Conclusions: Informed consent in any form constitutes the autonomy right of the subject. Digital formats provide better prospects in facilitating communication to research subjects. But this ease must be accompanied by the consistency of the application of the standard informed consent process, even in intervention studies with biological samples this is more stringent. Informed consent given to the subject must use language that is easy to understand, and transparent. The subject of the study is given the right at any time to exit the research. In the future, the issue of morals and ethics of research will grow, and more dynamic informed consent is needed, especially for interventional clinical research.
Keywords: digital, informed consent, research

Abstrak

Pendahuluan : *Informed consent merupakan bentuk konkrit nilai moral dan etik yang sangat perlu ditekankan terutama pada penelitian yang membutuhkan peran manusia sebagai subjek dan biasa berhubungan dengan penelitian eksperimental. Informed consent sendiri terdiri dalam dua bentuk cetak maupun digital, seiring perkembangan zaman banyak pihak yang mulai mengkaji bagaimana peran dari informed consent, kelebihan kekurangan antara cetak dan digital, pengaplikasian digital informed consent yang baik, dan bagaimana seharusnya informasi tentang penelitian disampaikan kepada subjek penelitian sehingga mudah dipahami dan sesuai standar moral dan etik. Tujuan artikel ini adalah untuk menjawab isu yang berkaitan dengan informed consent digital pada penelitian klinis.*
Metode: *Kami melakukan pencarian pada database SpingerLink pada bulan Maret 2022 untuk melihat berbagai publikasi pada 2 tahun terakhir terkait elektronik informed consent dengan menggunakan kata kunci: digital, informed consent, research.*
Hasil*: Total 4 jurnal sebagai literatur review. Penelitian terkini menunjukkan kecenderungan subjek penelitian untuk memilih informed consent digital karena konten lebih mudah dipersonalisasi, memudahkan dalam memahami konten yang hanya dibutuhkan oleh subjek, dan mudahnya penambahan konten digital dalam bentuk media tertentu seperti audio, dan video ke dalam format digital. Dari sisi peneliti akan meningkatkan partisipasi aktif dan jumlah dari subjek penelitian, memudahkan untuk interaksi jangka panjang terutama penelitian lanjutan. Terdapat 4 jenis informed consent berdasarkan pemanfaaatan untuk penelitian dan 5 proses informed consent yang harus dilakukan pada penelitian klinis, yang diupayakan menggunakan bahasa yang mudah dipahami oleh subjek penelitian dan bersifat dinamis untuk penelitian lanjutan.*
Kesimpulan*: Informed consent dalam bentuk apapun merupakan hak autonomi subjek. Format digital memberikan prospek yang lebih baik dalam memudahkan komunikasi ke subjek penelitian. Namun, kemudahan tersebut harus diiringi dengan konsistensi penerapan proses informed consent yang standar, bahkan pada penelitian intervensi dengan sampel biologis hal ini lebih ketat. Informed consent yang diberikan kepada subjek mesti menggunakan bahasa yang mudah dipahami, dan transparan. Subjek penelitian diberikan hak sewaktu-waktu untuk keluar dari penelitian. Ke depannya isu tentang moral dan etik penelitian akan semakin berkembang, dan dibutuhkan informed consent yang lebih dinamis khususnya untuk penelitian klinis intervensi.*
Kata kunci: *digital, informed consent, research*

Introduction

In modern civilization in the 20th century, research is an integral part of the world of education and development of science. This is to further provide convenience and comfort to the community which of course requires a lot of time.[1] Good research will provide a "complete" picture and solution of an "event" in the community with evidence-based and able to be integrated in the values and policies of a company or state. What is known is that some policies in the company are "direct language transfer", without adjustments based on local conditions. For this reason, research and periodic publications in Indonesia are needed so that there is continuity and correction in every policy implementation, it will also help avoid unnecessary burdens on workers and companies due to unreliable policies, especially during outbreaks and pandemics in Indonesia.[2,3]

