CHANGER

CHALLENGES AND INNOVATIVE CHANGES IN RESEARCH ETHICS REVIEWS

E-consent

Ethical landscape: challenges and innovations

Pascal Borry (KUL)

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What is the meaning of an informed consent?

- “protect the **dignity and identity of all human beings** and guarantee everyone, without discrimination, respect for their integrity and other rights and fundamental freedoms” (art. 1 Oviedo Convention)
- “**interests and welfare** of the human being” (art. 2 Oviedo Convention)
- “An intervention in the health field may only be carried out after the person concerned has given **free and informed consent** to it. This person shall **beforehand** be given **appropriate information** as to the *purpose and nature of the intervention* as well as on its *consequences and risks*. The person concerned may freely *withdraw consent* at any time” (art. 5 Oviedo Convention)

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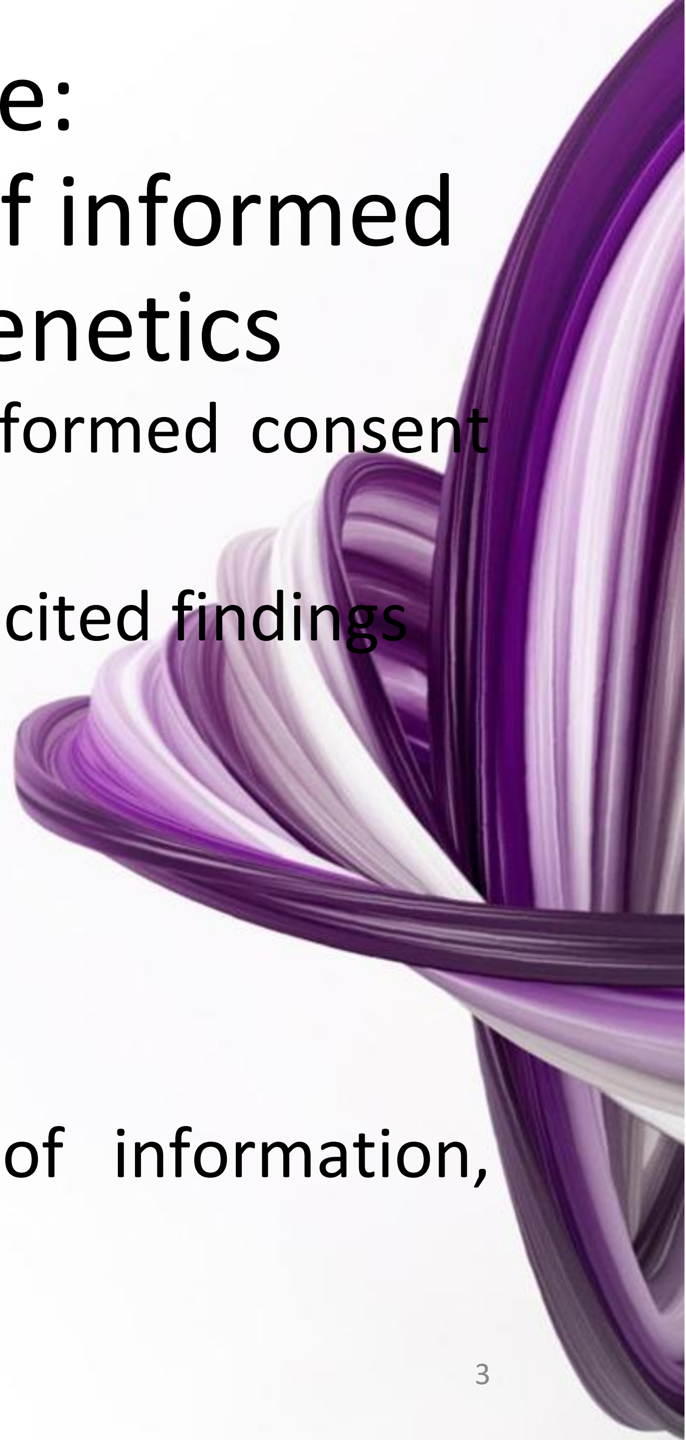
Case example: Challenges of informed consent in genetics



As genetic tests have grown in complexity, a truly informed consent has become more difficult to achieve

- Possibility of identifying secondary findings or unsolicited findings
- Possibility of recontacting
- Impact for family members
- Data sharing and access to raw data
- Variants of unknown significance
- Challenges at the level of comprehensiveness of information, understanding, facilitating choices

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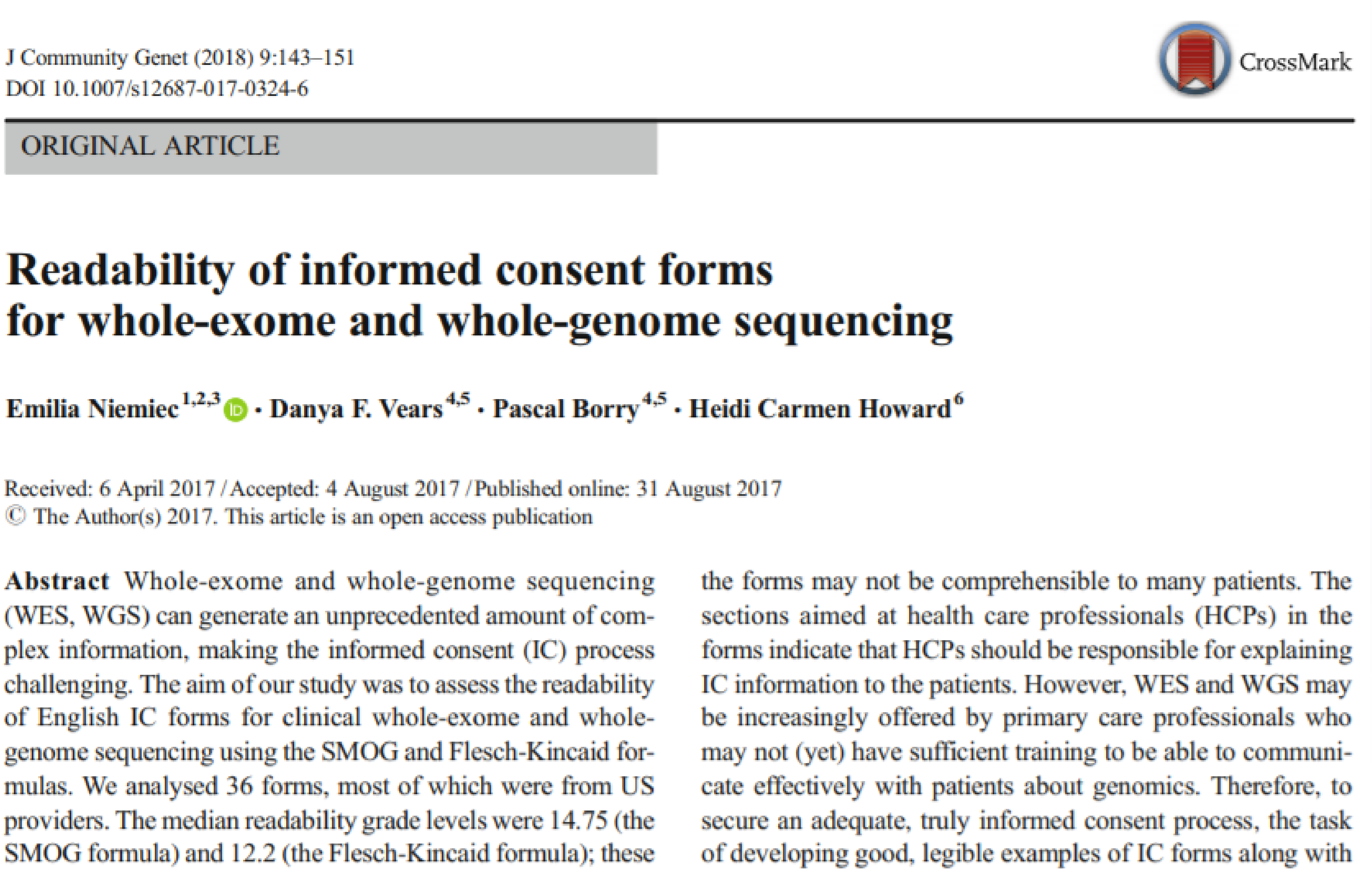

