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# Four reasons why too many informed consents to clinical research are invalid: a critical analysis of current practices



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# Four reasons why too many informed consents to clinical research are invalid: a critical analysis of current practices

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## *Abstract*

**Objective** Informed consent (IC) is a central ethical and legal requirement for clinical research that aims to protect the autonomy of participants. In order to enable an autonomous decision and valid consent adequate understanding must be ensured. However, a considerable proportion of participants does not understand the relevant aspects about participation in research, e.g., approximately 45% could not name at least one risk. As such, the inadequate understanding of IC has been known for several decades and it still constitutes a severe problem for the ethical conduct of research. Through delineating the most pressing deficits of current IC procedures that lead to insufficient understanding, we aim to encourage the discussion amongst stakeholders, e.g., clinical researchers, and to provide the grounds for practical solutions.

**Main arguments** (1) Informed consent documents are too long to be read completely, thus, make it very difficult for potential participants to identify the material facts about the trial. (2) The low readability of the IC documents disadvantages persons with limited literacy. (3) The therapeutic misconception frequently prevents participants to realize that the primary purpose of clinical research is to benefit future patients. (4) Excessive risk disclosures, insufficient information about expected benefits and framing effects compromise a rational risk/benefit assessment.

**Conclusion** Due to these deficits, practices of informed consent in clinical research too often preclude adequate understanding of prospective participants, thus, invalidating informed consent. The gap between the well-specified ethical norm to enable informed consent and its insufficient translation into practice can no longer be accepted, as participant rights and the public trust in responsible research are at stake. Hence, immediate action is needed to address the prevailing deficits.

# Four reasons why too many informed consents to clinical research are invalid: a critical analysis of current practices

The ethical relevance of informed consent (IC) in health care and research is rooted in the appreciation for persons' autonomy – that is, the right and capability to develop own preferences and goals as well as to choose and act accordingly. As such IC became a central ethical and legal requirement for medical research involving humans. In Germany, the first guidelines articulating the principle of consent in research were issued as early as 1900 and 1931.[1] Yet, these guidelines did not prevent extensive crimes during medical experiments in Nazi Germany. In consequence, the verdict of the Nuremberg Doctors Trial emphasized as first principle that: "The voluntary consent of the human subject is absolutely essential."[2] The Nuremberg Code provided substantive groundwork for the concept of IC to evolve as an indispensable prerequisite for medical research. Today, the requirement of IC can be found in all international guidelines as well as in national and EU law. The Declaration of Helsinki in its current version defines the necessary elements of valid IC:" 25. Participation by individuals capable of giving informed consent as subjects in medical research must be voluntary. […] 26. In medical research involving human subjects capable of giving informed consent, each potential subject must be adequately informed of the aims, methods, sources of funding, any possible conflicts of interest, institutional affiliations of the researcher, the anticipated benefits and potential risks of the study and the discomfort it may entail, post-study provisions and any other relevant aspects of the study. The potential subject must be informed of the right to refuse to participate in the study or to withdraw consent to participate at any time without reprisal. […] After ensuring that the potential subject has understood the information, the physician or another appropriately qualified individual must then seek the potential subject's freely-given informed consent […] ".[3] Only if these elements are met can IC be regarded valid.

Translation of these ethical requirements into practice is vital to safeguard participants' autonomy in clinical research. Systematic reviews however indicate that a considerable proportion of participants did not understand essential components of IC such as potential risks

and benefits of the trial, procedures being applied (e.g. randomization), voluntariness of participation as well as nature and purpose of clinical research – that is, acquiring generalizable knowledge to benefit future patients.[4-6] In this light it must be assumed that current practices of IC considerably fail to deliver on the ethical standard of autonomy. In the following we aim to dissect the most pressing insufficiencies of IC that cause inadequate understanding. Hereby, we hope to inspire the development of practical solutions in support for more self-determination of research participants.

