Digital tools in the Informed Consent process: a systematic review

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Abstract
Background: Providing understandable information to patients is necessary to achieve the two main aims of the Informed Consent process: respecting and promoting patients’ autonomy and protecting patients from harm. In recent decades, new, primarily digital, technologies have been used to apply and test innovative formats of Informed Consent. We conducted a systematic review to explore the impact of using digital tools for Informed Consent in both clinical care and clinical trials. Understanding, comprehension, satisfaction and participation were compared for digital tools versus the traditional Informed Consent process. Methods: We searched for studies on available electronic databases, including Pubmed, ISI web of science (WoS), and Cochrane. Studies were identified using specific Mesh-terms/keywords. We included studies, published from January 2012 to April 2018, that focused on the use of digital Informed Consent tools for surgery, diagnostic procedures, therapeutic interventions, and clinical research. Digital interventions were defined as interventions that used multimedia or audio-video to provide information to patients. We classified the interventions into 3 different categories: video only, non-interactive multimedia, and interactive multimedia. Results: Our search yielded 1046 publications. After title and abstract screening 182 studies were retained for full-text analysis, of which 38 publications were included. Studies examined interactive multimedia (17/38), non-interactive multimedia (11/38), and videos (10/38), and most (34/38) studies were conducted on adults. Innovations in consent were tested for clinical/surgical procedures (26/38) and RCTs (12/38). For RCTs, 21 outcomes were explored, with a positive effect on at least one of the studied outcomes being observed in 8/12 studies. For clinical/surgical procedures 49 outcomes were explored, and 21/26 studies reported a positive effect on at least one of the studied outcomes. Conclusions: Digital technologies for informed consent were not found to affect negatively any of the outcomes, and overall, interactive multimedia tools seem desirable. Interactive multimedia tools indicated a higher impact than passive videos. Presence of a researcher may potentially enhance efficacy of different outcomes. Studies were heterogeneous in design, making evaluation of impact challenging. Robust study design including standardisation is needed to conclusively assess impact. Background
In 1967, the World Medical Association Declaration of Helsinki (1) set the framework for the practical application of the notion of Informed Consent in clinical research for the years to come. The declaration built upon the foundations put in place by the Nuremberg Code, which stated that the primary consideration in research is the subject’s voluntary consent (2). After more than a half a century, these principles are still valid. Providing understandable information to patients is necessary to achieve the two main aims of Informed Consent: respecting and promoting patients’ autonomy and protecting patients from harm (3). Informed Consent is a cornerstone of clinical practice, used to describe diagnostic or therapeutic procedures clearly and concisely to patients prior to a procedure (4). In clinical research, informed consent is used to explain clinical studies before enrolling participants. Informed Consent for randomized clinical trials (RCT), also includes relatively complex methodological concepts, such as randomization and blinding.

Patients’ comprehension of Informed Consent is crucial, but comprehension varies both in developed and developing countries (5). Frequently, comprehension is too limited for an autonomous decision to be made. Only one third of study participants in pre-surgery studies published before 2006 showed a correct understanding of risks associated with surgery (6), and a meta-analysis conducted on 135 cohorts of participants in clinical trials showed that Informed Consent comprehension varied between 52% and 76% for different components (7). According to Tam et al., the proportion of participants understanding Informed Consent documents has not increased over the past 30 years (7). Comprehension of Informed Consent can be hampered by the format of the information provided to patients. Readability of Informed Consent is often insufficient (8) due to complex content and the length of the text. In several studies, short and/or enhanced Informed Consent documents have had a positive effect on patients through reduced anxiety and increased satisfaction, although the effect on understanding has been found to be variable (3).

Comprehension of informed consent does not seem to be directly associated with patient satisfaction or participation (3): patients may decide to participate in a study or express satisfaction towards a consent format without having a comprehensive understanding of its contents. To facilitate an informed decision, efficacious techniques are required to communicate abstract concepts such as
experimental study methods, and enable their comprehension. Information content and format may need to be tailored to the socio-cultural characteristics of patients. Factors including age, gender, and cultural background may affect the communication process and the comprehension of Informed Consent, and therefore bias the decisions taken by patients (9, 10, 11).