J Community Genet (2018) 9:143–151
DOI 10.1007/s12687-017-0324-6

CrossMark

ORIGINAL ARTICLE

Readability of informed consent forms for whole-exome and whole-genome sequencing

Emilia Niemiec[1,2,3] · **Danya F. Vears**[4,5] · **Pascal Borry**[4,5] · **Heidi Carmen Howard**[6]

Received: 6 April 2017 / Accepted: 4 August 2017 / Published online: 31 August 2017

Abstract Whole-exome and whole-genome sequencing (WES, WGS) can generate an unprecedented amount of complex information, making the informed consent (IC) process challenging. The aim of our study was to assess the readability of English IC forms for clinical whole-exome and whole-genome sequencing using the SMOG and Flesch-Kincaid formulas. We analysed 36 forms, most of which were from US providers. The median readability grade levels were 14.75 (the SMOG formula) and 12.2 (the Flesch-Kincaid formula); these the forms may not be comprehensible to many patients. The sections aimed at health care professionals (HCPs) in the forms indicate that HCPs should be responsible for explaining IC information to the patients. However, WES and WGS may be increasingly offered by primary care professionals who may not (yet) have sufficient training to be able to communicate effectively with patients about genomics. Therefore, to secure an adequate, truly informed consent process, the task of developing good, legible examples of IC forms along with

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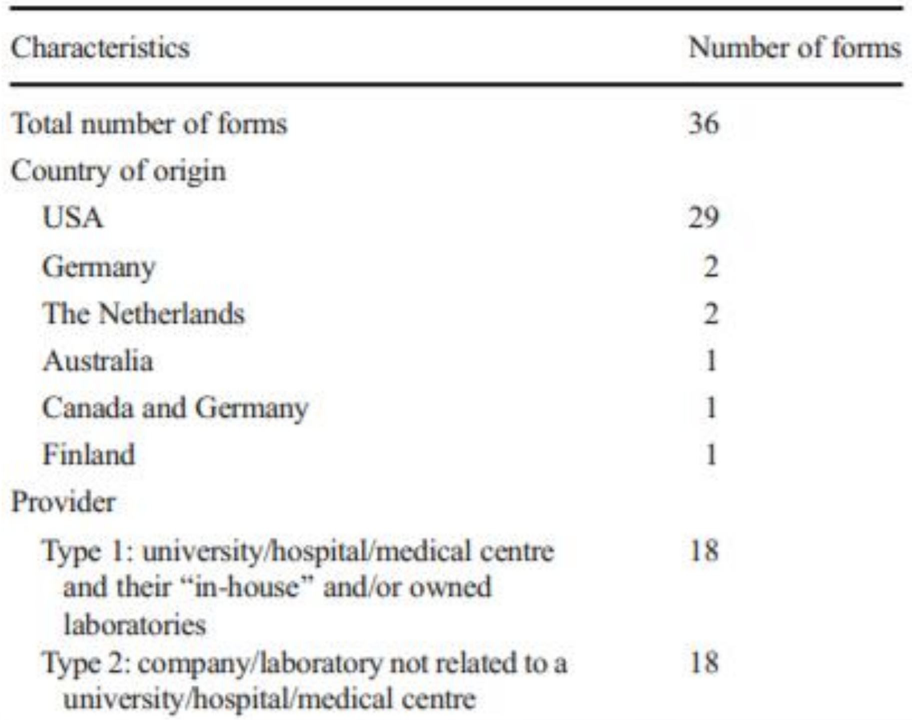
Readability

Are they understandable for the target audience?
Professional organizations recommend reading grade level of 8 (e.g. US medical schools Institutional Review Boards)



Characteristics	Number of forms
Total number of forms	36
Country of origin	
USA	29
Germany	2
The Netherlands	2
Australia	1
Canada and Germany	1
Finland	1
Provider	
Type 1: university/hospital/medical centre and their "in-house" and/or owned laboratories	18
Type 2: company/laboratory not related to a university/hospital/medical centre	18

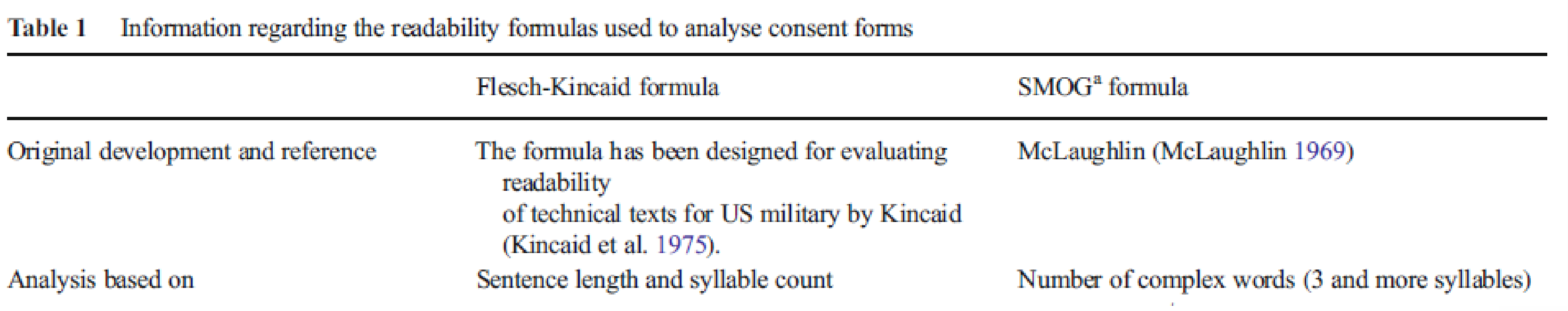


Table 1 Information regarding the readability formulas used to analyse consent forms

