# Replacing Paper Informed Consent with Electronic Informed Consent for Research in Academic Medical Centers: A Scoping Review

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**Abstract**

*Although experts have identified benefits to replacing paper with electronic consent (eConsent) for research, a comprehensive understanding of strategies to overcome barriers to adoption is unknown. To address this gap, we performed a scoping review of the literature describing eConsent in academic medical centers. Of 69 studies that met inclusion criteria, 81% (n=56) addressed ethical, legal, and social issues; 67% (n=46) described user interface/user experience considerations; 39% (n=27) compared electronic versus paper approaches; 33% (n=23) discussed approaches to enterprise scalability; and 25% (n=17) described changes to consent elections. Findings indicate a lack of a leading commercial eConsent vendor, as articles described a myriad of homegrown systems and extensions of vendor EHR patient portals. Opportunities appear to exist for researchers and commercial software vendors to develop eConsent approaches that address the five critical areas identified in this review.*

**Introduction**

Academic medical centers, pharmaceutical sponsors, and other stakeholders have identified benefits of electronic consent (eConsent) for research (1,2). Following a successful pilot of replacing paper informed consent with eConsent at our institution (3), we sought to understand how other institutions implemented eConsent for research at the enterprise level. Although multiple review articles have addressed participant understanding of informed consent procedures, to our knowledge the literature lacks a comprehensive understanding of approaches for replacing paper informed consent with eConsent in an academic medical center. To address this gap, we performed a scoping review guided by five areas identified as critical to success of our pilot including ethical, legal, and social issues; user interface/user experience; comparison to paper; enterprise scalability; and changes to consent.

**Methods**

We conducted a scoping review following the Joanna Briggs Institute recommendations (4) and defined it using the population, intervention, comparison, and outcome (PICO) format. Specifically, we defined the population as centers performing clinical research with affiliations with major medical schools. The intervention of interest was the electronic informed consent process. With respect to comparison, we examined eConsent that may or may not have been contrasted with paper-based processes. For outcome, we examined the efficacy of eConsent.

Search strategy

A medical librarian (DD) and research specialist (KP) jointly developed and executed a search strategy for articles that described obtaining electronic informed consent. On December 11-15, 2017, searches were run in Ovid MEDLINE® (In-Process & Other Non-Indexed Citations and Ovid MEDLINE® 1946 to Present), Ovid Embase (1974 to present), the Cochrane Library (Wiley), Scopus (Elsevier), and ABI/Inform (ProQuest). Search terms for all databases included controlled vocabulary and/or keywords as appropriate. Complete database search strategies are available at https://www.github.com/wcmc-research-informatics. In February, 2019, we retrieved additional records in two ways: 1) by reviewing the bibliographies of articles that met inclusion criteria, and 2) identifying papers that had cited included articles since their publication.