On the other hand, not all research subjects can be covered and represent a population, some under-served populations such as racial minorities may not be included. This has become a common concern of institutions and governments to strive for the implementation of inclusive values and equality to get a suitable place in research. The effort begins with develop and refine a programme theory that explains the factors that influence the decision to take part in health research in under-served population[4]

Before the research is carried out there are several stages that must be passed one of the most important is related to moral and ethical values. Biological research today for example is more directed as *translational research* which means continuity between different scientific fields including which differences in knowledge sets, methodologies, and findings should result in research into the form of practice, or simply sample from the patient's bed to the experimental process by the researcher and the usefulness returns to the patient. So this requires the storage of big data (integrated digital big data) that can be accessed at any time by interested parties (researchers) who have been given access through *the initial informed consent* of the study, so that it can benefit humanity in the future.[5]

Informed consent is a concrete form of moral and ethical values that urgently needs to be emphasized, especially in research that requires the role of humans as subjects and is commonly associated with experimental research.[1,6,7] The provision of understandable information to the subject is necessary to achieve the purpose of informed consent, namely respecting and promoting patient *autonomy* and protecting patients from dangerous risk (*do no harm principal*).[6,8]

Informed consent itself consists of two: print-out and digital forms, along with the times many parties began to examine how the role of informed consent, the advantages of the shortcomings between print and digital, the application of good digital informed consent, and how information about research should be conveyed to the research subject so that it is easy to understand and in accordance with moral and ethical standards.[6,7,9]

Method

We conducted a search on the SpingerLink database in March 2022 to see various publications in the last 2 years, up-to-date relevant article journal related to electronic informed consent using keywords: digital, informed consent, research.

For searches with such keywords are more focused on filtering in the title section, and abstracts of the research. Research journals that meet these criteria are then included as inclusions. While the exclusion criteria are various journals that do not meet the previous criteria.

Result

After performing article extraction and filtering in terms of relevance and quality, 8 articles are selected for assessment (see table 1). Recent research points to the tendency of research subjects to choose digital format informed consent because content is easier to personalize, makes it easier to understand content that is only needed by the subject, and the ease of adding digital content in certain forms of media such as audio, and video into digital formats. From the researcher's side will increase the active participation and number of subjects, making it easier for long-term interactions, especially follow-up research.[6,7,10]

Evidence of this is seen in one of the studies in the field of surgery that proves the addition of a digital educational platform (DEP) online module to a standard verbal consent for laparoscopic Roux-en-Y gastric bypass (LRYGB) resulted in improved patient's understanding of the procedure-specific risks and benefits, high patient

satisfaction, and over 50%-time savings for the bariatric surgeon conducting the consent discussion. DEP consisted of a 29-slide video-supplemented module detailing the risks, benefits, expectations and outcomes for the LRYGB[10]

While conventional paper-based informed consent tends to have more complex (long and too much) content that is only read by half of the study subject, formalized documents (immutable and inflexible), which leads to repeated searching for a participant's specific written statement, uncontrolled storage of paper-based forms, and availability at only one location, but have added value make it easier for the subject to interact directly with the researcher.[7,9]

On the other hand, with these various advantages, digital format informed consent has its own challenges, especially the form of a mutually agreed standard format, and the openness of information that can be accessed by the subject if at any time there is a change in content. [1,9]

To answer these challenges, the H2020 i-CONSENT project conducted a multi-faceted literature review and systematic review to establish "The Guidelines for Tailoring the Informed consent Process in Clinical Studies". After testing using the RAND/UCLA method it is declared as "appropriate" by policy makers in Europe.[1]

i-CONSENT is an acronym, and a key element of the informed consent process as follows.[11]

1. i: Information
   Complete and clear information is essential for the potential participant to be able to make an autonomous decision[11]