In recent decades, innovative technologies have improved clinical care and research, including Informed Consent: using primarily digital means, we can implement and test a variety of Informed Consent formats. Studies have aimed to improve the access and comprehension of the “traditional” written Informed Consent format, by providing information using a diverse range of instruments including videos, audio-video formats, and computer-based techniques (12)(13). Several different outcome measures have been taken into account, but results are often inconsistent, and the generalisability of studies is limited. At present, no evidence of the impact of specific innovative Informed Consent processes is available.

We conducted a systematic review to explore the challenges and assess the impact of digital tools for Informed Consent for clinical care and for clinical trials in the context of a H2020 funded project dedicated to improving the process of acquisition of Informed Consent in Europe (i-CONSENT, Grant Agreement nº 741856). Comprehension, knowledge, acceptance, anxiety, satisfaction and participation were compared for digital Informed Consent tools versus traditional Informed Consent.

Methods
Our study was conducted following the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) guidelines (14).

Search strategy
We conducted a systematic literature review following an a-priori defined, unpublished protocol. We searched for studies published between 1 January 2012 and 1 April 2018 on available electronic databases including Pubmed, ISI Web of Science (WoS) and Cochrane. The term “Informed Consent” was combined with mesh-terms/keywords for technologies considered relevant for innovative Informed Consent processes (computer, computerized, audiovisual aids, smartphone, mhealth, telemedicine, online systems, mobile application, multimedia).
**Eligibility criteria**

We included studies, published from January 2012 to April 2018, that focused on the use of digital tools for Informed Consent for surgery, diagnostic procedures, therapeutic interventions and clinical research. Digital interventions were defined as interventions that used multimedia or audio-visual means to provide information to patients.

We included randomized controlled trials (RCT) for which full-text was available in English, Italian or French, that compared the effect of digital Informed Consent vs. standard forms of Informed Consent (written on paper and/or face-to-face discussion). We excluded articles that reported the results of cohort studies, systematic reviews or meta-analyses.

**Study selection**

One researcher (PV) screened the titles and abstracts of the unique references to identify potentially relevant papers. After this primary screening, full texts were reviewed to assess eligibility criteria for inclusion in the review.

**Data Extraction and definitions**

Data were extracted by two researchers (FG and EP), using a standardized extraction form. The two datasets were then evaluated and in case of conflicting results a decision was taken by a third researcher (CR).

For each study, information was extracted about the population and setting; type of Informed Consent intervention (video, interactive multimedia, non-interactive multimedia); the standard Informed Consent process used in the comparison group; type of study/procedure for which the consent was requested (clinical study, diagnostic test, therapy/vaccine, surgery); outcome measured (knowledge, comprehension, satisfaction, acceptability, anxiety, study participation) and effect value for the comparison of the intervention and control groups.

Quality of included studies was assessed using criteria selected through discussion among the involved researchers: sufficient sample size (according to a priori or post-hoc sample size calculation - studies not reporting a sample size calculation were considered as not meeting the criteria); sufficient description (based on researchers’ judgement) of RCT or clinical procedure for which the consent was
requested, intervention (innovative tools in the consent process) and comparison; objective criteria to measure outcome; consideration of limitations (any limitation that affected both study arms equally, e.g. sample size); and consideration of bias (any element producing a differential effect on the two study arms).

Interventions were classified into 3 different categories: video only, non-interactive multimedia, and interactive multimedia. Video was defined as the passive provision of audio-visual content only. Multimedia interventions were defined as software that provided consent information in various format combinations (images, audio, videos, graphics, etc.). Multimedia interventions were either navigated directly by the patients or used by the researcher as a support during the explanation of the study/procedure. Interaction was defined as patient interaction with the software, eg. providing responses to questions. The standard format of Informed Consent process was defined as reading a paper text presenting the Informed Consent and/or a standardized face-to-face discussion.

Regarding outcomes, the reported participation in the clinical study was either an actual participation, when the patient actually signed the Informed Consent for participating in the RCT or clinical procedures, or a hypothetical participation where patients declared their potential participation in a future RCT or clinical care procedures. Knowledge and comprehension were considered as different outcomes, based on the definitions provided in the original articles. In general, comprehension referred to the perceived understanding of the information provided, while knowledge was an objective measure based on the response to specific questions. Information retention and information recall were categorised as knowledge. We classified an intervention as effective on a specific outcome if the article reported a statistically significant effect (irrespective of the effect magnitude) of the studied intervention with respect to the comparison.