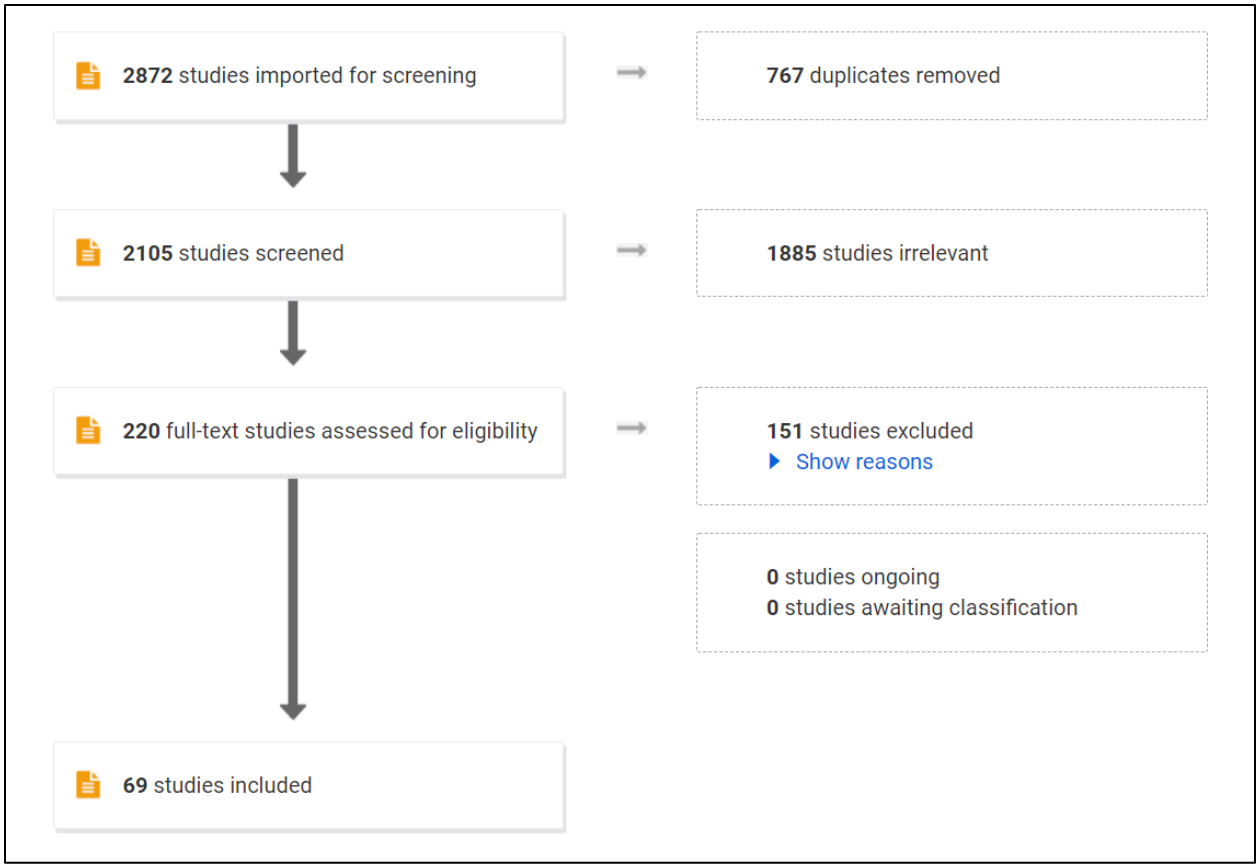


**Figure 1.** PRISMA workflow diagram of the review process

Screening and eligibility

We included articles that described electronic informed consent processes at clinical research centers or articles that compared the effectiveness, efficiency, and cost of paper-based versus electronic informed consent process. We excluded articles that only described using electronic content for recruitment or for conveying information without using electronic means to obtain consent. The literature search yielded 2872 articles and 767 duplicates were excluded. Two reviewers (CC, PL) screened 2105 articles for inclusion based on the title and abstract and then reviewed 220 full text articles. The final analysis included 69 studies (Figure 1).

Data extraction and summary

Three reviewers (CC, PL, TRC) categorized each paper according to its geographic area, article type as defined by the Journal of the American Medical Informatics Association (i.e., original research, perspective, review), disease area, study population (i.e., adult, pediatric), and purpose (i.e., clinical trial, biobank). Additionally, drawing from institutional experience, we determined whether each paper described ethical, legal, and social issues; user interface/user experience considerations; comparison of electronic and paper methods; enterprise information technology scalability; and the ability for participants to change consent elections. The reviewers compared ratings and resolved disagreements through discussion. For details on selected studies and search strategy, please visit the online supplement described above.

**Results**

As described in Table 1, 75% (n=52) of articles described activities in North America with the preponderance (n=50) in the United States. The majority of articles presented original research describing novel approaches and evaluations of methods. More than half of articles (n=38) did not focus on a particular disease area with the remainder detailing initiatives across different medical specialties, the bulk of which addressed collection of biospecimens and data to enable precision medicine. Nearly all articles (94%) described efforts in adult populations with pediatric-focused

articles originating from one institution. About half (52%) of articles described consent for specific clinical trials while nearly a third described efforts for biobanking.

