Special issue

# New Strategies for Increasing Participation of Patients from Diverse Cultural and Religious Backgrounds in Clinical Trials

***Laura Palazzani, Fabio Macioce, Margherita Daverio, Loredana Persampieri, Valeria Ferro****

ABSTRACT: Cultural differences between researchers and potential participants in clinical trials could result in communication barriers, which are likely to hinder awareness and pose challenges to the informed consent process. An intercultural communication approach to the informed consent process could facilitate potential participants' understanding; strategies such as the involvement of family members, cultural insiders, cultural mediators during the consent process should be adopted to overcome language and cultural barriers. The article highlights as well barriers related to the interaction between gender and multicultural issues in cross-cultural communication and stresses some culturally-sensitive strategies for the inclusion of pregnant women in clinical research. Consent procedures tailored to local cultural patterns with a focus on the use of new technologies are discussed.

KEYWORDS: Informed consent; intercultural communication; community engagement; gender; ICT

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* *Laura Palazzani, Professore Ordinario di Filosofia del Diritto, Libera Università Maria Ss. Assunta (LUMSA), Roma. E-mail: palazzani@lumsa.it; Fabio Macioce, Professore Ordinario di Filosofia del Diritto, Libera Università Maria Ss. Assunta (LUMSA), Roma. E-mail: fmacioce@libero.it; Margherita Daverio, ricercatore Libera Università Maria Ss. Assunta (LUMSA), Roma. E-mail: m.daverio@lumsa.it; Loredana Persampieri, ricercatore Libera Università Maria Ss. Assunta (LUMSA), Roma. E-mail: l.persampieri@lumsa.it; Valeria Ferro, ricercatore Libera Università Maria Ss. Assunta (LUMSA), Palermo.* E-mail: *v.ferro@lumsa.it. The article was subject to a double-blind peer review process.*

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## 1. Introduction

The purpose of this literature and ethical guidelines' review is to consider cultural challenges in the informed consent process, in order to increase participation of people of different cultures and religious beliefs. By "increasing participation", we mean focusing on avoiding an unfair exclusion of subjects from diverse cultural backgrounds (and religious, insofar as religion influences culture generating communication barriers, that can cause someone not to participate in a clinical study due to their religious beliefs) from clinical research. Cultural diversity includes several cultural elements that can affect health, such as nutrition, gender differences, the family structure, the concepts of autonomy and solidarity. The objective of this contribution is to make sure that cultural/language barriers in the communication process do not exclude these populations from accessing potential benefits, in those cases where they are envisaged in the study design. Overcoming culturally-driven communication challenges may ultimately lead to an improved access to research participation. Therefore, we will discuss an intercultural approach to communication and a participatory approach to the informed consent process (e.g. taking into account the perspectives of different cultural groups in the development of information materials, etc.). This approach can empower culturally-diverse subjects to make autonomous decisions with regard to their participation/non-participation in clinical research. The analysis of findings focuses also on verifying whether reliance on technological developments in information, which offer new opportunities for the implementation of informed consent, as well as the selection of digital tools according to cultural patterns, may help to modernize and improve the informed consent process, overcoming possible communication barriers between researchers and participants in clinical trials.

## 2. The informed consent process involving participants from diverse cultural and religious backgrounds: barriers and challenges to global clinical research

### 2.1. Communication barriers to recruitment of research participants in international multicenter and multicultural clinical trials

Informed consent is not only a written form or a bureaucratic procedure, but also, above all, an essential communication process between the participant and the researcher in clinical research. In many cases, obtaining informed consent may be difficult with people from diverse cultural and religious backgrounds, as it is in the case of international multicenter studies where researchers and the potential participants belong to different cultural contexts[1]. In order to overcome communication barriers and avoid misconceptions and misunderstandings, interaction in a multicultural setting cannot overlook cultural diversity[2], as it contributes to shaping subjective identities, thus, it has an impact on the way people process and understand information[3].

[1] H. TEN HAVE, B. GORDIJN (eds.), Handbook of Global Bioethics, Dordrecht, 2013, p. 154.

[2] The UNESCO Universal Declaration on Cultural Diversity, 2001, available at https://unesdoc.unesco.org/ark:/48223/pf0000127162, last visited April 26th, 2019, sets out that "culture takes diverse forms across time and space. This diversity is embodied in the uniqueness and plurality of the identities of the groups and societies making up humankind (…)" (Article 1). It equally stresses that "the defence of cul-



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Cultural differences between researchers and potential participants in clinical trials could result in communication barriers, which are likely to hinder awareness and pose challenges to the informed consent process[4]. In 2015, WHO underlined that **"**a challenge in global health ethics concerns international research, especially where investigators from wealthy countries conduct research in impoverished settings where participants are especially vulnerable or where language and cultural barriers make informed consent difficult**"**[5]. In cross-cultural communication – as in the case of certain international multicenter clinical trials –special care is recommended in collecting informed consent, in order to avoid the risk of possible poor communication due to language differences[6]. The difference of values and beliefs (even if not limited to cases of multicultural settings) could generate difficulties in communication itself[7]: for example, certain cultural practices and expectations may impact negatively on communication to prospective participants in clinical trials, e.g., in some settings the belief that for a medicine to be effective it has to be bitter or it must hurt[8]. Sound comprehension of infor-

tural diversity is an ethical imperative, inseparable from respect for the dignity of the human person" (Article 4). Culture refers to the set of spiritual and material, intellectual and affective traits that characterize a society or a social group (see UNESCO Universal Declaration on Cultural Diversity, 2001, cit., Preamble); moreover, it "encompasses in addition to art and literature, lifestyles, ways of living together, value systems, traditions and beliefs" (see UNESCO Universal Declaration on Cultural Diversity, 2001, cit.). It is important to keep in mind that cultural diversity and religious diversity do not overlap, as in the same cultural group one can find different religious beliefs, and the same religious group can embrace diverse cultural patterns.

[3] As highlighted by the Italian Committee for Bioethics, cultural backgrounds influence individual and collective behaviours: in the researcher-participant relationship, the researcher acts according to his/her heritage of knowledge grounded in medical and professional education/experience gained in particular cultural and social contexts, whereas culturally heterogeneous participants may carry with them a broad spectrum of cultural values and religious beliefs, which influence their lifestyles, health habits and views of medical interventions and therapies, different understandings of modesty in public areas, and more generally, different philosophical interpretations of medical duties, goals and practices (i.e. diverse concepts of health, illness, disease, corporeity) (see ITALIAN COMMITTEE FOR BIOETHICS (NBC), Opinion on Migration and Health, 2017, available at http://bioetica.governo.it/en/works/opinions-responses/migration-and-health/, last visited April 8th, 2019).

[4] D. SCHROEDER, J. COOK, F. HIRSCH, S. FENET, V. MUTHUSWAMY, *Ethics Dumping Case Studies from North-South Research Collaborations*, New York, 2018, pp. 134.

[5] WHO, *Global Health Ethics. Key issues*, 2015, available at https://www.who.int/ethics/publications/global-health-ethics/en/, last visited March 25th, 2019 .

[6] UNESCO INTERNATIONAL BIOETHICS COMMITTEE (IBC), Report of the IBC on Consent, 2008, available at https://unesdoc.unesco.org/ark:/48223/pf0000178124, last visited March 25th, 2019; THE COUNCIL OF EUROPE, *Guide for Research Ethics Committee Members, Steering Committee on Bioethics*, April 2012, https://www.coe.int/t/dg3/healthbioethic/activities/02_biomedical_research_en/Guide/Guide_EN.pdf, last visited March 25th, 2019; CIOMS, *International Ethical Guidelines for Epidemiological Studies*, 2009, available at https://cioms.ch/wp-content/uploads/2017/01/International_Ethical_Guidelines_LR.pdf, last visited March 25th, 2019; CIOMS, *International Ethical Guidelines for Health-Related Research Involving Humans*, Geneva, 2016, https://cioms.ch/wp-content/uploads/2017/01/WEB-CIOMS-EthicalGuidelines.pdf, last visited March 25th, 2019.