2. C: Co-creation
   The inclusion of potential participants during the design and review of study information materials is key to ensuring that they are understandable and address the target population's needs and preferences[11]

3. O: Ongoing process
   Consent should be a two-way continuous communication process that begins at first contact with the potential participant, and continues until the end of the study[11]

4. N: New technologies, methods, and (innovative) processes
   The consent process should include technical and methodological innovations to facilitate the participant's experience. Their appropriateness from a social, methodological, legal, and ethical point of view should always be taken into consideration.[11]

5. S : Self-determination(autonomy)
   Autonomy is a fundamental principle. The purpose of the informed consent is to ensure that the potential participants can make an autonomous and free decision.[11]

6. E: Empowerment
   Participants should be empowered to make their own decisions.[11]

7. N: Non-standard (inclusive and tailored)
   Research should be inclusive to meet the needs of the potential participants and respect the basic bioethics principle of justice. There is no single best way to conduct the consent process. The 'ideal' solution will differ in every setting and therefore needs careful design. Where possible, the consent process should be tailored to the needs of the target population.[11]

8. T: Trusted
   Good practices are essential to build trust between investigators and potential participants, and to increase society's trust in research.[11]

Informed consent has a process stage that are: [1]

1. First contact with the research subject
   Aimed at raising awareness, purpose, important study information to prospective subjects including inclusion and exclusion criteria, relevant study procedures and contacts that can be contacted. Can be done through social media, letters, posts or ads, press/radio/tv, health professionals, patient organizations, investigator expertise, institutional websites[1]

2. Information for prospective subjects
   Information is inclusive and clear, and well personalized. Received through web links, videos, images, printed paper, applications (android/ios) and others. The use of multimedia is preferred subject rather than just using video. It is important to convey information in simple language that is easy to understand without

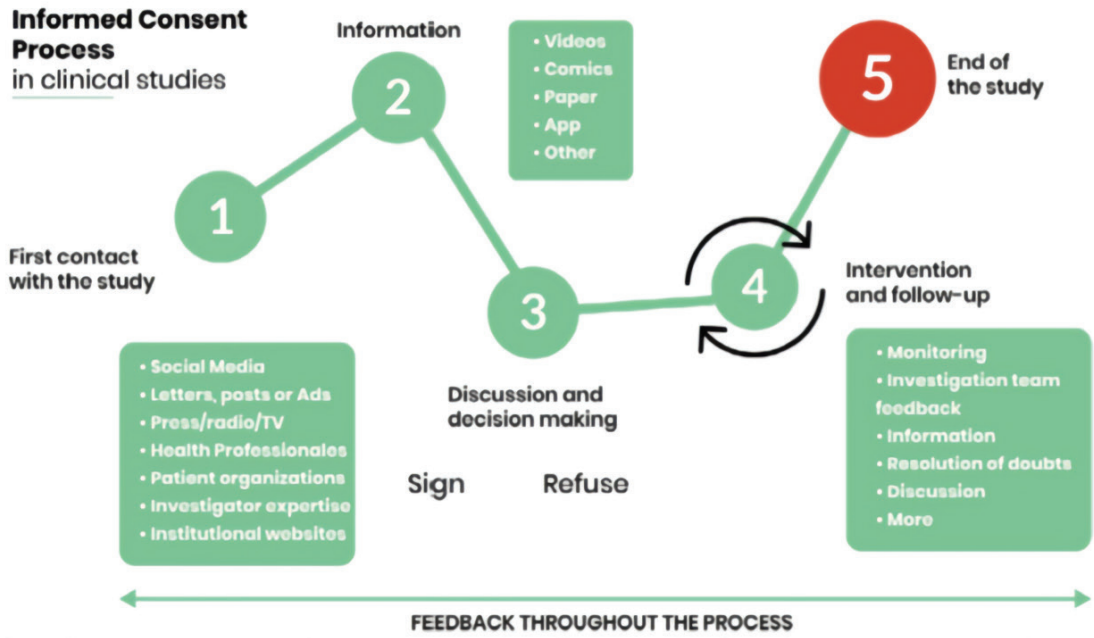

Figure 1. Informed consent process in clinical research [1]

the need for follow-up expert consultation (rather than the use of technical language such as medical terms, whenever possible). If not, an explanation of the term is given directly in the document. All must pay attention to the views of social aspects, methodology, legal and ethical. [1]