**Table 1.** Characteristics of papers meeting inclusion criteria.

| **Domain of Interest** | **N=69** |
|---|---|
| Geographic area | |
| North America, n (%) | 52 (75) |
| Europe | 13 (19) |
| Asia | 2 (3) |
| Oceania | 2 (3) |
| Article type | |
| Original research | 50 (72) |
| Perspective | 14 (20) |
| Review | 5 (7) |
| Disease area | |
| None | 38 (55) |
| Precision medicine | 9 (13) |
| Other | 9 (13) |
| Asthma | 3 (4) |
| Genetic disorders | 3 (4) |
| Neurology | 3 (4) |
| Mental health | 2 (3) |
| Diabetes | 2 (3) |
| Population | |
| Adult | 65 (94) |
| Pediatric | 3 (4) |
| Both | 1 (1) |
| Purpose | |
| Clinical trial | 36 (52) |
| Biobank | 22 (32) |
| Both | 11 (16) |
| Description | |
| Ethical, legal, and social issues | 56 (81) |
| User interface/user experience | 46 (67) |
| Comparison to paper | 27 (39) |
| Enterprise scalability | 23 (33) |
| Changes to consent | 17 (25) |

More than 80% of articles described ethical, legal, and social issues while about two thirds described user interface/user experience design considerations. 33% of articles described enterprise information technology scalability, and 25% described methods to enable participants to change their consent elections.

Ethical, legal, and social issues

*Digital divide*

Younger users were found to be more satisfied with using technology for informed consent (5). Conversely, older participants may be more skeptical of mobile technology and thus more concerned about their privacy and confidentiality while using their phones (6–8). In a focus group study, minorities and rural area residents expressed

concern over access to computers and the internet, computer literacy, privacy and confidentiality, relating to the use of eConsent for research (9).

*Biobank-specific issues*

Biobanks, which aim to recruit a large number of participants to contribute samples, have created unique challenges in informed consent: the sheer number of participants from whom researchers must obtain consents; and the need to link the samples with participants' electronic medical record (EMR), and other information such as family history, lifestyle and environmental risk factors; and the requirement that participants must broadly consent to any type of research (10). In many cases, studies are retrospective and therefore information about them are difficult to communicate to participants in advance, when they initially signed the consents (11). In addition, biobanks typically operate under different protocols approved by various IRBs; separate consents may be needed and a way of tracking them is essential (12).

Many researchers have suggested using technology to allow participants to monitor and keep track of use of their biological samples over time (13). In addition, methods for protecting the privacy of participants (e.g., de-identification) are not well-suited for genetic research because genetic information identifies the participants and their families as predisposed to certain hereditary diseases (14). Further, it was found that participants who use eConsent to enroll in biobanks are generally less diverse than the population that enrolls using traditional consent (10,15). Computer literacy was found to be a factor affecting user uptake in electronic biobank consent (16).

*Electronic signature validity*

In the US, electronic signatures for consent must comply with 21 CFR 11(c), a federal regulation which states that an electronic signature must be unique to one individual, and organizations must verify the identity of the individual. European countries impose similar requirements on researchers (7,17). A study revealed that some institutional review boards (IRBs) were uncertain whether electronic signatures were valid, which laws would apply, and how the electronic signatures would be stored (18).

*Ensuring trust*

Participants are concerned about privacy breaches, data misuse, and anonymity relating to eConsent (19). To secure the participants' information, researchers have used encryption for data in transit, not storing information on a server (20). However, researchers are not consistently applying encryption to both data in transit and at rest (21). Some researchers expressed concerns about storing biometric information on cloud storage and suggested storing the information on the users' local devices instead (22). Others pseudonymize the data (21).

Due to the European Union's newly implemented General Data Protection Regulation (GDPR), digital consent management systems will have to be upgraded across the globe (13). GDPR states that research participants have the right to determine how and with whom their medical information is shared. Implicit consent or research requiring opting-out is not acceptable informed consent (23).