[7] EGE, Ethical aspects of clinical research in developing countries. Opinion n. 17, 2003, available at https://publications.europa.eu/en/publication-detail/-/publication/6339dcbf-c156-4e7f-9e43-9928acf82118/language-en/format-PDF/source-77404483, last visited March 25th, 2019.

[8] CIOMS, Drug development research in Resource-Limited Countries. How to succeed in implementation of Good Clinical Practice Guidelines. Draft report of the Joint CIOMS/WHO Working Group, CIOMS, Geneva, December 2005, available at https://cioms.ch/wp-content/uploads/2017/05/DrugDevelopRpt14Dec2005.pdf, last visited March 3rd, 2019.

mation can moreover become complex when those who intervene do not use the same references in approaching health problems (for example, the scientific approach of a research team is different from a mystic, supernatural approach to health which could be found in some communities)[9].

Main barriers in cross-cultural communication can be identified with language barriers[10]; as a matter of fact, in some communities, there could not even be the word to express some scientific concepts related to research, e.g. for the term 'randomization'[11]. Other barriers can concern a lack of awareness about trials and in particular poor understanding of the concept of research, which may be confused with the direct health services provision[12], and with a lack of trust in researchers and low health literacy regarding immunization; concern about adverse events and fears about exploitation (especially in the case of healthy volunteers, as it is in the case of experimental vaccines)[13].

In this review, we will focus mainly on language barriers. If not addressed, communication barriers between the participants and the researchers may influence comprehension of potential benefits

[9] UNESCO INTERNATIONAL BIOETHICS COMMITTEE (IBC), Report of the IBC on Consent, 2008, available at https://unesdoc.unesco.org/ark:/48223/pf0000178124, last visited March 25th, 2019.

[10] J. BODDY, *Research across cultures, within countries: Hidden ethics tensions in research with children and families?*, in *Progress in Development Studies*, 14(1), 2014, pp. 91-103; P. AMORRORTU ET AL., *Recruitment of racial and ethnic minorities to clinical trials conducted within specialty clinics: an intervention mapping approach*, in *Trials* 19, 2018, p. 115; L. CONDON ET AL., *Engaging Gypsy, Roma, and Traveller Communities in Research: Maximizing Opportunities and Overcoming Challenges*, in *Qualitative Health Research*, 2019, available at https://www.ncbi.nlm.nih.gov/pubmed/30600758; D. SCHROEDER, J. COOK, F. HIRSCH, S. FENET, V. MUTHUSWAMY, *Ethics Dumping Case Studies from North-South Research Collaborations*, cit., pp. 99-106; L. PALAZZANI, *Innovation in Scientific Research and Emerging Technologies. A Challenge to Ethics and Law*, Cham (Switzerland), 2019, pp. 157.

[11] G. OKELLO ET AL., *Challenges for consent and community engagement in the conduct of cluster randomized trial among schoolchildren in low-income settings: experiences from Kenya*, in *Trials* 14, 2013, p. 142. In addition, a study from UK about the inclusion of non-English-speaking patients in research reported language barriers and the unavailability of translators for different reasons (R. BERNIER, E. HALPIN, S.J. STAFFA, L. BENSON, J.A. DI NARDO, V.G. NASR, *Inclusion of non-English-speaking patients in research: A single institution experience*, in *Paediatric Anaesthesia Journal*, 28(5), 2018, pp. 415-420).

[12] This could result in difficulties in understanding research process in general (see J. BODDY, *Research across cultures, within countries: Hidden ethics tensions in research with children and families?*, in *Progress in Development Studies*, cit.; S. GEORGE, N. DURAN, K. NORRIS, *A systematic review of barriers and facilitators to minority research participation among African Americans, Latinos, Asian Americans, and Pacific Islanders*, in *American Journal Public Health*, 104(2), 2014, pp. 16-31; T.W. QUAY ET AL., *Barriers and facilitators to recruitment of South Asians to health research: A scoping review*, in *British Medical Journal Open*, 2017, available at https://bmjopen.bmj.com/content/bmjopen/7/5/e014889.full.pdf, last visited May 5th, 2019; P. AMORRORTU ET AL., *Recruitment of racial and ethnic minorities to clinical trials conducted within specialty clinics: an intervention mapping approach*, cit.; L. PALAZZANI, *Innovation in Scientific Research and Emerging Technologies. A Challenge to Ethics and Law*, Cham (Switzerland), cit., pp. 16-17.

[13] J. BODDY, *Research across cultures, within countries: Hidden ethics tensions in research with children and families?*, cit.; T.W. QUAY ET AL., *Barriers and facilitators to recruitment of South Asians to health research: A scoping review*, cit.; P. AMORRORTU ET AL., *Recruitment of racial and ethnic minorities to clinical trials conducted within specialty clinics: an intervention mapping approach*, cit.; J.L. BROWNE, C.O. REES, J.J.M. VAN DELDEN ET AL., *The willingness to participate in biomedical research involving human beings in low- and middle-income countries: a systematic review*, in *Tropical Medicine & International Health,* 24(3), 2019, pp. 264-279; S. GEHLERT, J. MOZERSKY, *Seeing Beyond the Margins: Challenges to Informed Inclusion of Vulnerable Populations in Research*, in *The Journal of Law, Medicine & Ethics*, 46, 2018, pp. 30-43; B. BODEN-ABALA ET AL., *Examining Barriers and Practices to Recruitment and Retention*, in *Stroke Clinical Trials*, 46(8), 2015, pp. 2232-7.

and risks related to clinical studies[14], leading to misconceptions with respect to an overestimation of envisaged benefits deriving from inclusion in a clinical trial (the so-called "therapeutic misconception")[15] or, in general, the expectation of receiving health services in the context of severely resource-constrained public health systems[16].

### 2.2. Reconciling autonomy with community: an intercultural approach to communication

International guidelines for scientific research involving humans recommend individual, free and informed consent as a general ethical standard[17]. The same ethical guidelines highlight that consent presents always a social and cultural context that must be taken into account and respected[18]. This is particularly important in the case of some international scientific research, where subjects with different cultural backgrounds are involved in clinical trials, at least as potential participants. As a matter of fact, there are cultures in which the community perspective can prevail on individual informed consent[19]; or there are communities, such as some south Asian ones, where there are decisional hierarchies within families[20]; moreover, in many settings community leaders or family members play

[14] J. BODDY, *Research across cultures, within countries: Hidden ethics tensions in research with children and families?*, cit.; G. BERNAL ET AL., *Methodological challenges in research with ethnic, racial, and ethnocultural groups*, in F.T.L. LEONG ET AL. (Eds.), *APA handbook of multicultural psychology, Vol. 1. Theory and research*. Washington, DC, 2014, pp. 105-123; T.W. QUAY ET AL., *Barriers and facilitators to recruitment of South Asians to health research: A scoping review*, cit.; P. AMORRORTU ET AL., *Recruitment of racial and ethnic minorities to clinical trials conducted within specialty clinics: an intervention mapping approach*, cit.; R. BERNIER ET AL., *Inclusion of non-English-speaking patients in research: A single institution experience*, cit.