**Informed consent documents are too long**

In the last three decades, the average length of IC documents has increased 10 times with consequences on participants' understanding.[7] A study that analysed IC documents of neuro-oncological RCTs in 2011/2012 found an average word count of 7069 words and an average of 19 pages.[8] Since then, the length of IC documents has continuously increased. In our experience, IC documents for oncological studies comprising 40 pages plus additional 5 pages on data protection are common. Beardsley et al.[9] already showed in 2007 that longer documents are associated with a lower level of understanding. According to this analysis, objective understanding, measured by the Quality of Informed Consent (QuIC-A) questionnaire, was increased when page count remained below seven pages. Sharp et al.[10] even concluded that IC documents should not exceed 1250 words, since longer document are usually read incompletely. Similarly, the CIOMS Guidelines of 2016 demand: "The wording of the leaflet must be short and preferably not exceed two or three pages."[11]

**Low readability of IC documents hinders understanding of participants with limited literacy**

Poor readability of IC documents is another reason accounting for limited understanding. According to the OECDs' PIAAC study[12], just half of the population of OECD member states (51,2%) showed a higher proficiency in literacy allowing to understand multi-page texts with high information density, whereas, 15,5% had such limited reading skills that they were only

able to capture isolated information in relatively short texts. The readability of IC documents is usually low as several studies using the Flesch-Kincaid scale indicate, thus, a high grade level is required to understand the assessed documents.[7, 13] Reinert et al.[8] classified eight of the nine IC documents examined as difficult or fairly difficult to read (e.g., Flesh Reading Ease below 30), hence, only high school graduates or even university graduates will be able to understand the given information. Consequently, the complex language typically used in IC document may prevent up to half of the population in OECD member states to access relevant information on their trial participation.

**The therapeutic misconception is widespread**

In 1982, the therapeutic misconception was first addressed as a serious obstacle for proper understanding and valid IC in research with humans.[14] While standard medical care focusses solely on the benefit for the individual patient, the primary goal of clinical research is to generate generalizable knowledge on a specific scientific question, e.g., which treatment is superior for a given disease. Thus, clinical trials are primarily oriented towards the benefit for future patients. A therapeutic misconception exists when a research participant fails to recognize the difference between regular health care and the participation in a clinical trial, therefore, assuming that treatment decisions are tailored only to his or her personal needs, and/or holding disproportionate beliefs on his or her own personal benefit from participating in the trial, which is uncertain by nature.[15] In the meta-analysis by Tam et al.[4] 37.6% of the participants showed a therapeutic misconception. Joffe et al.[16] depicted that 30% of the participants in oncological studies assumed that the experimental treatment had already been proven as the most effective option. In the same study, only 46% of physicians recognized that the main goal of clinical trials is to gain scientific knowledge and benefit future patients. The therapeutic misconception presumably precludes participants' valid consent, since they lack correct views on the specific conditions of participation in research, which has direct implications for a proper assessment of benefits and risks.[17, 18] In addition, participants often do not know that there are alternative treatments. According to Tam et al.[4], only 64.1% of the

participants understood that other therapies would be available if they withdrew from the study. In this context, a lack of understanding can have negative ramifications on the voluntariness of the participation, especially when participants fear that their withdrawal would result in insufficient treatment.

**Potential benefits of the trial participation are not sufficiently addressed**

Another frequent shortcoming of IC documents in clinical research lies in an imbalanced description of possible risks versus expected benefits that often impedes a rational risk/benefit assessment. Essential but also extremely rare adverse effects are generally depicted in exceeding detail, whereas information on the expected benefits remain vague and brief. In our experience, information on adverse effects can cover up to 12 pages, but explanations on expected benefits usually do not exceed more than 12 lines. Comparably, Kirby et al.[19] reported that only one third of the assessed IC documents mentioned potential benefits; in these cases, information on benefits were usually found after description of adverse effects and presented by relatively shorter text. Along similar lines, the aforementioned study within a neuro-oncological research centre found that none of the analysed IC documents allowed a profound risk-benefit assessment.[8] The emphasis on risks and legal aspects may seem comprehensible with regard to liability issues, but it does not justify the lack of adequate information on the expected benefit. For, a valid IC can only be given if a risk/benefit assessment is made possible through comprehensible and balanced information. Additionally, too little attention is paid to framing effects in risk disclosures. Patients' or research participants' decisions between two alternative options can substantially differ depending on whether a positive frame (e.g., gains like survival rate related to a therapy) or a negative frame (e.g., losses like mortality rate) is used to communicate risks.[20] Consequently, framing effects can distort adequate understanding. Moreover, framing the likelihood of adverse effects negatively (e.g., 10% will experience fatigue versus positively framed, e.g., 90% will not experience fatigue) can even affect participants' wellbeing as it may contribute to increased fears and negative expectations that itself cause adverse effects in the sense of a nocebo effect.[19, 21]

## Discussion

To decide autonomously on the participation in medical research potential participants must have understood the advantages and disadvantages as well as the consequences of their decision. Given the four prevailing deficits in the practice of informed consent summarized here, it must be questioned whether research participants will find the pertinent information in the overlong, hardly readable IC documents and thus, will be able to balance potential risks and expected benefits in agreement with their individual goals. Even if participants adequately capture the risks and benefits, they may not recognize how research substantially differs from standard clinical care, therefore, misconceiving the very nature of their participation. In conclusion, under the current circumstances a significant proportion of participants does not understand the material facts about research, consequently precluding valid informed consent.