3. Discussion information and subject decision making
   The subject is entitled to accept or reject the research and can give feedback during the study. [1]

4. Intervention and follow-up
   Include monitoring, investigation team feedback, information, resolution of doubts, discussion and others.[1]

5. End of Study
   Researchers are allowed to submit study results and add feedback from subjects such as the use of the *Study Participant Feedback Questionnaire Toolkit.*[1]

Ultimately, the key aspects for improving understanding of the informed consent process in clinical studies are:[1]

- Consider consent as an ongoing two-way communication process that begins at the time of first contact with potential participants, and continues until the end of the study
- Improvement of research communication skills
- Creation of shared informational materials
- The use of layered approaches, including information to compensate for the possible lack of health literacy on the subject's part and a list of terms to facilitate the research subject.

The application of the use of biological samples for various studies presents its own challenges in the informed consent process. One of the cancer organizations in the European country of France, The Cancer Research for Personalized Medicine (CARPEM) SIRIC, accredited by the French National Institute of Cancer (INCa), is an expert consortium in translational research and precision medicine in the field of cancer.[5]

They used centralized data sharing to be re-used in follow-up research with the aim of obtaining hypotheses, adaptation of treatment and finding new indications for

treatment in cancer patients. In this case it is divided into two categories of interventional and non-intervention research and is given informed consent to the subject. The research complies with the declaration in Taipei and the Declaration of Helsinki and the European General Data Protection Regulation (GDPR). The GDPR defines informed consent as "a clear affirmative action that establishes a freely, specific, informed, and unambiguous indication of the data subject's consent for the processing of personal data relating to it, such as through written statements, including through electronic means, or oral statements[5]

In the withdrawal of data on the 5-year research activity report (2012-2017) by investigators obtained infomed consent content after being classified based on flesch score (level readability-index to understand the level of language use in informed consent versus understanding of the language in the general population) which is classified into high school level as rather complex, undergraduate as complex and academic as very complex. It turns out that some (22 of the 53 documents) are academic levels, 29 of the 53 undergraduate levels, and the rest are high school levels. This suggests that some informed consent requires in-depth understanding and use of specific language that not necessarily all research subjects understand.[5]

Informed consent in similar studies has more detailed specific in the context of using specimens e.g. "specific informed consent" (SC) for specific research use as written or delivered, "broad informed consent"(BC) collection and storage of bio-specimen for unspecified future research, which will occur under the conditions specified at the time of approval. , "either broad or specific informed consent" (BSC) allows the subject to choose between the use of specimens for specific research or also for unspecified research in the future, or "opt-out informed consent"(OC) subjects are informed of the "use of bio-specimen research and offered the opportunity to opt out(drop-out)".[5]

In other studies, such as in European countries they have started and are optimizing the utilization of dynamic informed consent with modular systems. Systematics of this can be seen in Figure 2. There are 3 important components, namely a template determines the content and structure of the consent form including an introductory text (header), selectable modules (e.g., accepted, declined, withdrawn) and a closure text (footer) as well as complementary information, e.g., order of modules, definition of obligatory modules as well as free text fields adjusting to the type and needs of research, a policy represents a decision or stated will, e.g. to allow data collection, or storage of biomaterials. Modules and policies can be freely combined, allowing for flexible and individualized usage for a large variety of studies. However, each policy must only occur once a template. This requirement results from the necessity to be consistent throughout the informed consent at any point in time.[9]