[15] P. MARSHALL, UNICEF/UNDP/WORLD BANK/WHO SPECIAL PROGRAMME FOR RESEARCH AND TRAINING IN TROPICAL DISEASES & WORLD HEALTH ORGANIZATION, *Ethical challenges in study design and informed consent for health research in resource-poor settings*, 2007, available at http://www.who.int/iris/handle/10665/43622, last visited March 1st, 2019; L. PALAZZANI, *Innovation in Scientific Research and Emerging Technologies. A Challenge to Ethics and Law*, cit.

[16] P. AMORRORTU ET AL., *Recruitment of racial and ethnic minorities to clinical trials conducted within specialty clinics: an intervention mapping approach*, cit.

[17] WORLD MEDICAL ASSOCIATION, *Declaration of Helsinki*, 1964 last version 2013, available at https://www.wma.net/policies-post/wma-declaration-of-helsinki-ethical-principles-for-medical-research-involving-human-subjects/, last visited April 8th, 2019; CIOMS, *International Ethical Guidelines for Health-Related Research Involving Humans*, Geneva, 2016, cit.

[18] UNESCO INTERNATIONAL BIOETHICS COMMITTEE, *Diversity of cultural expressions*, 2005, available at https://en.unesco.org/creativity/sites/creativity/files/article_18en.pdf, last visited March 25th, 2019; UNESCO INTERNATIONAL BIOETHICS COMMITTEE (IBC), *Report of the IBC on Consent*, 2008, available at https://unesdoc.unesco.org/ark:/48223/pf0000178124, last visited March 25th, 2019; CIOMS, *International Ethical Guidelines for Health-Related Research Involving Humans*, 2016, cit.; P. MARSHALL, *Ethical challenges in study design and informed consent for health research in resource-poor settings*, cit.

[19] P.E. EKMEKCI, B. ARDA, *Interculturalism and Informed Consent: Respecting Cultural Differences without Breaching Human Rights*, in *Cultura (Iasi)*, 14(2), 2017, pp. 159-172; C. T. ANDOH, *African Communitarian Bioethics and the Question of Paternalism*, in *British Journal of Education, Society & Behavioural Science*, 15(4), 2016, pp. 1-16.

[20] T.W. QUAY ET AL., *Barriers and facilitators to recruitment of South Asians to health research: A scoping review*, in *British Medical Journal Open*, 2017, available at https://bmjopen.bmj.com/content/bmjopen/7/5/e014889.full.pdf, last visited May 5th, 2019.

an important role in the decision-making process for participation in research[21]. To respond to this challenge, **"**it is necessary that the issue of consent be envisaged in a more global context of education, making persons autonomous whilst keeping in mind the primacy of the interests of the person concerned in their social setting. It is necessary to ensure the respect for the will of the person concerned, and to promote education towards autonomy and individual responsibility**"**[22]. This aim can be achieved through an improved intercultural communication in the informed consent process. An intercultural communication presupposes embracing intercultural bioethics as the underlying theoretical framework through which to interpret and understand a culturally-sensitive communication, preventing communication barriers, as far as possible, or re-thinking ways to overcome them, by taking into account the intercultural perspective. Interculturalism values cultural diversity and pluralism, alongside emphasizing integration and social inclusion. As the UNESCO *Declaration on Cultural Diversity* points out **"**no one can invoke cultural diversity to threaten human rights guaranteed by international law, nor to limit their scope**"**[23], and it makes clear that **"**everyone must be able to participate in the cultural life of his choice, and exercise its forms, within the limits imposed by respect for human rights and fundamental freedoms**"**[24].

In an intercultural approach to communication, it is crucial to overcome stereotypical thinking and a "one for all" communication method, devoting attention to the cultural backgrounds of patients or research participants and to personal specificity among individuals belonging to same culture, contributing to the achievement of a more respectful, complete and effective informed consent process. Starting from the knowledge of the cultural tradition researchers face with, respect is recognized as one of the ethical principles of conduct in research in general, but in particular in research in developing countries[25]; anything in the nature of the research which the participant may find morally or culturally sensitive should entail some corresponding sensitivity in obtaining consent (see Singapore's Bioethics Advisory Committee (BAC), *Ethics Guidelines for Human Biomedical Research* (2015). Besides, the ways of conveying information should be adapted and tailored[26]. Information should be

[21] P. MARSHALL, *Ethical challenges in study design and informed consent for health research in resource-poor settings*, cit., p. 6 and pp. 27-31.

[22] UNESCO INTERNATIONAL BIOETHICS COMMITTEE (IBC), *Report of the IBC on Consent*, 2008, cit., III.3.3, n. 120.

[23] UNESCO, *Universal Declaration on Cultural Diversity*, 2001, cit., article 4.

[24] UNESCO, *Universal Declaration on Cultural Diversity*, 2001, cit., article 5.

[25] TRUST Project, *Global Code of Conduct for Research in Resource-Poor Settings*, 2018, available at http://www.globalcodeofconduct.org/wp-content/uploads/2018/05/Global-Code-of-Conduct-Brochure.pdf, last visited on March 1st, 2019; L. PALAZZANI, *Innovation in Scientific Research and Emerging Technologies. A Challenge to Ethics and Law*, cit.

[26] EGE remarks that the way information is given to patients and the procedure of obtaining consent may vary according to the specific situation of the country where a clinical trial takes place, namely regarding the level of literacy, the level of scientific understanding, the organisation of the community, etc. that may influence the consent procedures regarding the involvement of persons, in particular women, in a clinical trial (see EGE, *Ethical aspects of clinical research in developing countries. Opinion n. 17*, 2003, available at https://publications.europa.eu/en/publication-detail/-/publication/6339dcbf-c156-4e7f-9e43-9928acf82118/language-en/format-PDF/source-77404483; L. PALAZZANI, *Innovation in Scientific Research and Emerging Technologies. A Challenge to Ethics and Law*, cit.).

given in a culturally appropriate way[27]. An intercultural approach to communication should be adopted in all cases where there is cultural diversity between the research team and prospective research participants, insofar as this diversity becomes challenging in terms of communication effectiveness and affects the latter's autonomous decision-making throughout the entire informed consent process (before, during, and after the end of a clinical study, in the sense of having the proper information to be able to decide whether to participate in a clinical study, stay in or leave the study at any time without any form of retaliation, an adequate understanding of what is at stake, in terms of benefits and risks, as well as of required behaviours after the end of the study to protect participants' health). This approach to communication involves a global perspective; namely, it can apply both to clinical research conducted within Europe with participants from diverse cultural backgrounds, and clinical research beyond Europe (including but not limited to developing countries).

Potential participants' comprehension can be enhanced by researchers through previous consultation with cultural mediators and local representatives regarding the most effective ways of communicating the purpose of the study; investigators might consider conducting focus groups with representatives of those who may be recruited to a study, in order to understand issues and concerns associated with preparing the consent form and developing approaches to obtain consent[28]. In addition, adopting strategies to safeguard the understanding of the nature and the implications of the research, such as including sufficient time for subjects to consider their participation and discuss it with family and friends; provision of adequate information about what research entails (about research in general and the specific research in particular) from someone without a dependency relationship (such as between physician and patient)[29]. Establishing trust is also an important element, alongside with building long-term relationships between the community and the research team[30]. It should be equally underlined that in obtaining consent, in some cases, it may be appropriate to obtain before an agreement from the community or from a family member. If a person does not wish to partici-

[27] UN-REDD PROGRAMME, *Guidelines on Free, Prior and Informed Consent*, 2013, available at https://www.uncclearn.org/sites/default/files/inventory/un-redd05.pdf, last visited April 26th, 2019; UNESCO, *Policy on engagement with indigenous people*, 2018, available at https://unesdoc.unesco.org/ark:/48223/pf0000262748, last visited March 1st, 2019. In relation to intercultural communication in the specific case of vaccinations WHO, *Zika Strategic Response Plan*, 2016, available at https://www.who.int/emergencies/zika-virus/strategic-response-plan/en/, last visited March 1st, 2019.