Data synthesis

Some of the retrieved data were categorised (kind of study/procedure for which the consent was requested, type of innovative intervention, kind of outcome), and descriptive statistics were used to describe kind of interventions and main outcomes considered. A narrative synthesis of the main results is presented. The positive effect of digital tools on each outcome was presented as the
proportion of studies reporting statistically significant results (irrespective of the effect magnitude) on the total studies focusing on that specific outcome. As this study aimed to assess whether innovative interventions were superior to the standard Informed Consent process, a neutral effect of the intervention was considered as negative for statistical purposes.

Results

Results of the literature search

We identified 1046 publications through searching databases, and screening titles and abstracts of the records for study inclusion and exclusion criteria. We excluded 864 publications, and 182 articles were retained for full-text assessment. A total of 144 articles were excluded, and 38 publications were included in the review. Details of the study selection process are reported in Figure 1.

The majority of the study populations included in the systematic review were adult individuals; 5% (2/38) studies investigated consent provided for children, and 5% (2/38) studies investigated assent by adolescents. Of the selected studies, 58% (22/38) were set in North America, 21% (8/38) in Europe, 14% (4/38) in Oceania, 5% (2/38) in Asia and 5% (2/38) in Africa (Table 1).

Twelve studies (32%) investigated innovative Informed Consent processes for RCTs and 26 studies (68%) investigated innovative consent processes for clinical/surgical procedures. Overall, 17 studies used interactive multimedia (45%), 11 used non-interactive multimedia (29%), and 10 used videos (26%). Studied outcomes differed among included articles. Twenty-eight articles explored more than one outcome.

With regards to the quality of the included studies, 23 (61%) had a sufficient sample size; 36 (95%) reported a sufficient description of the RCT/clinical procedure for which the consent was requested, 38 (100%) reported a sufficient description of the intervention and 37 (97%) reported a sufficient description of the comparison; 38 (100%) used objective criteria to measure the outcome; 26 (68%) considered limitations and 9 (24%) considered bias.

RCTs

A total of 12 studies reported results on the efficacy of innovative Informed Consent processes for RCTs. Among those, 6 (50%) used interactive multimedia, 3 (25%) used non-interactive multimedia,
and 3 (25%) used videos. A total of 21 outcomes were explored across these 12 studies: all studies explored the effect of the digital intervention on comprehension, 3 articles explored the effect on knowledge, 3 on satisfaction. Only 3 studies investigated the effect of the innovative intervention on participation, which was always a hypothetical participation.

Among the 12 RCTs considered, 8 (67%) reported a positive effect on at least one of the studied outcomes. The efficacy of innovative interventions appeared high for interactive multimedia interventions: 5/6 studies reported a positive effect on at least one of the studied outcomes. For non-interactive multimedia interventions and videos, the proportion of studies reporting a positive effect was lower (2/3 studies and 1/3 studies respectively). Eight (67%) of the 12 studies investigating comprehension reported a positive effect. In 6 studies (50%), the researcher was present during the consent process. Of these, 5 studies (71%) showed positive effects on all studied outcomes, including participation. In the 6 studies that were conducted without the presence of the researcher, 3 (50%) reported a positive effect on at least one of the studied outcomes.

Clinical/surgical procedures

A total of 26 studies reported results on the efficacy of innovative Informed Consent processes for clinical/surgical procedures. The processes studied in the included articles were aimed at obtaining IC for surgery (58%), diagnostic tests (23%), and therapy/vaccine (19%).

Among these, 11 (42%) used interactive multimedia, 8 (31%) used non-interactive multimedia, and 7 (27%) used videos. A total of 49 outcomes were studied across these 26 studies: 13 articles explored the effect of the digital intervention on knowledge, 13 on satisfaction, 3 on acceptance, 11 on comprehension, 5 on anxiety, and 4 on participation.

Among the 26 articles considered, 21 (80%) reported a positive effect on at least one of the studied outcomes. The efficacy of innovative interventions was higher for interactive multimedia interventions (all 11 articles reported a positive effect on at least one of the studied outcomes) and non-interactive multimedia interventions (7/8 articles reported a positive effect on at least one of the studied outcomes); and lower for videos (only 3/7 studies reported a positive effect). The effect was generally positive for knowledge, comprehension and satisfaction (>60% of the studies reported a positive
effect for each of the 3 different outcomes).