<u>User interface/user experience (UI/UX)</u>

*User interface*

As comprehension is an important part of informed consent, using a multimedia electronic format could increase the comprehension effort and several studies measured that via the NASA Task Load Index (NASA-TLX) which assesses the perceived effort to complete a task (24,25). In addition to the participant's experience and time to complete the informed consent form, studies described the staff's task load (26,27). Some studies discussed the benefit of social annotation, where participants can see each other's comments about the eConsent, as a trusted way to question the research while lessening social pressure (28–30).

*User experience*

Two studies used an existing commercial telemedicine platform, Doxy.me, and found the ability for participants to complete the consent form in real-time with remote researchers to be interactive and similar to the in-person experience (5,20). One pilot of an online dynamic consent portal had overall positive user experience results and noted that the identity verification's multi-layer process had a negative impact on user experience but an advantage to data security (31). Researchers should remember that multimedia does not automatically meant interactive (32).

<u>Comparison to paper</u>

*Comprehension*

Some studies found that participants (including minors) using eConsent had a better understanding of the information presented to them, when such consent had interactive components, quizzes, tailored information, graphical media, and annotations (8,27,33–39). In one study focusing on underrepresented participants in research in the US, certain minorities and rural area residents expressed in their focus groups that eConsent was easier to use, more interesting, and better for understanding (9). In one case, the level of understanding is the same among participants without any mental illness, but a web-aided multimedia consent may facilitate understanding and provide better satisfaction in participants with schizophrenia (39).

Research has not consistently shown that eConsent is superior to paper consent in facilitating participants' understanding of information (40). Three studies found no significant difference in the level of understanding achieved by the participants using paper, a PDF, or a website/tablet version of consent in the United Kingdom, the US and Canada (41–43). While video-embedded eConsent can facilitate participant understanding, the format of the consent (digital versus paper) alone did not appear to affect understanding in one study (44).

Regardless of the form of consent, many studies have advocated that in-person interactions or other forms of communications with researchers remain a part of the eConsent process, to ensure participants' understanding of consent information and to foster trust, particularly for more complex and riskier studies. (11,13,32,33,37,41,45–47).

*Customization of amount of information*

eConsent may provide a solution that could tailor the amount of information presented based on users' choice (8). One study showed that when participants were given the choice to receive more, the same, or less information in the eConsent form than presented on a paper consent form, a majority of them choose less information, suggesting that the amount of information in the paper consent was more detailed than what participants are willing to read (41). Another study similarly found that participants read informed consent documents quickly, particularly on paper, and preferred to have shorter and simpler consent forms (34,43,48). However, there is also evidence indicating that users do not thoroughly review click-through agreements online (40), or eConsent for a genetic study (49). Many participants think less than half of the consent form is vital, and perceive the consent form as providing legal protection for researchers, rather than informing participants (30,39). With respect to user satisfaction, participants found the use of eConsent to be less stressful compared to paper because they could proceed at their own pace and have more control over the consent process (24,50).

Enterprise scalability

*Systems integration*

To scale eConsent for research across the enterprise, multiple studies cited the need for information technology infrastructure (10), including wifi connectivity (16,42,51), informatics personnel for development (15,16), and helpdesk personnel for support (16,52). Four studies emphasized benefits of integrating research consent data with electronic health record (EHR) systems and electronic data warehouses (16,23,27,37,52,53), including through the use of emerging HL7 FHIR standards (23). Three articles described use of EHR participant portals to collect consent for research from participants (37,52,54). Three studies emphasized the need for academic medical centers to consider ontological models of consent (12,27,51).

*Authentication*

Studies also emphasized a need for proper authentication through usernames and passwords, finger-drawn signatures (10,22,55), biometrics (22), and blockchain (56). Of note, Li described a novel system called USign, a signature verification method that can integrate with existing eConsent systems and provide a new authentication token (55). Two studies (51,56) described approaches to tracking versions of protocols and informed consent forms to which participants consented.