Although the challenges of informed consent reach beyond the deficits outlined above[22], insufficient understanding is a particularly pressing shortcoming as it dates back at least to the 1980s[23], so far without having improved substantivly.[4] Accumulating data on research participants' understanding revealed a striking discrepancy between well-defined ethical requirements for IC at one side and inadequate translation into practice at the other that can no longer be accepted. While advanced therapeutics as well as novel scientific methods are constantly implemented to foster ongoing medical progress, IC practices remain untouched from substantial progress. However, an IC process that ensures the participants' basic right for an autonomous decision should be regarded as an equivalently important research infrastructure. The EU Clinical Trial Regulation (CTR) 536/2014 emphasizes the need for a better understanding of IC as it requires in Article 29(5) that "it shall be verified that the subject has understood the information".[24] Yet, some questions have to be clarified before the CTR presumably becomes legally effective at the end of 2021. Most importantly, how is the verification to be implemented in practice and which parts of the IC document must be understood for a valid IC, as it is apparent that comprehension of a document of 10 pages or longer cannot be verified in detail.

A very fundamental obstacle affecting the understanding lies in the increasing complexity of the issues to be disclosed for IC, such as complex study designs, novel methods like next-generation sequencing and processes like biobanking or data sharing. Usually, these concepts reach beyond the knowledge and experience of the general population and are thus, intuitively difficult to understand and prone to misunderstandings.

The principle of respect for autonomy in medicine entails more than solely acknowledging the choices of patients and research participants. It also requires to actively encourage their decision making, e.g., through providing pertinent information in an appropriate form or through resolving misconceptions when necessary. We do not argue for an unrealistic ideal of *full* understanding. As Beauchamp and Childress outlined, "From the fact that actions are never fully informed, voluntary, or autonomous, it does not follow that they are never adequately informed, voluntary, or autonomous."[25] Accordingly, we urge for a practice of informed consent that supports *adequate* understanding of material facts about the participation in research – that are, regarding international guidelines, information on the nature and purpose of research, its risks and expected benefits as well as the applied methods and possible alternatives. To achieve this, we claim for immediate action regarding the development of understandable IC documents.[26] In addition, more emphasis to substantive conversations between investigators and participants is needed.[27] These actions should be accompanied by empirical research which needs to pay attention to a cohesive definition of 'understanding'.[26] What is at stake if passiveness persists, are no less than the indispensable participant rights and ethical standards of legitimate medical research as well as the public trust in responsible research practices.

**Authors**

AW is research fellow at the Association of Medical Ethics Committees in Germany. She is a trained physician with a special interest in bioethics and scientific experience in the field of neuroimmunology

JH is professor for medical biometry and epidemiology with extensive experience with clinical trials. Since 1998 he serves as a member of a Medical Ethics Committee, since 2012 as president of the Association of Medical Ethics Committees in Germany (in an honorary function). As the Informed Consent materials and forms got longer and longer, and harder to read and understand, even for him, he realized that something has gone wrong with the current IC.

**Authors' contributions**

JH developed the concept of the article. AW reviewed the relevant literature and drafted the first version. AW und JH contributed substantially to the several versions of the manuscript prior to submission. Both authors read and approved the final manuscript. JH serves as guarantor for the manuscript.

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## *Abstract*

**Objective** Informed consent (IC) is a central ethical and legal requirement for clinical research that aims to protect the autonomy of participants. To enable an autonomous decision and valid consent, adequate understanding must be ensured. However, a considerable proportion of participants do not understand the relevant aspects about participation in research, e.g., approximately 45% could not name at least one risk. As such, the inadequate understanding of IC has been known for several decades and it still constitutes a severe problem for the ethical conduct of research. Through delineating the most pressing deficits of current IC procedures that lead to insufficient understanding, we aim to encourage the discussion amongst stakeholders, e.g., clinical researchers, and to provide the grounds for practical solutions.