	Flesch-Kincaid formula	SMOG[a] formula
Original development and reference	The formula has been designed for evaluating readability of technical texts for US military by Kincaid (Kincaid et al. 1975).	McLaughlin (McLaughlin 1969)
Analysis based on	Sentence length and syllable count	Number of complex words (3 and more syllables)

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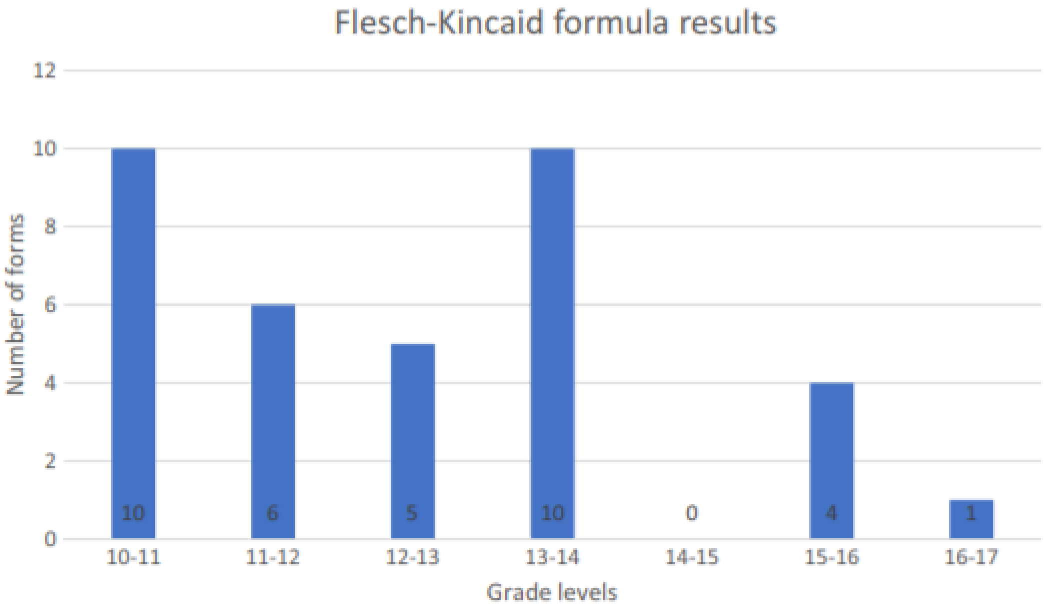
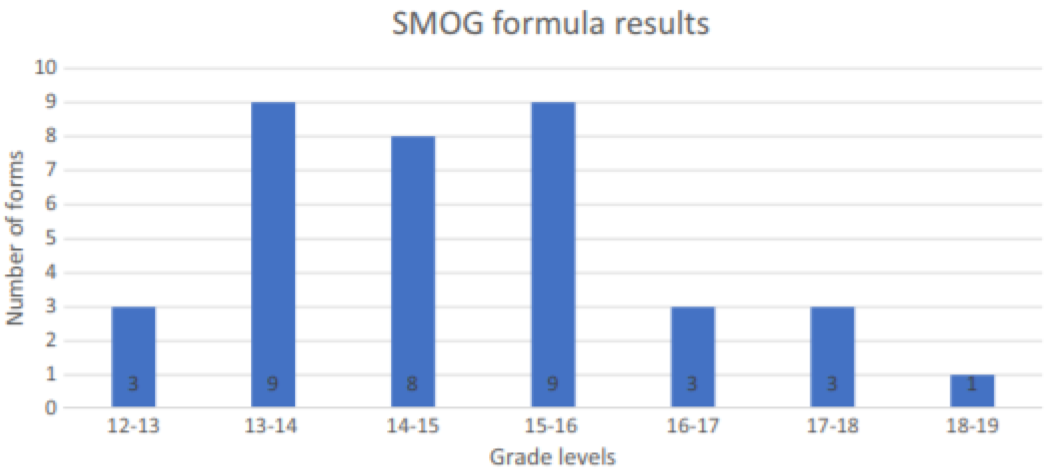
Readability





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Readability

- The results indicating **low readability** of IC forms are not surprising, particularly when comparing them to studies of IC forms in the context of other medical procedures (Sugarman et al. 1999).
- **None** of the forms in this study, or other previous studies investigating IC for WGS, **reaches the average recommended readability level** of 8th grade (Henderson et al. 2014; Jamal et al. 2013).
- This indicates that IC forms may **fail to fulfil their intended function** of providing understandable information to patients and facilitating communication.
- The high scores obtained in the SMOG and Flesch-Kincaid formulas indicate that the documents studied use many **complex, long words**, which may often be **technical** and therefore difficult to understand to an average reader.

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Understanding

- “We found that the **level of comprehension** regarding informed consent components, such as voluntary participation, blinding, and freedom to withdraw, **was low, being understood by only half of the patients.** This seriously undermines the ethical foundations of current practices for obtaining consent in clinical trials, potentially also challenging the standard approach to safeguarding patients’ autonomy in ordinary medical settings.”

Pietrzykowski and Smilowska *Trials* (2021) 22:57
https://doi.org/10.1186/s13063-020-04969-w

Tri

REVIEW Open Acc

The reality of informed consent: empirical studies on patient comprehension—systematic review

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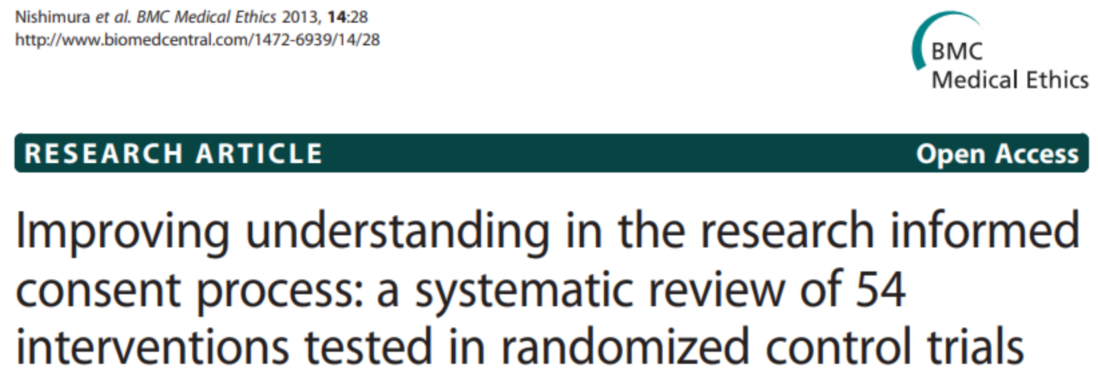
Improve understanding

- Systematic review of 54 interventions and meta-analysis of 22 interventions that sought to improve the rates of participant understanding in the informed consent process.
- The findings of our study suggest that **enhanced consent forms** and **extended discussions** are most effective in improving participant understanding.
- **Multimedia interventions** are effective, though not significantly so, and appear to be more useful for **improving long-term knowledge retention rates**.