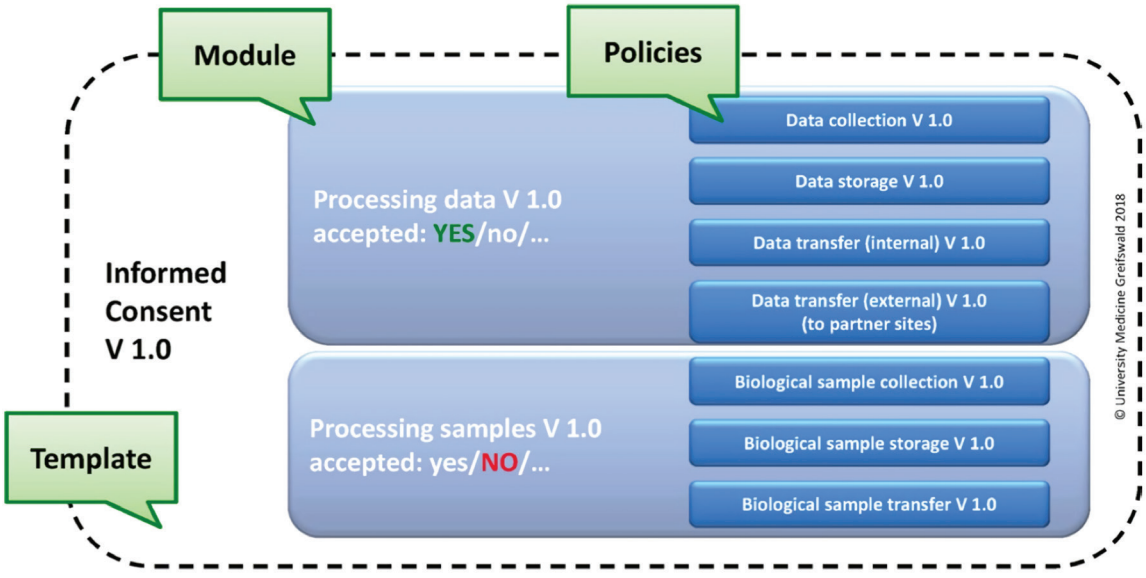

Figure 2. Structure of a modular Informed Consent within gICS[9]

Policies, modules, and templates are always version-specific. Therefore, subsequent changes of contents and wording in already consented policies, modules and templates lead automatically to a new version, respectively. Therefore, contents and wording of already consented parts remain untouched. This means that each change results in a new version of a study's consent. Contextual domains are used as organizational unit to manage policies, modules, and templates. Domains can be projects, study sites, or institutions and support the provision of context-related data, e. g. logos or versioning details.[9]

Discussions

For conditions such as the above requires more dynamic informed consent by not complicating the research process but also providing autonomy and facilitating understanding for research subjects to be able to update at any time when needed. Because it is impossible to update informed consent at any time that can take a lot of time and cost, even cause psychic fatigue in charging informed consent as well as lead to an increase in drop-out of research subject. Subjects are given the freedom to control their personal data while they are given up-to-date news about who used the sample, for what, what it would look like to be used when there is further research. This principle of transparency is only possible when using a digital format with centralized data that is always monitored and updated by the independent scientific community consistently.[5,9]

Modular systems seem to open more opportunities to simplify the process with periodic updates of data without changing the content and words in the previous informed consent. However, we need optimal security forces on the server's main database to prevent data leakage while maintaining the privacy of the research subject. This type of informed consent can be referred as dynamic informed consent, but this kind need eligible and standardized form for future sustain informed consent especially in clinical interventional and translational research.[5]

Conclusions

Informed consent in any form is the autonomy right of the subject. The digital format provides better prospects for facilitating communication to research subjects in the form of digital informed consent. But this ease must be accompanied by the consistency of the application of the standard informed consent process, even in intervention studies with biological samples this is more stringent. Informed consent given to the subject must use language that is easy to understand, and transparent. The subject of the study is given the choice of the right at any time to exit the research. In the future, the issue of morals and ethics of research will grow, and more dynamic informed consent is needed, especially for clinical interventional and translational research. [5,8,11]