**Main arguments** (1) Informed consent documents are too long to be read completely, thus, make it very difficult for potential participants to identify the material facts about the trial. (2) The low readability of the IC documents disadvantages persons with limited literacy. (3) The therapeutic misconception frequently prevents participants to realize that the primary purpose of clinical research is to benefit future patients. (4) Excessive risk disclosures, insufficient information about expected benefits and framing effects compromise a rational risk/benefit assessment.

**Conclusion** Due to these deficits, practices of informed consent in clinical research too often preclude adequate understanding of prospective participants, thus, invalidating informed consent. The gap between the well-specified ethical norm to enable informed consent and its insufficient translation into practice can no longer be accepted, as participant rights and the public trust in responsible research are at stake. Hence, immediate action is needed to address the prevailing deficits.

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Translation of these ethical requirements into practice is vital to safeguard participants' autonomy in clinical research. Systematic reviews however indicate that a considerable proportion of participants do not understand essential components of IC such as potential risks

and benefits of the trial, procedures being applied (e.g., randomization), voluntariness of participation as well as nature and purpose of clinical research – that is, acquiring generalizable knowledge to benefit future patients.[4-6] In this light it must be assumed that current practices of IC considerably fail to deliver on the ethical standard of autonomy. Moreover, from a legal standpoint the EU Clinical Trial Regulation that will enter into force by the end of January 2022 sets an urgent need for improved IC practices to support participants' understanding. It states in Article 29(5) that "it shall be verified that the subject has understood the information".[7] In the following we aim to dissect the most pressing insufficiencies of IC that cause inadequate understanding. Hereby, we hope to inspire the development of practical solutions in support for more self-determination of research participants.

**Informed consent documents are too long**

In the last three decades, the average length of IC documents has increased 10 times with consequences on participants' understanding.[8] A study that analysed IC documents of neuro-oncological RCTs in 2011/2012 found an average word count of 7069 words and an average of 19 pages.[9] Since then, the length of IC documents has continuously increased. In our work experience from research ethics committees, IC documents for oncological studies comprised of 40 pages plus additional 5 pages on data protection are common. Beardsley et al.[10] already showed in 2007 that longer documents are associated with a lower level of understanding. According to this analysis, objective understanding, measured by the Quality of Informed Consent (QuIC-A) questionnaire, was increased when page count remained below seven pages. Sharp et al.[11] even concluded that IC documents should not exceed 1250 words, since longer documents are usually read incompletely. Similarly, the CIOMS Guidelines of 2016 demand: "The wording of the leaflet must be short and preferably not exceed two or three pages."[12]

**Low readability of IC documents hinders understanding of participants with limited literacy**

Poor readability of IC documents is another reason attributing to limited understanding. According to the OECD PIAAC study[13], just half of the population of OECD member states (51.2%) showed a higher proficiency in literacy allowing to understand multi-page texts with high information density, whereas, 15.5% had such limited reading skills that they were only able to capture isolated information in relatively short texts. The readability of IC documents is usually low as several studies using the Flesch-Kincaid scale indicate, thus, a high grade level is required to understand the assessed documents.[8, 14] Reinert et al.[9] classified eight of the nine IC documents examined as difficult or fairly difficult to read (e.g., Flesh Reading Ease below 30), hence, only high school graduates or even university graduates will be able to understand the given information. Consequently, the complex language typically used in IC documents may prevent up to half of the population in OECD member states to access relevant information on their trial participation.

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In 1982, the therapeutic misconception was first addressed as a serious obstacle for proper understanding and valid IC in research with humans.[15] While standard medical care focusses solely on the benefit for the individual patient, the primary goal of clinical research is to obtain generalizable knowledge on a specific scientific question, e.g., which treatment is superior for a given disease. Thus, clinical trials are primarily oriented towards the benefit for future patients. A therapeutic misconception exists when a research participant fails to recognize the difference between regular health care and the participation in a clinical trial, therefore, assuming that treatment decisions are tailored only to their personal needs, and/or holding disproportionate beliefs on their own personal benefit from participating in the trial, which is uncertain by nature.[16] In the meta-analysis by Tam et al.[4] 37.6% of the participants showed a therapeutic misconception. Joffe et al.[17] depicted that 30% of the participants in oncological studies assumed that the experimental treatment had already been proven as the most effective option. In the same study, only 46% of physicians recognized that the main goal of clinical trials is to gain scientific knowledge and benefit future patients. The therapeutic

misconception presumably precludes participants' valid consent, since they lack correct views on the specific conditions of participation in research, which has direct implications for a proper assessment of benefits and risks.[18, 19]

In addition, participants often do not know that there are therapeutic alternatives outside the study. According to Tam et al.[4], only 64.1% of the participants understood that other therapies would be available if they withdrew from the study. In this context, a lack of understanding can have negative ramifications on the voluntariness of the participation, especially when participants fear that their withdrawal would have negative consequences such as insufficient treatment. Finally, misunderstandings may also give rise to fears of being treated inappropriately, either, because participants hold the misconception that the clinical trial offers the best treatment and a discontinuation would cause insufficient treatment, or, because they think that physicians would treat them improperly or with less care if they withdrew or refused.