[28] P. MARSHALL, *Ethical challenges in study design and informed consent for health research in resource-poor settings*, cit.; K. CHATFIELD ET AL., *Research with, not about, communities – Ethical guidance towards empowerment in collaborative research*, a report for the TRUST project, 2018, available at http://trust-project.eu/wp-content/uploads/2018/07/TRUST-Community-Participation-in-Research-Final.pdf, last visited March 1st 2019.

[29] J.L. BROWNE, C.O. REES, J.J.M. VAN DELDEN, ET AL., *The willingness to participate in biomedical research involving human beings in low- and middle-income countries: a systematic review*, cit.

[30] P. MARSHALL, *Ethical challenges in study design and informed consent for health research in resource-poor settings*, cit.; J.J.M. VAN DELDEN, R. VAN DER GRAAF, *Revised CIOMS International Ethical Guidelines for Health-Related Research Involving Humans*, in *Journal of the American Medical Association,* 317(2), 2017, pp. 135-136; P. AMORRORTU ET AL., *Recruitment of racial and ethnic minorities to clinical trials conducted within specialty clinics: an intervention mapping approach*, cit.; K. CHATFIELD ET AL., *Research with, not about, communities – Ethical guidance towards empowerment in collaborative research, a report for the TRUST project*, 2018, cit.

pate, his/her will must always be respected[31]. A 'relational' view of autonomy, which includes in the autonomy of the individual also the reference to dialogue with the researcher/physician as well as with wife/husband/relatives[32] can provide solutions to ethical and practical problems in clinical practice and research[33].

### 2.3. Elements for an interculturally-sensitive informed consent

Given the social and cultural context of informed consent recalled above, the informed consent process must take into account some aspects, in order to be interculturally-sensitive. First, through community consultation[34] and other community engagement strategies researchers should verify that informed consent takes into account cultural practices and the health service context. Informed consent procedures should be tailored to local requirements to achieve genuine understanding[35]. Second, one should recall that the process of "back-translation" of the informed consent form (after the translation of the consent form in another language, the form is then given to a native speaker who translates the document back to the original language) is a process which ensures the validity of the translated form and provides opportunities for corrections to be made. Particular attention must be given to the appropriate use of local dialects and terminology that effectively conveys the meanings of words to potential research participants[36]; with some populations, where the language is generally spoken and not written, there could be offered the possibility to read the document in Eng-

[31] EMA, *Reflection paper on ethical and GCP aspects of clinical trials of medicinal products for human use conducted in third countries and submitted in marketing authorisation applications to the EMA*, 2010, available at https://www.ema.europa.eu/en/documents/regulatory-procedural-guideline/draft-reflection-paper-ethical-good-clinical-practice-aspects-clinical-trials-medicinal-products_en.pdf, last visited March1st, 2019; EGE, *Ethical aspects of clinical research in developing countries. Opinion n. 17*, 2003, available at https://publications.europa.eu/en/publication-detail/-/publication/6339dcbf-c156-4e7f-9e43-9928acf82118/language-en/format-PDF/source-77404483, last visited March1st, 2019; TRUST PROJECT, *Global Code of Conduct for Research in Resource-Poor Settings*, 2018, available at http://www.globalcodeofconduct.org/wp-content/uploads/2018/05/Global-Code-of-Conduct-Brochure.pdf, last visited March1st, 2019;

[32] ITALIAN COMMITTEE FOR BIOETHICS (NCB), *Opinion on Migration and Health*, 2017, cit.: L. PALAZZANI, *Innovation in Scientific Research and Emerging Technologies. A Challenge to Ethics and Law*, cit.; i-CONSENT D1.4, *Ethical issues concerning informed consent in translational/clinical research and vaccination*, cit.

[33] E.S. DOVE, S.E. KELLY, F. LUCIVERO, B. PRAINSACK, ET AL., *Beyond individualism: Is there a place for relational autonomy in clinical practice and research?*, in *Clinical Ethics*, 12 (3), 2017, pp. 150-165.

[34] CIOMS, *Drug development research in Resource-Limited Countries. How to succeed in implementation of Good Clinical Practice Guidelines. Draft report of the Joint CIOMS/WHO Working Group*, 2005, cit.; CIOMS, *International Ethical Guidelines for Health-Related Research Involving Humans*, Geneva, 2016, cit.; CIOMS, *International Ethical Guidelines for Epidemiological Studies*, 2009, cit.

[35] TRUST PROJECT, *Global Code of Conduct for Research in Resource-Poor Settings*, 2018, cit., in particular art. 21: **"**Lower educational standards, illiteracy or language barriers can never be an excuse for hiding information or providing it incompletely. Information must always be presented honestly and as clearly as possible. Plain language and a non-patronising style in the appropriate local languages should be adopted in communication with research participants who may have difficulties comprehending the research process and requirements".

[36] P. MARSHALL*, Ethical challenges in study design and informed consent for health research in resource-poor settings*, cit.

lish but discuss it in the local language[37]; pre-testing consent forms with individuals from the study population provides useful direction concerning the need to revise consent forms so that they are meaningful and understandable for study participants[38]. Third, researchers have historically used strategies such as storytelling, performance or theatre, and more recently have looked into using visual tools, such as creating small video clips where a community member explains the research and the consent process in their mother tongue[39].

Community engagement is a recognized ethical requirement[40] and it is also a crucial element of an interculturally sensitive informed consent. Potential cultural sensitivities should be explored in advance of biomedical research with local communities, research participants and local researchers to avoid violating customary practices[41], often through the contribution of the local trusted "spokesperson", a person who not only can translate but also help to understand cultural values and perceptions[42], such as a contact person between the community and the research team[43]. Consultation with community members[44], in particular on how to work with the community, e.g. providing a forum for discussing and addressing issues arising from participants and community representatives[45], alongside an ongoing "dialogue" between researchers and the community about the proposed study and

[37] H3Africa Working Group on Ethics and Regulatory Issues for the Human Heredity and Health in Africa (H3Africa) Consortium, *Guidelines for informed consent* (2017), available at https://h3africa.org/wp-content/uploads/2018/05/H3A%202017%20Revised%20IC%20guideline%20for%20SC%2020_10_2017.pdf, last visited March 25th, 2019.

[38] P. Marshall, *Ethical challenges in study design and informed consent for health research in resource-poor settings*, cit.

[39] K. Chatfield et Al., *Research with, not about, communities – Ethical guidance towards empowerment in collaborative research, a report for the TRUST project*, 2018, cit.

[40] See CIOMS, *International Ethical Guidelines for Health-Related Research Involving Humans*, 2016, cit., guideline 7, *Community engagement*; see also EGE, *Ethical aspects of clinical research in developing countries. Opinion n. 17*, 2003, cit., n. 2.4, Partnership; CIOMS, *International Ethical Guidelines for Epidemiological Studies*, 2009, cit., guideline 4, *Individual informed consent*, par. on *Cultural considerations, consultation with community members* et seq.; J.J.M. van Delden, R. van der Graaf, *Revised CIOMS International Ethical Guidelines for Health-Related Research Involving Humans*, cit.; K. Chatfield et al., *Research with, not about, communities – Ethical guidance towards empowerment in collaborative research, a report for the TRUST project*, 2018, cit.

[41] See Trust Project, *Global Code of Conduct for Research in Resource-Poor Settings*, 2018, cit., art. 8, "Respect".