Nishimura *et al. BMC Medical Ethics* 2013, **14**:28
http://www.biomedcentral.com/1472-6939/14/28

BMC Medical Ethics

RESEARCH ARTICLE **Open Access**

Improving understanding in the research informed consent process: a systematic review of 54 interventions tested in randomized control trials

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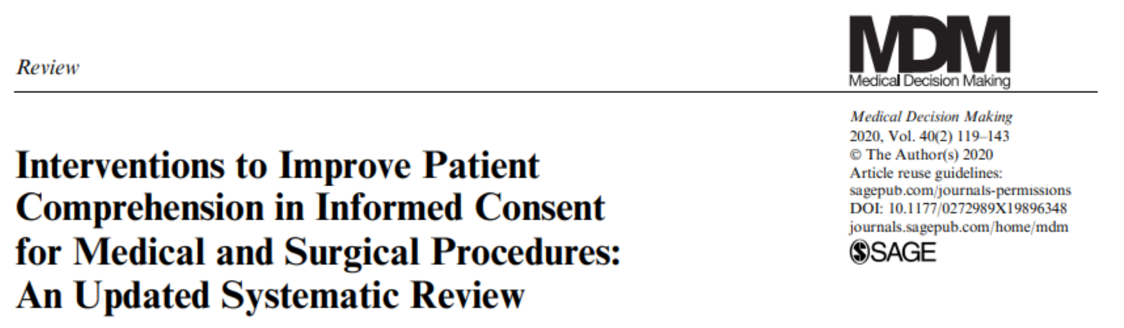
Improve understanding

- Our findings suggest, however, that **interactive informed consent interventions** (i.e., those that intentionally *promote active patient involvement and bidirectional communication*), may be superior to noninteractive interventions.
- Noninteractive interventions, such as those in which patients independently read additional information or reviewed visual aids, were less likely to improve patient comprehension.



Review

MDM
Medical Decision Making

Medical Decision Making
2020, Vol. 40(2) 119–143
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Interventions to Improve Patient Comprehension in Informed Consent for Medical and Surgical Procedures: An Updated Systematic Review

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Improve understanding

- defining adequate patient comprehension encompassing the **key elements** of informed consent
- developing validated measures **to assess** the attainment of adequate patient **comprehension**
- consistently using **easy-to-understand, linguistically and culturally appropriate materials** to specifically ensure adequate comprehension for patients facing language barriers and for patients with limited education and health literacy
- including **interactive components** within the informed consent process, particularly test/feedback and teachback techniques

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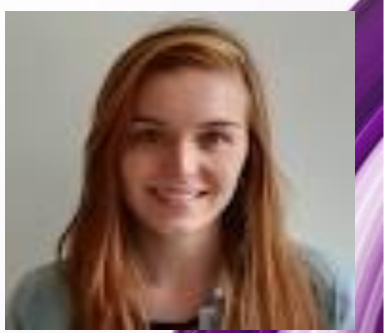
Glaser, Johanna, et al. "Interventions to improve patient comprehension in informed consent for medical and surgical procedures: an updated systematic review." Medical Decision Making 40.2 (2020): 119-143.

PhD project Evelien De Sutter

Towards participant-centric electronic informed consent in clinical research



> *“An electronic informed consent refers to the use of any digital media (e.g. text, graphics, audio, video, podcasts or websites) firstly to **convey information** related to the clinical trial to the trial participant and secondly to **document informed consent via an electronic device** (e.g. mobile phones, tablets or computers).”*

European Medicines Agency: Good Clinical Practice Inspectors Working Group. 2023.

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Semi-structured interviews

ORIGINAL RESEARCH article

Front. Pediatr., 01 September 2021

Sec. Neonatology

Volume 9 - 2021 | https://doi.org/10.3389/fped.2021.724431

Clinical Research in Neonates: Redesigning the Informed Consent Process in the Digital Era

Evelien De Sutter[1*] Birte Coopmans[1] Femke Vanendert[1] Marc Dooms[1] Karel Allegaert[1,2,3] Pascal Borry[4] Isabelle Huys[1]

Five stakeholder groups (n=39)
Active in EU Member States / pan-European level

Healthcare professionals (n=31)
Active in Belgium / the Netherlands
Neonatal setting

RESEARCH Open Access

Informing a European guidance framework on electronic informed consent in clinical research: a qualitative study

Evelien De Sutter[1*], Pascal Borry[2], Isabelle Huys[1†] and Liese Barbier[1†]

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Personalised approach

Functionalities

Consult **multiple layers** of information

Highlight information

✓ *Advantages*

May increase participant **empowerment**

May solve the **issue of flooding** the participants with information

Long-term interaction

Repeated informed consent **discussions**

Reconsenting

Return of **results**

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Potential bottlenecks

Concerns about participants who lack digital literacy

Concerns about personal interaction investigator – research participants

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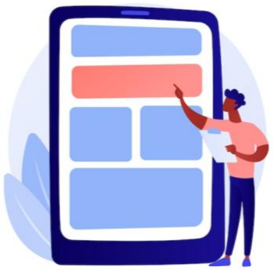
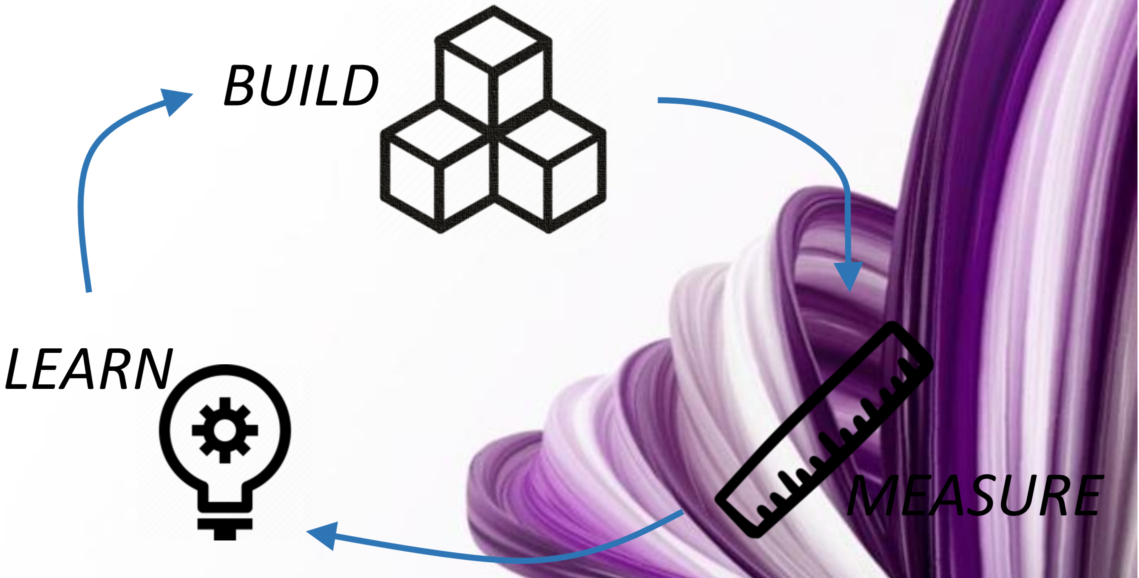