**Potential benefits of the trial participation are not sufficiently addressed**

Another frequent shortcoming of IC documents in clinical research lies in an imbalanced description of possible risks versus expected benefits that often impedes a rational risk/benefit assessment. Essential but also extremely rare adverse effects are generally depicted in exceeding detail. Whereas, information on expected benefits remains vague and brief, often restricted to phrases like "you may or may not benefit".[20] In our experience, – that is, regularly assessing IC documents for research ethics approval – information on adverse effects can cover up to 12 pages out of a total of 40 pages, e.g., for oncological trials that test new treatments. But explanations on expected benefits usually do not exceed more than 12 lines. Kirby et al.[21] reported that only one third of the assessed IC documents mentioned specific potential benefits such as an expected delay of cancer progression; in these cases, information on benefits were usually found after description of adverse effects and presented by relatively shorter text. Along similar lines, the aforementioned study within a neuro-oncological research centre found that none of the analysed IC documents allowed a profound risk-benefit assessment.[9] The emphasis on risks and legal aspects may seem comprehensible with regard

to liability issues, but it does not justify the lack of adequate information on the expected benefit. A valid IC can only be given if a risk/benefit assessment is made possible through comprehensible and balanced information.

So far, little guidance exists on how to communicate potential benefits in the context of research where no benefits have reliably been established. Obviously, to avoid therapeutic misconception, information needs to emphasize the inherent uncertainty about personal benefits as well as refrain from overly optimistic wording. At the same time, vague notions of potential benefits do not suffice in weighing risks and benefits. Thus, experts demand that descriptions of potential benefits should at least specify the expected beneficial outcomes, e.g., improvements of symptoms or survival.[20] Moreover, Kahrass et al.[20] also discuss different approaches to describe the likelihood of potential benefits. However, further investigation is necessary to determine best practices.

Additionally, almost no attention is paid to framing effects in risk disclosures for IC. A patient's or research participant's decision between two alternative options can substantially differ depending on whether a positive frame (e.g., gains like survival rate related to a therapy) or a negative frame (e.g., losses like mortality rate) is used to communicate risks.[22] Consequently, framing effects can distort adequate understanding. Moreover, framing the likelihood of adverse effects negatively (e.g., 10% will experience fatigue versus positively framed, e.g., 90% will not experience fatigue) can even affect participant wellbeing as it may contribute to increased fears and negative expectations that itself cause adverse effects in the sense of a nocebo effect.[21, 23]

## Discussion

Given the four prevailing deficits in the practice of informed consent summarized here, it must be questioned whether research participants will find the pertinent information in the overlong, hardly readable IC documents and thus, will be able to balance potential risks and expected benefits in agreement with their individual goals. Even if participants adequately capture the risks and benefits, they may not recognize how research substantially differs from standard

clinical care, therefore, misconceiving the very nature of their participation. In conclusion, under the current circumstances a significant proportion of participants do not understand the material facts about research, consequently precluding valid informed consent.

When speaking of validity, we refer to the ethical sense of informed consent that is grounded in its primary purpose to protect autonomy.[24] In this sense, IC is valid if a person capable of deliberating own goals, free of controlling influences, and with sufficient understanding, intentionally decides about participating in a proposed trial – hence, expresses an autonomous choice. However, a second sense of IC exists that aims at legally effective permissions of research procedures.[24, 25] Laws and institutional practices in this sense are sometimes less rigorous regarding autonomy instead focussing on documented authorization and detailed risk disclosure. Whereas consents under these conditions are legally valid and shield from liability, they often do not allow a participant's autonomous decision-making.