[42] A. Halkoaho et al., *Cultural aspects related to informed consent in health research: A systematic review*, in *Nursing Ethics* 23(6), 2016, pp. 698-712; J. Hughson et al., *A review of approaches to improve participation of culturally and linguistically diverse populations in clinical trials*, in *Trials*, 17 (2016), 263; K. Chatfield et al., *Research with, not about, communities – Ethical guidance towards empowerment in collaborative research, a report for the TRUST project*, 2018, cit.; V. Angwenyi, *Complex realities: community engagement for a paediatric randomized controlled malaria vaccine trial in Kilifi*, Kenya, cit.; L. Condon et al., *Engaging Gypsy, Roma, and Traveller Communities in Research: Maximizing Opportunities and Overcoming Challenges*, cit.

[43] K. Chatfield et al., *Research with, not about, communities – Ethical guidance towards empowerment in collaborative research, a report for the TRUST project*, 2018, cit.

[44] See CIOMS, *International Ethical Guidelines for Epidemiological Studies*, 2009, cit., guideline 4, *Individual informed consent*, par. on *Consultation with community members*; CIOMS, *International Ethical Guidelines for Health-Related Research Involving Humans*, 2016, cit.; P. Marshall, *Ethical challenges in study design and informed consent for health research in resource-poor settings*, cit.; L. Palazzani, *Innovation in Scientific Research and Emerging Technologies. A Challenge to Ethics and Law*, Cham (Switzerland), 2019, cit.

[45] V. Angwenyi, *Complex realities: community engagement for a paediatric randomized controlled malaria vaccine trial in Kilifi*, Kenya, cit.

its potential implications, or a more structured consultation taking into account the concerns of a community or a socially identifiable group[46] are recommended advices.

## 3. Interaction between gender, culture and education in cross-cultural communication

### 3.1. Gender and health literacy

There are some specific barriers related to the interaction between gender and multicultural issues in cross-cultural communication, within geographically different research settings. In this regard, a study conducted by Killawi *et al* in the Arabian Gulf Region (particularly in the high-density multicultural setting of Qatar) describes how prospective research participants perceive their potential participation. As for the participant recruitment procedure, cultural norms in Qatar require that interactions between men and women occur in public space except for purely medical reasons or necessity depending on the task.

The mostly Muslim and all-female research assistants involved in the study believed it would be culturally inappropriate for them to be in a private room with a man. In addition, more women in the Arabic language group declined participation compared to any other language group (they felt compelled to discuss with a family member whether to participate and were concerned about recorded interviews for privacy reasons).

The study devises some best practices relating to a gender and culturally-tailored approach to recruitment procedures: culturally-competent and language concordant female research assistants were involved in research procedures to avoid neglecting cultural patterns regarding gender interactions; findings show that relying on male research assistants to recruit female subjects is more likely to clash with cultural sensitivities about gender interactions in the geographical context under consideration and, thus, lead to a negative impact on the research, compared to female research assistants recruiting male individuals. Recruitment took place in "gender specific waiting areas"[47] with female research assistants wearing white research coats to convey their official status and mitigate cultural patterns of gender separation. In this case, consent procedures were tailored to local cultural and social patterns; this empirical study has led to the conclusion that taking into account cultural influences results in an increased participation rate[48].

Moreover, research ethics guidelines and scientific studies identify a number of recommended practices taking into account women's health literacy: emphasis is placed on the need to improve the understanding of information: "[…] providing information through health workers (and particularly female health workers when the research will involve women), rather than physicians so that participants feel more at their ease to discuss and ask questions". Another key element concerns "providing information about a research project in various ways that are appropriate to the community (i.e. in

[46] See CIOMS, *International Ethical Guidelines for Epidemiological Studies*, 2009, cit., *Commentary on Guideline 4, Individual Informed Consen*t, par. on *Consultation with community members*.

[47] A. KILLAWI ET AL., *Procedures of recruiting, obtaining informed consent, and compensating research participants in Qatar: findings from a qualitative investigation*, in *BMC Medical Ethics*, 15, 2014, p. 9.

[48] A. KILLAWI ET AL., *Procedures of recruiting, obtaining informed consent, and compensating research participants in Qatar: findings from a qualitative investigation*, cit.

parts of Africa, information has been supplied on audio or video tape, on the radio and through ballad singers); in some communities, particular care will need to be taken to ensure that the methods of providing information and aiding understanding which are adopted will ensure that the information reaches all members of the community. For example, if public meetings are used, it must be borne in mind that young women may feel unable to ask questions during such a meeting"[49].

Other recommended practices focus on the importance of increasing understanding of cervical cancer perceptions and beliefs: in this regard, Mwaka *et al.* explore community perceptions, beliefs and knowledge, in Northern Uganda, about local names, causes, symptoms, course, treatment, and prognosis of cervical cancer in order to inform targeted interventions to promote early help-seeking. The study suggests that "awareness campaigns to promote early help-seeking for cervical cancer symptoms need to be culturally-sensitive and context-specific; and include messages on symptoms, risk factors, course, treatment and prognoses"[50].

In order to improve awareness of Muslim women health beliefs, a study by Walton *et al*. stresses that although Muslim women prefer to make autonomous decisions concerning their health and not delegate this role to male family members, ultimately they believe it is important to consult with them during the decision-making process. Muslim women think that interacting with a female health care provider is imperative. In particular, they are inclined to access medical and rehabilitation services if provided by a female, but not when provided by a male health care provider; they are equally persuaded that relying on prayer, recitation of Quran, fasting, charity could be beneficial to their health, and are at ease with the use of physical touch in medicine and rehabilitation evaluation and treatment, if the care provider is female[51].

In the context of best practices aimed at improving informed consent of women in an intercultural setting, a number of studies point out the usefulness of multimedia tools for facilitating the communication process: Muhammed Olanrewaju Afolabi *et al.*, in this respect, assessed the effectiveness of a multimedia informed consent tool for adults participating in a clinical trial in the Gambia. A computerized, audio questionnaire was used to assess participants' comprehension of informed consent. This was done immediately after consent had been obtained and at subsequent follow-up visits (days 7, 14, 21 and 28). The acceptability and ease of use of the multimedia tool were tested in focus groups. Poorer comprehension was independently associated with female sex. A multimedia informed consent tool significantly improved comprehension and retention of consent information by research participants with low levels of literacy: research concepts that are known to be difficult to understand were clearly illustrated using video recordings and animations and explained by sound tracks in three local languages[52].

In a study on HIV research in South Africa, Staunton *et al.* highlight that obtaining consent in low-and middle-income countries can be challenging, and they identify ethical issues in developing an educa-

[49] NUFFIELD COUNCIL ON BIOETHICS, *The ethics of research related to healthcare in developing countries*, 2002, p. 11.
[50] A.D. MWAKA ET AL., *Understanding cervical cancer: an exploration of lay perceptions, beliefs and knowledge about cervical cancer among the Acholi in northern Uganda*, in *BMC Women's Health*,14:84, 2014.
[51] L.M. WALTON ET AL., *Health Beliefs of Muslim Women and Implications for Health Care Providers: Exploratory Study on the Health Beliefs of Muslim Women*, in *Online Journal of Health Ethics*, vol. 10, 2, 2014.
[52] M.O. AFOLABI ET AL., *A multimedia consent tool for research participants in the Gambia: a randomized controlled trial,* in Bulletin World Health Organization, 93(5), 2015, pp. 320–328A.

tional video to empower potential participants during consent processes. This tool has been prepared taking into account gender differences and some critical points emerged. Low levels of education, complexity of science and research processes, confusion about basic elements of research, and socio-economic conditions that make access to medical care difficult have led to concerns about the adequacy of the consent process. Evidence showed the importance of early community engagement in educating potential research participants and promoting community acceptance of research. This study reported that a 15-minute educational video entitled 'I have a dream: a world without HIV' was developed to educate and empower potential research participants to make informed choices during consent processes in future HIV cure clinical trials. The decision to include two women as the HIV-positive actors, instead of a male and female actor, turned out to be problematic as it may fuel misconceptions that women are carriers of the disease. In South Africa, women are generally in charge of the care of a child, and thus the caregiver needed to be female; equally, issues such as rape and female contraceptive methods, also required a female actor. This video prototype could be used in research targeted at different populations, and coupled with a variety of different media[53].