To test and evaluate electronic informed consent modules



Usability testing

Patients / healthy volunteers (n=30)
Belgian setting
Three rounds

Semi-structured interviews

Three stakeholder groups (n=17)
Mainly active in Belgium

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Original Research

DIGITAL HEALTH

Digital Health
Volume 8: 1–11
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SAGE

Co-creation with research participants to inform the design of electronic informed consent

Evelien De Sutter[1], David Geerts[2], Pascal Borry[3], Kristien Coteur[4], Dorien Bamps[1], Heleen Marynissen[1], Els Ampe[5], Els Geenens[5], Marleen Depré[5] and Isabelle Huys[1]

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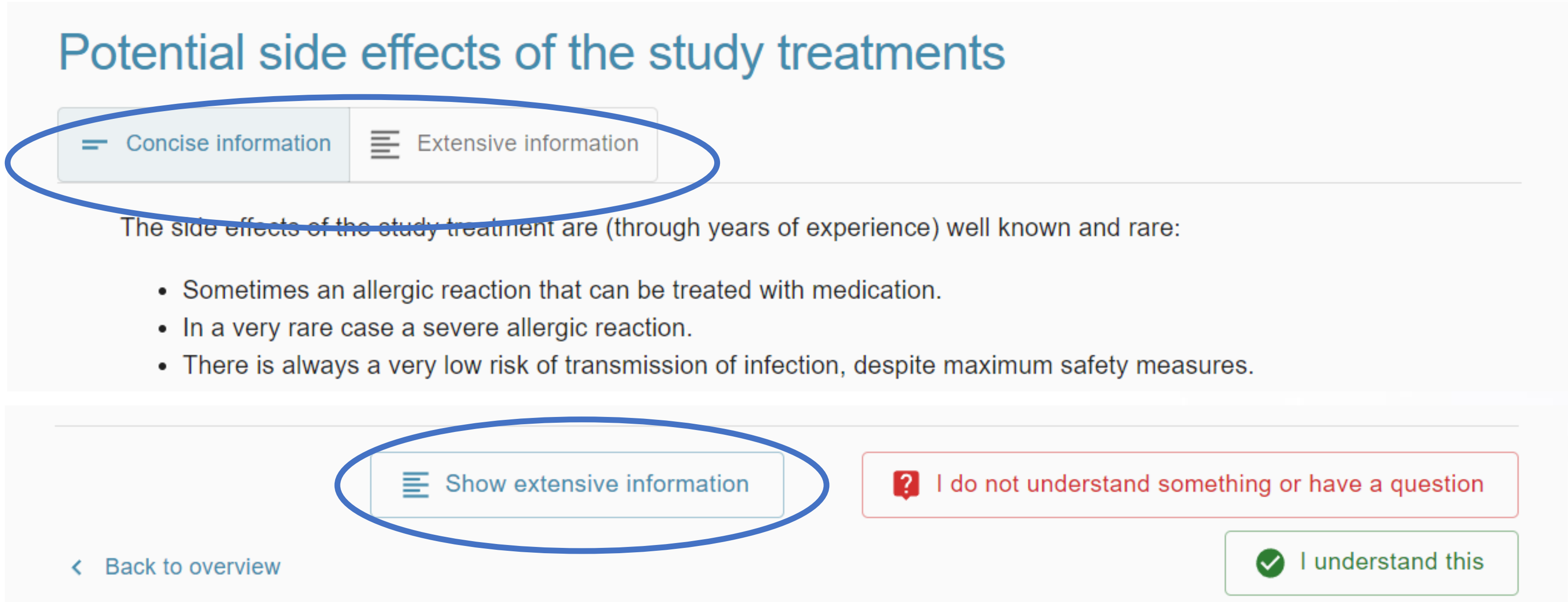
Interface: personalisation



Potential side effects of the study treatments

The side effects of the study treatment are (through years of experience) well known and rare:

- Sometimes an allergic reaction that can be treated with medication.
- In a very rare case a severe allergic reaction.
- There is always a very low risk of transmission of infection, despite maximum safety measures.

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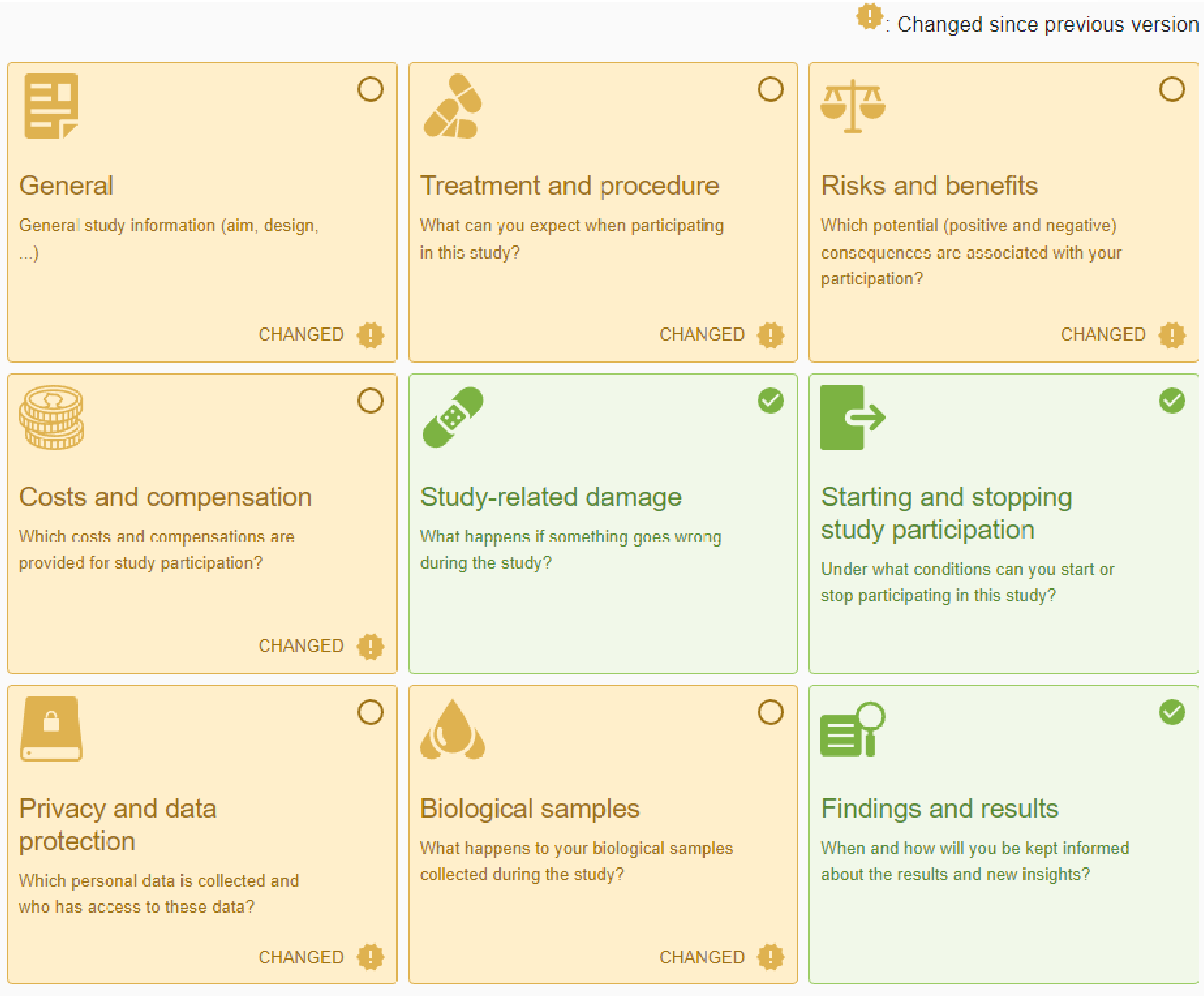
Interface: long-term interaction