At this point, a debate in research ethics that is relevant to our argument needs recognition. Ethicists have proposed dissenting views of what is required for valid IC, especially when it comes to the level of understanding a potential participant should have. On the "minimalist account", necessary understanding is limited to a few items to make sure that a participant is consenting to a specific proposal, i.e., comprehension of how to consent or refuse and of the procedures the person will undergo.[26] The minimal understanding requirement appears to be tied to a rather narrow conception of respect for autonomy solely focusing on non-interference with a person's rights. We hold against – following Beauchamp and Childress[24] – that respect for autonomy poses more than a negative obligation to *avoid* rights violation and illegitimate control, it also contains a positive obligation to *enable* autonomous decisions through establishing meaningful understanding. We take both obligations as foundational and from that, derive what constitutes adequate understanding. It should not be misunderstood as a full understanding of every study detail. Rather, it is a grasp of core information that allow research participants to evaluate *what* they consent or refuse to and which *advantages and disadvantages* it might have, thus, allowing them to weigh the information against their interests and goals. What therefore needs to be understood for a valid IC, is the nature and

purpose of the research, it's potential risks and benefits, applied procedures, right to refuse or withdraw, and alternatives outside the study.

Despite efforts in support for better IC practices, the impact on participants' understanding has been relatively modest. Recent strategies to improve IC have focused for instance on documents with a short section on "key information" as introduced by the revised US Common Rule, on multimedia approaches, and on test/feedback interventions. However, effectiveness of some of these measures is still unclear, partly due to the high heterogeneity of studies on IC interventions,[27, 28] and strategies that show efficacy like enhanced IC documents[27] are far from being implemented comprehensively. In result, the actual understanding of participants has not improved substantively over three decades.[4] The challenges of informed consent clearly reach beyond the deficits outlined above.[25, 29] But insufficient understanding remains a particularly pressing shortcoming as it dates back at least to the 1980s[30] and points to an unacceptable, yet unresolved gap between the ethical principle of IC and its ineffective translation into practice. One acute force to act is set through the verification requirement in Article 29(5) of the EU Clinical Trial Regulation (CTR).[7] Yet, some questions have to be clarified before it becomes legally effective by the end of January 2022 – i.e., by means of which methods shall understanding be verified and which parts of the IC document must be understood for a valid IC, as it is apparent that comprehension of a document of 10 pages or longer cannot be verified in detail.

A very fundamental obstacle affecting understanding lies in the increasing complexity of the issues to be disclosed for IC, such as complex study designs, novel methods like next-generation sequencing and processes like biobanking or data sharing. Usually, these concepts reach beyond the knowledge and experience of the general population and are thus, intuitively difficult to understand and prone to misunderstandings.

The principle of respect for autonomy in medicine entails more than solely acknowledging the choices of patients and research participants. It also requires to actively encourage their decision making, e.g., through providing pertinent information in an appropriate form or through

resolving misconceptions when necessary. To achieve meaningful understanding, we urge for immediate action on informed consent practices. A few considerations may be helpful in doing so. First, informed consent should be regarded as a process rather than a form and as such, will require a combination of interventions to improve understanding. According to a first meta-analysis,[27] this needs to involve at least the development of understandable IC documents *as well as* strategies for substantive conversation between participants and the research team. Second, improving consent will also mean to engage patients and patient experts to a greater extent. Patient involvement facilitates IC processes that place informational needs and interests of participants in the centre,[31] e.g., in rendering IC documents more understandable and relevant through testing.[32] To reach a broader implementation in practice, specific guidelines are necessary. Third, actions should also involve stakeholders who prepare written information, e.g., sponsors and investigators, to shift emphasis on legal precautions to autonomy-driven consent and to identify barriers that hinder good practices. Fourth, robust evidence is required to select effective interventions for better understanding. Empirical research should thus adopt a cohesive definition of 'understanding'[32] and standardized study designs.[27] Finally, what is at stake if substantial change holds off, are no less than the indispensable participant rights and ethical standards of legitimate medical research as well as the public trust in responsible research practices.

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JH is professor for medical biometry and epidemiology with extensive experience with clinical trials. Since 1998 he serves as a member of a Medical Ethics Committee, since 2012 as president of the Association of Medical Ethics Committees in Germany (in an honorary function). As the Informed Consent materials and forms got longer and longer, and harder to read and understand, even for him, he realized that something has gone wrong with the current IC.

**Authors' contributions**
JH developed the concept of the article. AW reviewed the relevant literature and drafted the first version. AW and JH contributed substantially to the several versions of the manuscript. JH deceased before acceptance of the article. The final approval of the article was signed off by the surviving author AW.

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