*Enterprise examples*

Institutions with multiple publications describing enterprise deployment included Partners Healthcare (10,52), Medical University of South Carolina (MUSC) (20,26,53), University of California San Diego (27,57), and University of Greifswald in Germany (23,51). At MUSC, Sanderson noted the success of piloting eConsent in "high-volume but low-pressure" clinical areas and the "overwhelmingly positive" reception from MUSC staff that led to roll-out to additional practices (53). Welch described extension of Sanderson's approach from physical patient visits to telemedicine encounters (20). Although nearly all articles described novel system implementations, one study

described commercial eConsent offerings from six software vendors (58). Two studies described use of Apple ResearchKit in smartphone app-based eConsent for lower-risk studies (59,60).

Changes to consent

Changes to consent range from protocol updates and amendments to withdrawal. One study proposed a dynamic consent model that allows for personalization and flexibility, such as allowing a biobank participant to amend their broad consent based on new research activities (15). Dynamic eConsent can be further defined as utilizing the technology to allow for on-going engagement with the participants to maintain their consent preferences (19). Multiple papers (19,27,30,57) described identifying the organization type of the data recipient as participants may only wish to consent to providing limited data to for-profit organizations. There are numerous technical approaches to electronically tracking this data, ranging from blockchain (56) to HL7 FHIR (23). Two studies described trusted third-party organizations that would securely maintain the data and govern who could access the data (56,61).

**Discussion**

Based on the results of the selected articles, there was no unified approach or guideline for replacing paper consent with eConsent. Academic medical centers described diverse implementations and addressed the five areas of interest – ethical, legal, and social issues; user interface/user experience; comparison to paper; enterprise scalability; and changes to consent – variably. However, the differences do not appear to be dictated by the disease areas or the purposes for which eConsent is obtained (i.e., whether it was for a clinical trial or a biobank). In addition, research studies did not consistently find that eConsent is superior in facilitating participants' comprehension of information (62). While the traditional paper-based consent is widely accepted for authentication, there is not yet universal acceptance of electronic signature.

The selected articles were predominantly about US adults, but some studies focused on the pediatric population. For research involving children, researchers needed to modify the process to obtain consent from parents or guardians (21), which can be a challenge for scheduling in-person paper consent. eConsent that can be provided remotely from home may be a solution in pediatric clinical trials (63).

Although biobanking studies represented 32% of studies and clinical trials were 52%, our analysis addressed biobank studies at length because of unique challenges, such as participants' genomic data being considered a commodity (11). Compared with clinical trials, biobanks tend to have a larger number of participants and therefore, the consent process must be scalable to accurately track changes in consent in order to gain participants' trust (9,19,61,62).

The usage of eConsent should not replace human interaction – rather it can provide another medium for interaction. Participants should nonetheless have the ability to ask researchers questions and could also have the ability to ask each other through social annotations. However, lack of access to and familiarity with the technology itself can create additional obstacles to consent. As the access to technology increases, the pool of participants could increase too as they are no longer limited by physical proximity to an academic medical center. However, until that increase, there is a potential for participation skewing to younger, more affluent participants who currently have access. This digital divide not only impacts UI/UX, but also impacts the enterprise scalability as under-represented communities tend to have limited access to eConsent's technical requirements such as stable, high-speed wifi.

This review may not have identified all relevant articles, despite attempts to be as comprehensive as possible, such as an additional search in February 2019 to increase timeliness. The reviewers (CC, PL, TRC) are not physicians, but have a diversity of professional backgrounds. It was the reviewers' first time using the systematic review software, Covidence, in conjunction with the reference manager, F1000Workspace, but the usage enabled accounting for the articles during the review process.

Due to the HITECH Act and the transition to EHRs, a monoculture emerged as many healthcare organizations shifted to a single vendor of clinical information systems (64). As paper consent transitions to eConsent, our review showed a lack of a leading commercial eConsent solution, as articles described a myriad of homegrown systems (1–3) and extensions of vendor EHR patient portals (1,2). Using a multitude of systems can result in inefficiencies and the need for researchers to develop additional workflows and interfaces to address gaps as seen in the PCORI ADAPTABLE and NIH *All of Us* Research Program studies (65,66). Opportunities appear to exist for researchers and commercial software vendors to develop eConsent approaches that address the five critical areas discussed in this review.

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