!: Changed since previous version

○ **General** General study information (aim, design, ...) CHANGED !	○ **Treatment and procedure** What can you expect when participating in this study? CHANGED !	○ **Risks and benefits** Which potential (positive and negative) consequences are associated with your participation? CHANGED !
○ **Costs and compensation** Which costs and compensations are provided for study participation? CHANGED !	✓ **Study-related damage** What happens if something goes wrong during the study?	✓ **Starting and stopping study participation** Under what conditions can you start or stop participating in this study?
○ **Privacy and data protection** Which personal data is collected and who has access to these data? CHANGED !	○ **Biological samples** What happens to your biological samples collected during the study? CHANGED !	✓ **Findings and results** When and how will you be kept informed about the results and new insights?

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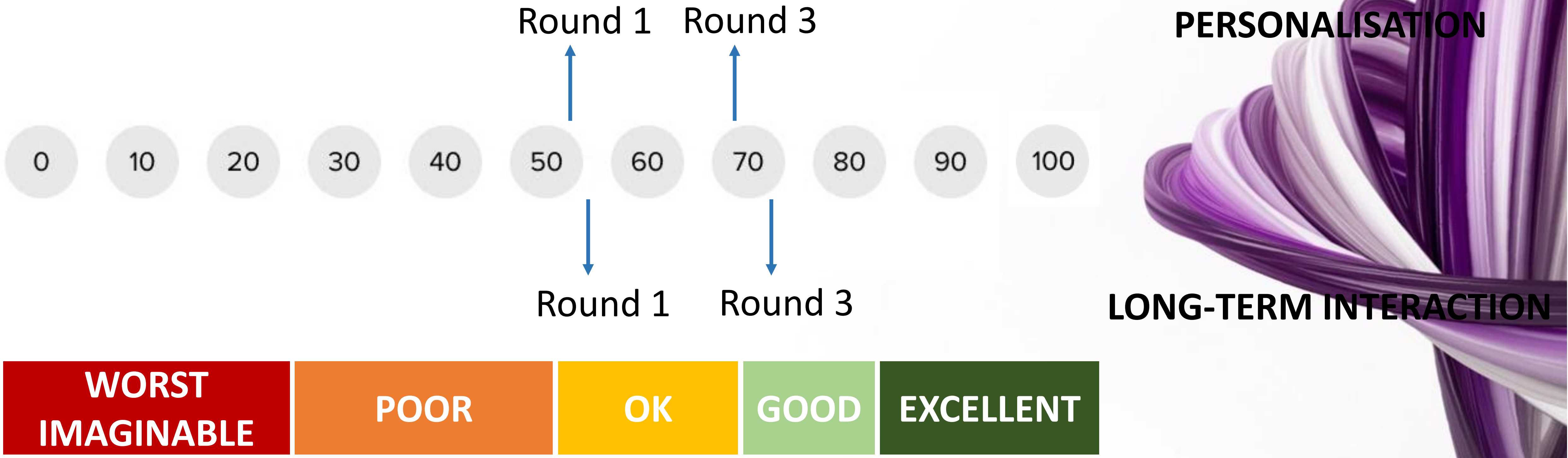
Published on 19.12.2023 in Vol 25 (2023)

Preprints (earlier versions) of this paper are available at https://preprints.jmir.org/preprint/46306, first published February 08, 2023.

Testing and Practical Implementation of a User-Friendly Personalized and Long-Term Electronic Informed Consent Prototype in Clinical Research: Mixed Methods Study

Evelien De Sutter[1]; David Geerts[2]; Koen Yskout[3]; Stef Verreydt[3]; Pascal Borry[4]; Liese Barbier[1]; Isabelle Huys[1]

System usability scale score



Round 1 Round 3

0 10 20 30 40 50 60 70 80 90 100

Round 1 Round 3

PERSONALISATION

LONG-TERM INTERACTION

WORST IMAGINABLE	POOR	OK	GOOD	EXCELLENT

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To test and evaluate electronic informed consent modules

- ✓ Usability testing is key to design a user-friendly application
- ✓ The designed electronic informed consent module has the potential to be usable by a wide audience
- ✓ Importance of providing participant support or alternatives to an electronic informed consent application