The researcher was present during the innovative consent process in 18 (69%) of the 26 studies considered. Contrary to what happened in consent processes for RCTs, a researcher was present in all of the studies that reported no positive effect of the innovative intervention in any of the studied outcomes.

Discussion

Innovative, digital tools for Informed Consent published in the medical literature from January 2012-April 2018 fell into three main categories: videos (passively received by patients), non-interactive multimedia tools, and interactive multimedia tools. Included studies were limited in number and heterogeneous in terms of study population, intervention, outcome measures and results. The study hypothesis of this review was the superiority of digital technologies compared with traditional Informed Consent. While we were unable to ascertain superiority due to heterogeneity in study designs, we found that the digital technologies evaluated in this review did not affect any of the outcomes negatively, and a higher impact was observed for interactive multimedia tools than passive videos, for which impact appears limited.

We included fewer studies on innovative consent for RCTs than for clinical care (surgery, therapy, vaccines, diagnostic procedures). Several studies initially selected were excluded because of their non-experimental design. Few articles on consent in RCTs evaluated participation as an outcome and, in most cases, participation was only hypothetical. There is a need to promote studies for evaluating the impact of digital tools for the consent process, in particular for RCTs, using an experimental design.

Most included studies explored the added value of digital tools for obtaining consent in adult populations. Articles dedicated to consent for studies or procedures involving children, adolescents and other minority groups (e.g. pregnant women or elderly individuals) were less represented, highlighting the need of focusing future research on these population subgroups (15),(16).

Previous reviews reported inconsistent conclusions about the use of audio-visual aids for Informed Consent (17),(18). Our review suggests that videos have a limited effect, in particular when the
consent aims to support the decision-making processes for patients regarding their participation in clinical trials. One reason for this could be that the information provided in videos does not add much beyond the information already provided in person by clinicians and researchers. This could be a worthwhile area for future research. Conversely, combining different multimedia formats (slides, audio, video, graphics) and engaging the patient through interaction with the digital technology (mainly questions to verify understanding), seemed to improve both satisfaction and understanding (subjective and objective). The value of interaction of the patients with digital tools deserves further research, as preliminary results seem promising (19).

The results of this review suggest that the researcher’s presence should be considered when designing innovative Informed Consent processes. When considering RCTs, our review suggests that the presence of the researcher may enhance the efficacy of innovative consent processes. We therefore recommend that presence of a researcher is carefully considered in research study design.

The mechanism for this was not established in this study, but we hypothesise that this could be due to the direct interaction between participants and researchers (e.g. question and answer). This supports the findings of Flory et al. (1920), that person-to-person interaction has a high impact on understanding. Conversely, the majority of studies on clinical and surgical procedures found that physical presence of the researcher does not add any benefit; which would lend support to the concept of a self-administered innovative consent in clinical and surgical procedures, which could reduce clinicians’ opportunity costs through time saved.

Comprehension was the most described outcome, followed by knowledge, satisfaction, participation, anxiety and acceptance. Acceptance and anxiety were not considered in any of the studies that investigated multimedia interactive Informed Consent. Results on the impact of digital technologies on anxiety were inconclusive.

Although we classified digital tools into different categories, technologies within the same category may differ in quality and/or performance. Quality could be affected by a range of factors that were usually not reported, including how the information presented was selected, the design of the tool including graphics, and the length of time given to the consent process. Outcomes and setting were
also heterogeneous, making comparisons of effect between studies difficult. Different dimensions of communication should be considered when planning future studies on this topic. For example, it would be interesting to assess whether using different technologies impacts upon specific issues such as therapeutic misconception. An attempt to standardize at least some of the outcomes would be helpful for supporting decisions to use digital tools.

We only found two studies that evaluated the effect of digital tools for Informed Consent in developing country settings (21). Both compared multimedia Informed Consents (one interactive and one not) with traditional paper-based consent methods, and showed positive effect on knowledge and comprehension with respect to paper-based traditional ICs. In some developing country settings, patients have accepted to participate in trials despite having a limited understanding of a study, with their decision being influenced by concerns about potential consequences of refusing to participate (5). In such contexts, it is unclear whether an improved understanding through of the digital tools would alter participation.