Table 1. Selected Article Overview

Article Title	Study Design	Population	Result
Digital tools in the informed consent process: a systematic review	Systematic literature review using PRISMA guideline	The published document on electronic databases Pubmed, Embase and Cochrane contain term "informed consent"	Digital technologies for informed consent were not found to negatively affect any of the outcomes, and overall, multimedia tools seem desirable. Multimedia tools indicated a higher impact than videos only
Personalized and long-term electronic informed consent in clinical research: stakeholder views	qualitative study: Semi-structured interviews	5 stakeholder groups: pharmaceutical industry representatives, patient organization representatives, regulator representatives, EC members, and physicians	Stakeholders expect several advantages to a personalized eIC platform that enables long-term contact between researchers and research participants.
Assessment of the appropriateness of the i-CONSENT guidelines recommendations for improving understanding of the informed consent process in clinical studies	qualitative study: validity of document review of informed consent process by expert	i-CONSENT guidelines using an adaptation of the RAND/UCLA Appropriateness Method	The RAND/UCLA method has demonstrated validity for assessing the appropriateness of recommendations in ethical guidelines. The recommendations of the i-CONSENT guidelines were mostly judged "appropriate" by all stakeholders involved in the informed consent process.

Facing new challenges to informed consent processes in the context of translational research: the case in CARPEM consortium	A qualitative analysis	A set of informed consent forms that were used by CARPEM researchers between 2012 and 2017	"Old fashion written ICFs" should be adapted to the translational research approach, to better respect individual rights and international research ethics principles. a digital tool allowing dynamic information and consent of participants, through an electronic interactive platform may be a good way to promote more active participation in research.
The generic Informed Consent Service gICS®: implementation and benefits of a modular consent software tool to master the challenge of electronic consent management in research	Literature research and practical experiences gathered by the Institute for Community Medicine (ICM), University Medicine Greifswald.	gICS as modular digital informed consent tool	To address the requirements, the free-of-charge, open-source software "generic Informed Consent Service" (gICS®) was developed by ICM to provide a tool to facilitate and enhance usage of digital ICs for the international research community covering various scenarios. gICS simplifies and supports sustained IC management as a major key to successfully conduct studies and build trust in research with human subjects. Therefore, interested researchers are invited to use gICS and provide feedback for further improvements.
A survey on the current status and future perspective of informed consent management in the MIRACUM consortium of the German Medical Informatics Initiative	A qualitatives study: survey using three standardised questionnaires with 46 questions to elicit requirements from the ten sites to improve generic Informed Consent Service® (gICS)	All participants in all MIRACUM partner sites	The results of the survey were classified according to their impact on the gICS. Feature requests of new functionalities, improvements of already implemented functionalities and conceptual support for implementing processes were identified. This is the basis for an improved gICS release to support the ten sites' individual consent management processes.
The informed consent process in health research with under-served populations: a realist review protocol	A realist review protocol has been written according to the PRISMA-P guidelines_	The published document in electronic databases (EMBASE, MEDLINE, Web of Science and PsycINFO), along with selected websites and grey trusted literature	Final programme theory and a set of recommendations informed consent include under-served population
Digital approach to informed consent in bariatric surgery: a randomized controlled trial	Prospective non-blinded randomized controlled trial	Patient data were collected at one Bariatric Centre of Excellence (Ontario, Canada) between December 2018 and December 2019	The addition of a digital educational platform (DEP) online module to a standard verbal consent for laparoscopic Roux-en-Y gastric bypass (LRYGB) resulted in improved patient's understanding of the procedure-specific risks and benefits, high patient satisfaction, and over 50%-time savings for the bariatric surgeon conducting the consent discussion.

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