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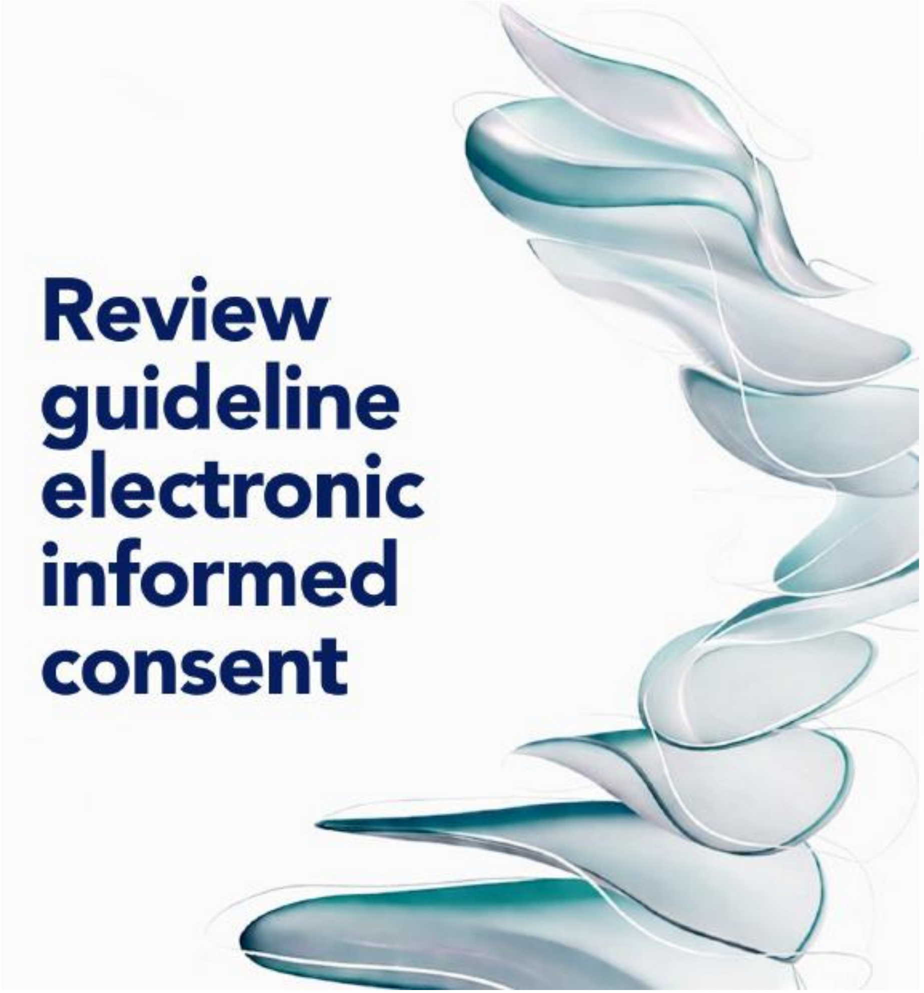
Review guideline electronic informed consent

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Comprehension

- The use of eIC highlights a **challenge to participant comprehension** that is less likely to occur in traditional informed consent evaluations, yet it is often overlooked.
- Besides informing the participant about the study, **the verbal, non-verbal interactions,** as well as the situated interaction between the participant and the researcher, provides the **participant indicators of whether to trust the researcher with safeguarding their interests** (e.g., as inferred from the researcher’s demeanor or affiliation).
- Both kinds of information are relevant to the consent decision. However, when the communication between researcher and participant is electronically mediated, **researchers may not pick up on and act upon subtle signs of a participant’s hesitancy or lack of comprehension.**

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Comprehension

- ► *Initial information provision: the consent information should be concise, clear, easy and highlighted, convey non-misleading trustworthiness indicators (e.g., university logo), and information on eIC personalization and long-term use (e.g., contacting participants for future studies).*
- ► *Personalized information: the information for participants can be tailored to their specific needs (e.g., disclosing pregnancy risks to women of childbearing age), layered (e.g., hover-over text for more information), customizable (e.g., allow changing font sizes or highlighting) or comprising of multiple formats (e.g., audio, video).*
- ► *Interaction: the eIC can be guided by the researcher (e.g., parallel video-call) or it can encourage participants to ask questions (e.g., through chat).*
- ► *Comprehension check: intermediate or final measures could assess participants' comprehension (e.g., quiz, teach-back) and contingently provide support (e.g., schedule a video call) or deny participation under certain levels of understanding (e.g., less than 80% correctly answered quiz questions).*

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Voluntariness

- The most well-known instances of research conduct that **reduce the voluntariness of consent**, such as coercion or offering clearly excessive financial incentives, are arguably similar between traditional informed consent and eIC. (persuasive design, push notifications…)
- *<u>Reduce persuasion, manipulation, nudging and related techniques:</u> researchers can remove persuasive or otherwise influencing elements that are not strictly necessary, indicate to participants that these techniques will be used, and/or allow participants to switch them off (e.g., change colors, notification frequency).*
- *<u>Future studies:</u> Researchers can allow participants to set their preferences for being contacted through the eIC interface about future studies.*

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Decision-making capacity

- eIC also poses particular **challenges to assessing and improving participants' decision-making competence** when it comes to consent decisions.
- *Due to the potential difficulties associated with authenticating a participant's true identity, **it can be difficult to assess whether that participant can be presumed to have decision-making competence** (e.g., is a child impersonating an adult?).*
- *Furthermore, decision-making competence is a **dynamic ability**, which can be affected by emotional or other affective states (e.g., feeling apathetic or overwhelmed with fear) as well as social support*
- *In eIC, **the decreased interaction between the researcher and the participant makes it more challenging for researchers to identify whether participants require more support related to study comprehension, emotional reassurance, or acquiring the necessary skills and resources to use digital means necessary for eIC.***
- ***INTERACTION AND SUPPORT***

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Authenticity

- eIC poses particular **challenges to signing and authentication**.
- *Ensure signature authenticity: researchers can ensure that the signature contains various identifiers (e.g., person, time, document version), and they can have an in-person interaction with the participant when the eIC is being signed (e.g., a video call).*
- *Protect signed documents from unauthorized access: researchers can provide unidentifiable data to certain parties (e.g., auditors, sponsors, RECs), assess whether unauthorized parties have access (e.g., eIC infrastructure providers), protect the data (e.g., limit and deidentify the collected consent data), the consent document (e.g., secure long-term storage, read-only documents) and the electronic infrastructure (e.g., the participants' device and their browser history, the eIC platform), and update protection measures.*