This systematic review gave us some insights about the potential limitations of the adoption of digital technologies for Informed Consent. Technology evolves constantly, and the continuous change in available tools makes keeping track of tools challenging. A repository of available innovative tools with a constant update system would be desirable. In addition, the digital divide has been reported to act as a barrier to access for some segments of the population such as the elderly, people from low socio-cultural backgrounds, or disabled persons (23),(24),(25). Additional considerations may be necessary to ensure inclusion of these populations. However, the importance of this divide could potentially decrease, as suggested by the growing penetration of digital messaging across all population segments. None of the studies included in this review seem to have discriminated against participants based upon their digital skills. This suggests that digital tools, rather than representing a barrier, could be used to personalise Informed Consent to improve understanding and informed participation.

This study has a number of limitations. Study heterogeneity made inter-study comparison problematic: while we attempted to grade study quality, it was difficult to conclusively distinguish one
study as being of higher quality than another, which also made it challenging to gauge the relative quality of the tools reported. We were able to broadly observe trends, but were unable to perform a meta-analysis of the results. Developing standard methods for studying and comparing innovative Informed Consents (in particular for clinical trials) would facilitate better evaluations of innovative consent tools in the future.

Conclusions
The objective of Informed Consent is to meet patients’ needs for clear and complete information. In recent years, the use of digital tools for improving patient comprehension, knowledge and satisfaction of Informed Consent seems to have had an impact. Digital tools, particularly interactive multimedia tools, may be useful in enabling the development of personalised Informed Consent that is tailored to an individual’s socio-cultural characteristics. Currently, studies are heterogenous. Developing standardised methods for the assessment of impact of innovative Informed Consents would facilitate better evaluation of innovative consent tools in the future.

List Of Abbreviations
RCT Randomised Controlled Trial
WoS ISI web of science
PRISMA Preferred Reporting Items for Systematic reviews and Meta-Analyses

Declarations

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Consent for publication: Not applicable
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Tables
Table 1. Description of the studies included in the systematic review (full reference information is provided below the table)

| Author, year | Consent for | Population | Intervention |
|--------------|-------------|------------|--------------|
| Bergenmar 2014¹ | RCT | adult | multimedia non interactive |
| Beulen 2016² | Diagnostic | adult | multimedia interactive |
| Blake 2015³ | RCT | adolescent | multimedia interactive |
| Gordon 2016⁴ | Surgery | adult | multimedia interactive |
| Hall 2017⁵ | RCT | adult | video |
| Krishnamurti 2016⁶ | RCT | adult | video |
| McCaughey 2016⁷ | Therapy/vaccine | adult | multimedia interactive |
| Mednick 2016⁸ | Surgery | adult | video |
| Pot 2017⁹ | Therapy/vaccine | adult | multimedia non interactive |
| Warriner 2016¹⁰ | RCT | adult | multimedia interactive |
| Winter 2016¹¹ | Surgery | adult | video |
| Yin 2015¹² | Surgery | adult | multimedia non interactive |
| Roberts 2016¹³ | Surgery | adult | multimedia interactive |
| Rowbotham 2013¹⁴ | RCT | adult | multimedia interactive |
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Table 2. Number of studies in which digital interventions had a positive effect by outcome (articles explored more than one outcome).
| Type of study:       | Outcome   |   |   |   |   |   |   |   |
|---------------------|-----------|---|---|---|---|---|---|---|
|                     |           | Comprehension | Knowledge | Acceptance | Anxiety | Satisfaction |
| Video               | RCT       |     |     |     |     |     |     |     |
|                     | C/S*      | 1/3 | 2/4 | 0/1 | 1/3 | 0/0 | 0/2 | 0/0 |
| Multimedia non      |           | RCT | C/S* | RCT | C/S* | RCTs | C/S* | RCT |
| interactive         |           |     |     |     |     |     |     |     |
|                     |           | 2/3 | 1/3 | 0/1 | 3/4 | 0/0 | 1/1 | 0/0 |
| Multimedia          |           |     |     |     |     |     |     |     |
| interactive         |           | 5/6 | 4/4 | 1/1 | 5/6 | 0/0 | 0/0 | 0/1 |
| Total studies by    |           |     |     |     |     |     |     |     |
| outcome and study   |           | 12  | 11  | 3   | 13  | 0   | 3   | 0   |
| type                |           | 23  | 16  | 3   | 5   | 5   | 16  |
| Total studies by    |           |     |     |     |     |     |     |     |
| outcome             |           | 23  | 16  | 3   | 5   | 5   | 16  |

*C/S = clinical or surgical

Figures
Figure 1

Flow diagram of the search process