### 3.2. Culturally-sensitive communication for the inclusion of pregnant women in clinical trials

Cultural issues and the scientific knowledge gap between researchers and participants, directly affecting the latter's capacity to clearly understand the underlying risks related to their specific health condition should be carefully weighed, especially in sensitive circumstances, such as those in which the involvement of pregnant women in clinical research is envisaged.

In this context, Frew *et al.* 2014 provide a number of interesting culturally-sensitive strategies for the inclusion of pregnant women in clinical research: community outreach to advise providers about studies: this aspect is key to helping women overcome unease and distrust of the research (the most common reason for women's unwillingness to enrol in studies was identified with a preference for protocols that enabled them to follow-up on study results with their clinician); face-to-face interactions with health providers; health staff education and message training, along with study promotion via clinic media, print material, and interpersonal communication, in order to enhance patient receptivity to recruitment; conducting research within a community space or offering home visits: low-income women may not have reliable access to research study sites, particularly if they rely on a friend or family member for transportation, or use of public transportation; explaining the objective of clinical trials for testing drugs for pregnant women in hospitals and obstetric offices has been successful in identifying and enrolling eligible pregnant women for immunization trials; in general, visits to community groups in their geographic area; giving the possibility to discuss with friends and family members; community engagement strategies, including focus groups among pregnant women to identify important barriers and facilitators to research participation, relying on targeted messages and culturally-sensitive information materials adapted to gender needs and preferences, as well as community-based participatory research methods; accommodation of time constraints of pregnant women by taking advantage of mobile technology and the prevalence of cellular phone usage. For

[53] C. STAUNTON ET AL., *Ethical challenges in developing an educational video to empower potential participants during consent processes in HIV cure research in South Africa*, in *Journal of Virus Eradication*, 4(2), 2018, pp. 99–102.


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example, the Text4baby (T4B) program, launched in 2011, attempted to improve health behaviour and perceptions among pregnant women by employing a text messaging program. T4B successfully changed attitudes toward pregnant women's health behaviour and thus it is recommended as method to alter perceptions of clinical trial practicality and overall potential benefits to their health. Disseminating messages via cellular phone usage allows investigators to educate eligible participants without taking additional time out of pregnant women's schedules. Education via mobile technology that has promoted significant changes in health behaviours and perceptions may also help providers restrained by clinical duties to reach eligible patients and use a similar program to educate them on available studies. Social networking sites have been employed as an effective method of increasing recruitment rates among pregnant women.

Culturally appropriate messages and research tailored to the need of prospective participants are among the most effective strategies contributing to successful retention of pregnant women in research trials. These findings further highlight the importance of recruitment methodology that is carefully tailored to interests and needs of pregnant women[54].

### 3.3. The role of the male partner in the informed consent process

There is broad consensus in international and European guidelines on the fact that in no case permission by the woman's partner may replace the individual informed consent of the woman herself, since this would result in a violation of the principle of respect for the person. However, if the woman wishes to consult with husband or partner before deciding to enrol in research, that is deemed to be not only ethically permissible, but in some contexts highly desirable[55]. In addition, different cultures may also have different views concerning privacy and personal data, which can impinge on the acceptability of certain aspects of research protocols, especially with regard to data collection, as well as the data subject's right of access and right to object[56].

The NBC stressed the fact that in some cultural contexts women tend to delegate decisions concerning their health to a partner, a male family member or the family group. In this perspective, the Italian Committee for Bioethics, proposes an interpretation of the concept of autonomy in terms of "relational autonomy", which may be better tailored to an intercultural approach aiming at accommodating the value of the community dimension in certain cultural settings and respect for the person[57].

In the context of research participation, women living in a social context of patriarchal authority, having a low literacy level, may adopt a passive behaviour with regard to enrolment procedures or not seek interaction with researchers in case of insufficient understanding of the study evolution. There-

[54] P.M. Frew Et Al., *Recruitment and Retention of Pregnant Women Into Clinical Research Trials: An Overview of Challenges, Facilitators, and Best Practices*, in *Clinical Infectious Diseases*, 59 (7), 2014, pp. S400–S407; Martinez Perez et Al.,'*Researchers have love for life': opportunities and barriers to engage pregnant women in malaria research in post-Ebola Liberia*, in *Malaria Journal*, 17(1) 2018, p. 132.

[55] Royal College Of Physicians, *Guidelines on the practice of ethics committees in medical research with human participants*, 2007.

[56] Ege, *Ethical aspects of clinical research in developing countries. Opinion n. 17*, 2003, available at https://publications.europa.eu/en/publication-detail/-/publication/6339dcbf-c156-4e7f-9e43-9928acf82118/language-en/format-PDF/source-77404483, p. 13.

[57] Italian Committee for Bioethics (nbc), *Opinion on Migration and Health*, 2017, p. 38.


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fore, as stressed by the UK Royal College of Physicians, "research ethics committees should exercise special care in examining the proposed consent process to ensure adequate time and a proper environment in which a decision to participate can be made"[58].

Involving particularly vulnerable women (for instance those living in poor socio-economic conditions) in clinical research should be carefully assessed, in order to avoid, on one side, any form of discrimination by excluding specific population groups from participation, which can directly (as individuals) or indirectly (as population group) benefit them; and, on the other, to prevent any form of coercion or undue inducement.

The role of male family members or partners may have a different impact on the woman's decision to participate in clinical research in diverse cultural groups. Looking into a number of geographical and cultural perspectives, the Nuffield Council on Bioethics highlights some considerations about women decision- making: in some South Asian regions, **"**women may not always be able to express personal opinions on even minor matters, let alone the issue of whether they would like to take part in research. The notion that individuals are free to make their own decisions will therefore be less familiar to such women**"**[59]; in China, women are usually not expected to obtain the permission of men or elders before deciding to participate in research. However, before consent can be sought, **"**a visiting research team's proposals will need to be discussed in an open manner through the offices of the village cadre committees**"**[60]; in many parts of Africa, women, especially in non-Muslim societies, have developed a more assertive position with regard to healthcare, often aided by mission hospitals, clinics and health focused non-governmental organisations. "As cultures are not fixed, researchers may need to find means of fostering discussion about what is required by cultural norms in a particular context. For example, research in South Africa has shown that even within a culture with strong beliefs about the importance of the community, many women favour the approach of requiring individual consent to research". In addition, in some areas of Uganda with traditional social and cultural values, men (husband/father as the head of the family) are expected to decide on all matters, especially sensitive ones affecting family members. Therefore, family members who do not submit to such decisions may face serious consequences including domestic violence and/or divorce. In this context, **"**women and children will tend not to participate in a study unless permission has been granted by the head of the household**"**[61]; in Latin America, unlike the cultural contexts mentioned above, community consent or other types of group consent are not common practice. Although collective information can be provided to rural communities or ethnic minorities, such as indigenous populations, consent by individual participants is accepted[62].