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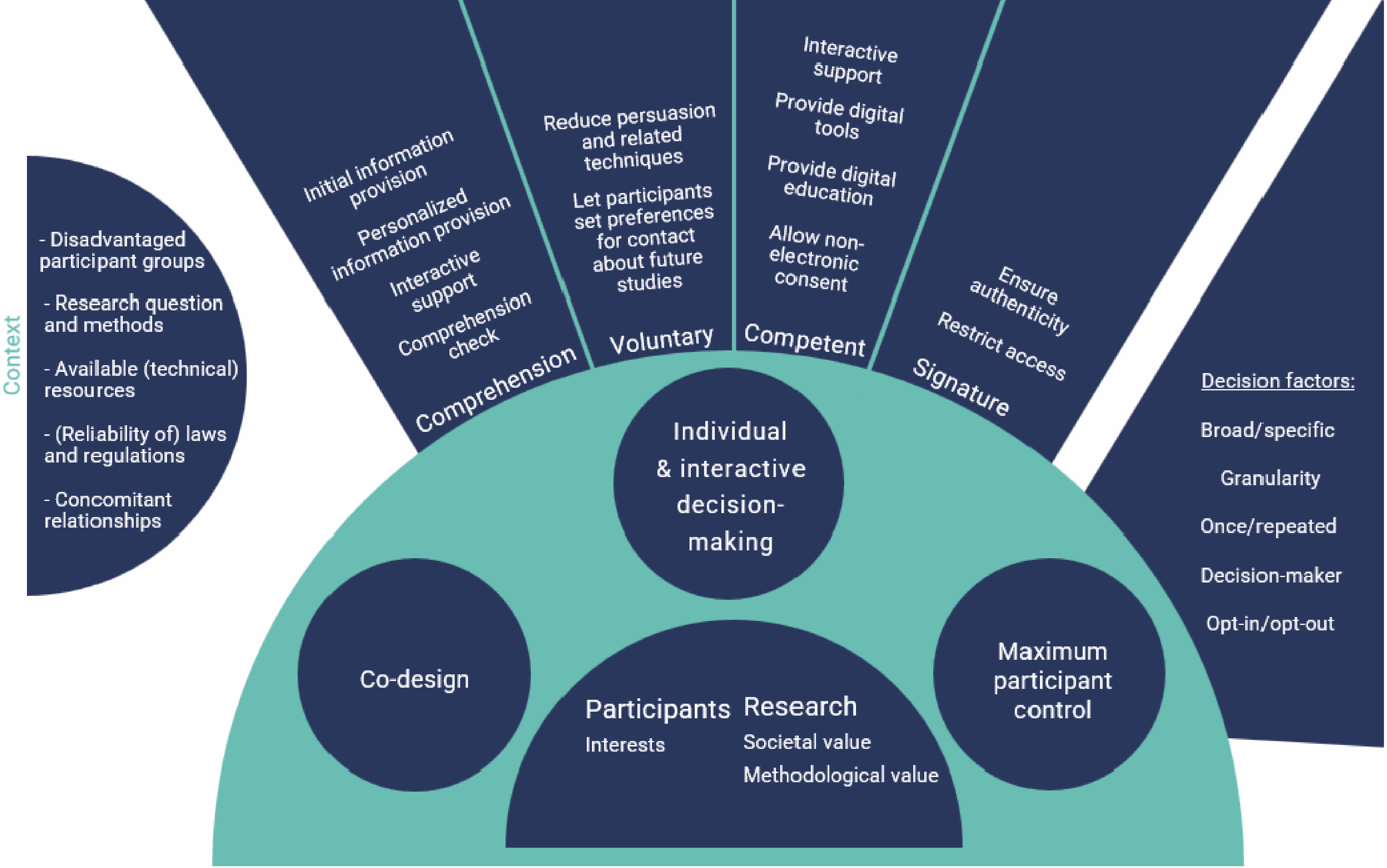


Context

- Disadvantaged participant groups
- Research question and methods
- Available (technical) resources
- (Reliability of) laws and regulations
- Concomitant relationships

Comprehension

Initial information provision

Personalized information provision

Interactive support

Comprehension check

Voluntary

Reduce persuasion and related techniques

Let participants set preferences for contact about future studies

Competent

Interactive support

Provide digital tools

Provide digital education

Allow non-electronic consent

Signature

Ensure authenticity

Restrict access

Decision factors:

Broad/specific

Granularity

Once/repeated

Decision-maker

Opt-in/opt-out

Individual & interactive decision-making

Co-design

Maximum participant control

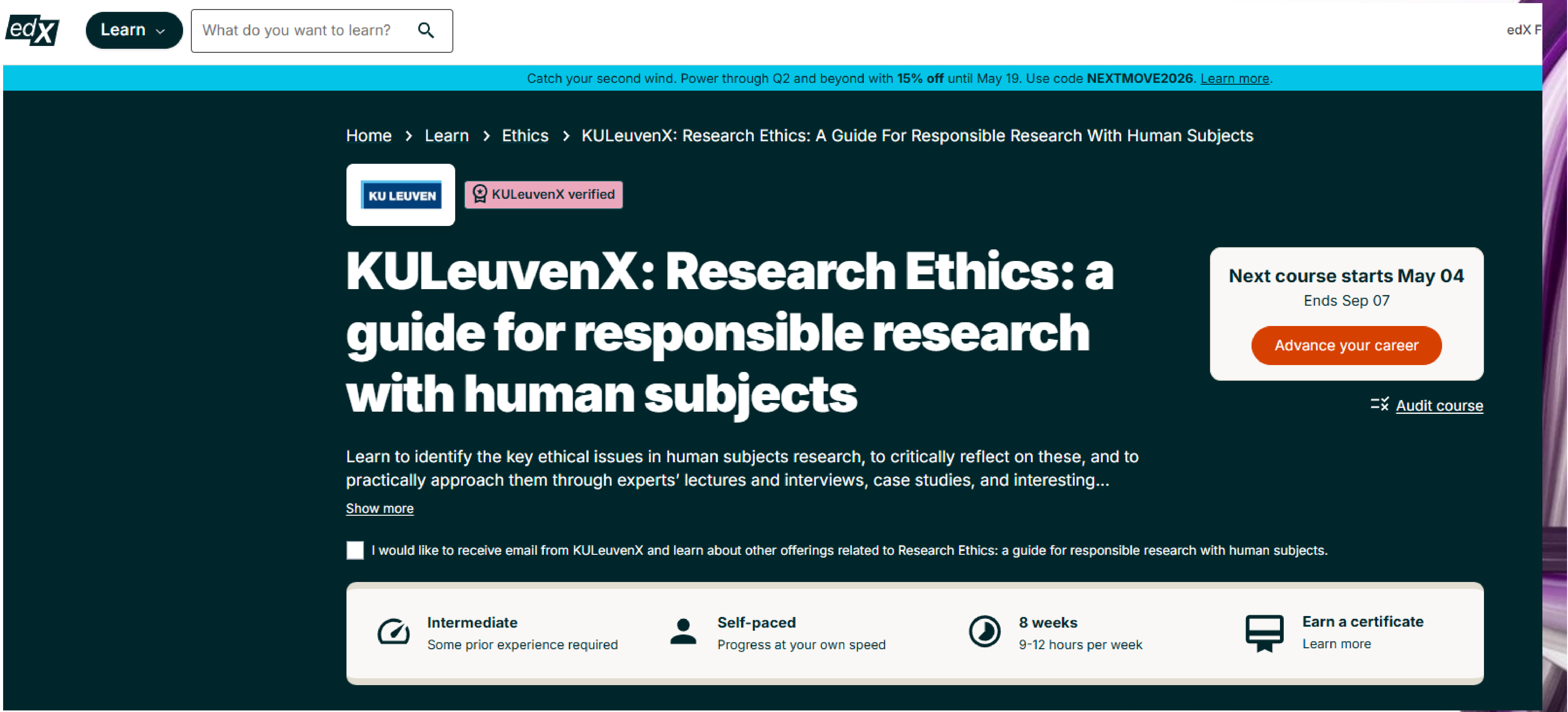
Participants

Interests

Research

Societal value

Methodological value



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MOOC informed consent

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NORSUS Norwegian Institute for Sustainability Research

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K&I Knowledge and Innovation

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