In this regard, the US National Bioethics Advisory Commission recommends that **"**researchers should use the same procedures in the informed consent process for women and men. However, ethics review committees may accept a consent process in which a woman's individual consent to participate in research is supplemented by permission from a man if all of the following conditions are met: a) it

[58] Royal College of Physicians, *Guidelines on the practice of ethics committees in medical research with human participants*, cit.

[59] Nuffield Council on Bioethics, *The ethics of research related to healthcare in developing countries*, cit.

[60] Nuffield Council on Bioethics, *The ethics of research related to healthcare in developing countries*, cit.

[61] Nuffield Council On Bioethics, *The ethics of research related to healthcare in developing countries*, cit.

[62] Nuffield Council On Bioethics, *The ethics of research related to healthcare in developing countries*, cit.



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would be impossible to conduct the research without obtaining such supplemental permission; and b) failure to conduct this research could deny its potential benefits to women in the host country; and c) measures to respect the woman's autonomy to consent to research are undertaken to the greatest extent possible. In no case may a competent adult woman be enrolled in research solely upon the consent of another person; her individual consent is always required"[63].

### 3.4. Best practices on culturally-tailored health communication programs with a gender perspective

The *Gender guide for health communication programs* issued by the US Center for Communications Programs (2003) points out the importance of including gender concerns in health communication initiatives, aimed at making health messages more effective and foster awareness of the necessity of equity in terms of gender needs. A gender perspective in communication should take into account ways in which gender influences health needs and concerns, different roles and interests of women and men, as well as the reception of health messages. Seeking feedbacks of effective communication strategies is highly recommended, also by conducting evaluations in different cultural communities. It is critical to speak to women and men separately to obtain reliable gender-informed perspectives.
In this context, it is possible to identify a set of culturally-sensitive communication strategies with a gender perspective (i.e. "the ways in which gender influences health needs and concerns, the reception of health messages, and access to and control over health communication interventions"[64]): health communication programs should take into account different needs, roles, and interests of women and men; spousal communication and power dynamics between men and women; decision-making processes; social and cultural constraints and opportunities; communication initiatives should assess potential positive and negative program impacts and communication capacity (e.g. access to media for women and men and their media habits: devising which communication channels, radio, tv, print, talks, community meetings, are used by women/men for health information and how this differs according to age and education levels); communication strategies should ensure that services, supplies, and practices of chosen media do not reinforce gender stereotypes; pretesting and re-testing messages, concepts, and intended program formats with women and men separately to determine what works well for women and what works well for men. These materials should be tailored to the different cultural groups they are addressed to.
In the context of a cultural adaptation of information, Brown *et al.* reported that ethnic-specific information about health risk associated with recipients' health condition increased recruitment of African American women into clinical trials. They provided evidence that "many patients and family members misunderstood trial information and that many felt that a question prompt lists and decision aids would assist in decision-making". In addition, they suggested that the best strategies to reduce enrolment barriers and retain participants are associated with the ability to keep constant contact with participants. Moreover, being respectful and showing a caring attitude are the important

[63] US NATIONAL BIOETHICS ADVISORY COMMISSION, *Ethical and Policy Issues in Research Involving Human Participants*, 2001, p. 4.
[64] JOHN HOPKINS UNIVERSITY CENTER FOR COMMUNICATION PROGRAMS, *The Gender Guide for Health Communication Programs*, 2003.

factors in this population. The authors equally stressed that findings may not be specific to African American population but can apply to other ethnic groups[65].

Among the innovative strategies aimed at the inclusion of women from diverse cultural backgrounds in clinical trials, Jones *et al.* illustrated a *Facebook* advertising of a clinical trial with African American women and provide a practical guide to create and publish a Facebook ad for a target population. This approach can be adapted to different study populations in diverse cultural settings. Although online recruitment lacks face-to-face contact, there is evidence that for many, such contact did not deter recruitment. Advertising for enrolment in clinical trials via social networking sites, specifically Facebook, has led to encouraging results in expanding geographic reach while still targeting a population and maintaining confidentiality. A broad representative distribution, including those less accessible via traditional venue sampling due to stigma may be reached online for participation in clinical trials[66].

## 4. Strategies to overcome communication barriers between researchers and research participants

### 4.1 Cultural competence training for researchers working with subjects from diverse cultural and religious backgrounds

For an adequate informed consent process, personal interaction between subjects involved in clinical trials and researchers is essential. The informed consent process involves an interactive conversation between the research participant and the research staff, during the whole process.

The research staff should be educated to deliver the information in an efficient and responsive manner. With training, research staff may become more confident in the accuracy of their knowledge and improve their interaction skills. CTTI Recommendations stressed the need that research staff obtaining consent should be trained to do so. An informed consent training program should aim to improve knowledge and communication skills of researchers[67].

Researchers should improve their ability to communicate effectively with diverse patients, especially when they are people from diverse cultural and religious backgrounds. In these cases, communication can be more challenging. It is therefore recommended that researchers develop cultural competence, namely awareness of cultural influences on patients' health beliefs and behaviours.

Cultural competence of the research team is recognised as very important[68]. More specifically, cultural competence training for researchers would guarantee an effective communication and interaction with participants from diverse cultural and religious backgrounds. The development of cultural

[65] R.F. Brown et al., *Perceptions of participation in a phase I, II, or III clinical trial among African American patients with cancer: what do refusers say?*, in J Oncol Pract. 9 (6), 2013, pp. 287-93.

[66] R. Jones, L.J. Lacroix, *Facebook Advertising to Recruit Young, Urban Women into an HIV Prevention Clinical Trial,* in *AIDS and Behavior*, 21(11), 2017, pp. 3141-3153.

[67] Clinical Trials Transformation Initiative, *CTTI Recommendations: Optimizing Mobile Clinical Trials by Engaging Patients and Sites*, Feb. 21, 2019, available at https://www.ctti-clinicaltrials.org/projects/engaging-patients-and-sites, last visited March 1st, 2019.

[68] M. Truong, Y. Paradies, N. Priest. *Interventions to improve cultural competency in healthcare: a systematic review of reviews*, in *BMC health services research*, 2014, 14:99.



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competence needs to be seen as an ongoing process. Strategies to develop cultural competence of researchers in order to increase the recruitment of participants who are unable communicate fully due to cultural barriers should be promoted. These strategies should include the following aspects. Firstly, an adequate education of researchers should be promoted: an increase in the intercultural skills of the researchers is recommended, in order for them to be able to interact appropriately with participants from diverse cultures, in the perspective of intercultural communication. It could be useful to devote adequate consideration, within university training paths, to studies focusing on the therapeutic relationship in an intercultural perspective (the so-called transcultural medicine).
Finally, it could be important to guarantee a continuity of the research team. In fact, when the researcher who interacts with each participant is the same through the different phases of a clinical trial, this helps build a bond of trust between researchers and prospective participants and maintain consistency in the conveyance of information;
These strategies aim at strengthening an intercultural sensitive approach to communication among researchers and potential participants in clinical trials and may contribute to improve participation of people from diverse cultural backgrounds in research. In this sense, open and understandable communication between researchers and participants during the whole research process could help creating trust in relationship and maintaining consistency in the information, thus, overcoming one of the main barriers in communication.

### 4.2. Innovative strategies to improve the informed consent process in an intercultural setting

Advances in technology enable novel communication approaches, allowing researchers to adapt the informed consent process to persons of diverse health literacy of all backgrounds[69]. Apps, tablets, video, interactive computers, robots, personal digital assistants, smartphones, and wearable technology, could help to modernize and improve methods for obtain informed consent. The adoption of digital tools within the IC process could facilitate and develop practices that are more culturally appropriate and that reflect the values, customs, and level of exposure of local communities to research[70].
At international level, the guidelines include an ethical analysis of the use of digital technologies in healthcare in general. The Report of the International Bioethics Committee of UNESCO (IBC) on Big Data and Health (2017) stressed the importance and problems about informed consent given electronically (informatic consent), specifying that electronic means in clinical research may be efficient and effective as long as there are safeguards implemented to ensure that the participants' autonomy is respected[71]. The CIOMS International Ethical Guidelines for Epidemiological Studies (2009), focus,

[69] J. KAYE, E.A. WHITLEY, D. LUND, M. MORRISON, H. TEARE, K. MELHAM, *Dynamic consent: a patient interface for twenty-first century research networks*, in *European Journal of Human Genetics*, 2015, 23(2), pp. 141-146; E. M. MESLIN, S.A. ALPERT, A.E. CARROLL, J.D. ODELL, W.M. TIERNEY, P.H. SCHWARTZ, *Giving patients granular control of personal health information: using an ethics 'Points to Consider' to inform informatics system designers*, in *International Journal of Medical Informatics*, 2013, 82 (12), pp. 1136-1143.
[70] A.C. JONES, E. SCANLON, G. CLOUGH, *Mobile learning: Two case studies of supporting inquiry learning in informal and semiformal settings*, in *Computers & Education*, 2013, 1-22.
[71] UNESCO INTERNATIONAL BIOETHICS COMMITTEE (IBC), *Report of the IBC on Big Data and Health*, 2017, available at https://unesdoc.unesco.org/ark:/48223/pf0000248724, last visited March 1st, 2019.

in the Guideline n° 6, on responsibility of the investigator for ensuring the adequacy of informed consent from each subject[72]. When subjects are enrolled in studies by mail or electronic means (e.g., e-mail, Internet, etc.), difficulties may arise in fulfilling investigators' duties to ascertain that subjects adequately understand relevant facts. Potential subjects enrolled in these ways should therefore be given a means (such as a toll-free phone number or email address) to enable them to pose questions to, and receive answers from, the research team concerning the study.

Tools to provide information are the following:

a) videos: the value of audio-visual interventions as a tool for helping to improve the informed consent process for people considering participating in clinical trials should be take into account. Audio-visual presentations can ensure the clear delivery of information that is complete, consistent and unbiased, to supplement or reduce staff time spent in seeking informed consent. A study of the feasibility of using multimedia technology during the informed consent process for clinical research reported that the use of the video made information more understandable[73];

b) animations: a study on 58 focus groups of African Americans, Latinos, Native Hawaiians, and Filipinos in Los Angeles/Hawaii demonstrated that via animation improved the communicating information about health research[74]. After viewing the video, participants appeared to be able to identify gaps in knowledge about research and to express an increased desire to seek information to address these gaps. In addition, the findings also suggest that animations may be augmented when accompanied by a community facilitator or a family member. The advantage of the animations is that are easier to be customized according to the subject's characteristics;

c) interactive tools: in general, interactive tools have a better impact in comprehension of information and long-term memory then non-interactive tools, so a combination of interactivity and animation could be a good solution to design innovative digital-based strategies[75].

Digital innovation and interactivity can indeed play a central role for the success of these strategies. Scientific evidence highlights the positive impact of a strategy blending personal relationship and innovative, video-based and digital tools[76].

A scientific study focused on a self-administered, web-based survey using an experimental between-group design to compare the effects of four informational aids on respondents' understanding of core aspects of research[77]. The aim was to verify what methods could improve informed consent in clinical research settings. Multimedia informational aids assessed were the following: animated videos (audio, character-driven); slideshows with voice-over (audio, not character-driven); comics (no audio, character-driven); text (no audio, not character-driven). Findings showed that knowledge

[72] CIOMS, *International Ethical Guidelines for Epidemiological Studies*, 2009, cit.

[73] A. SYNNOT, R. RYAN, M. PRICTOR, D. FETHERSTONHAUGH, B. PARKER, *Audio-visual presentation of information for informed consent for participation in clinical trials*, in *Cochrane Data base of Systematic Reviews*, 2014, 1-40.

[74] G. SHEBA ET AL., *Using Animation as an Information Tool to Advance Health Research Literacy among Minority Participants*, in *AMIA Annual Symposium Proceedings*, 2013, e16-e28.

[75] R.L. OWNBY ET AL., *Health literacy predicts participant understanding of orally presented informed consent information*, in *Clinical Research Trials*, 1 (1), 2015, pp. 15–19.

[76] A.R. TAIT, T. VOEPEL-LEWIS, *Digital multimedia: a new approach for informed consent?*, in Journal of American Medical Association, 2015, 463.

[77] S.A. KRAFT, *A randomized study of multimedia informational aids for research on medical practices: Implications for informed consent*, in *Clinical Trials,* 2017, pp. 94-102.

scores were significantly higher for the two informational aids with an audio component (animated videos and slideshows with voice-over) than in the two without (comics and text). Consequently, using multimedia informational aids (especially if with audio approach) could help to bridge the knowledge deficit about research and guarantee an information tailored to persons of diverse health literacy levels and of all backgrounds[78].

In this regard, the Clinical Trials Transformation Initiative (CTTI) developed a Project, with the objective to identify barriers to communication of informed consent elements and develop recommendations for improving the informed consent[79]. Among these:

1) engaging patients and sites to drive adoption of mobile technology in clinical trial; engaging patients and sites in planning clinical trials using mobile technology, including protocol design, technology selection, and pilot testing, in order to enhance satisfaction and engagement, recruitment and trial feasibility. Patients' perspectives can be identified through advisory panels, surveys, focus groups, simulation exercises and other methods (a range of relevant perspectives should be represented, including appropriate and diverse racial and cultural backgrounds);
2) select mobile technologies based on requirements of the study and needs of the intended user population, starting with the aspect that the assessment is intended to measure (engage patients and sites in technology selection; conduct feasibility studies to ensure that study participants find the technologies easy to learn, simple and convenient to use, physically comfortable);
3) when planning a trial using mobile technologies, identify and conduct necessary pilot studies with sites and a representative patient population. Mobile technologies can change the way sites and participants interact during a trial (For example, mobile technology can reduce the need for in-person visits and facilitating participation in the trial).

Improving the consent process for culturally and linguistically diverse population participants has been the focus of several studies, which emphasized the importance of adopting a multimethodological approach, including the use of culturally and linguistically sensitive multimedia tools, to tailor the information process to the needs of subjects from diverse cultural and religious backgrounds in clinical research. Multimedia resources may have key roles to play in addressing health research literacy by explaining medical research, enabling researchers to assess comprehension through testing, and improving participant comprehension of consent forms and procedures. Furthermore, multimedia tools could be used by researchers, who do not necessarily speak the language of the research participants[80].

Clinical trial participants in sub-Saharan Africa often have limited understanding of the study information provided during the informed consent process. In countries such as the Gambia, where local

[78] In the UK, the Guidance of Health Research Authority (HRA), with particular regard to clinical trials, stressed the importance of the use of media or non - text - based approaches (videos, cartoons, animations, info graphic cards, flipcharts, brochures and audio). These methods may be used as patient- friendly introductions to complement, or replace, the traditional paper information sheet. See THE HEALTH RESEARCH AUTHORITY, *Guidance relating to the inclusion or exclusion of participants in research who may have difficulties in adequate understanding of English*, 2018.

[79] CLINICAL TRIALS TRANSFORMATION INITIATIVE, *CTTI Recommendations: Optimizing Mobile Clinical Trials by Engaging Patients and Sites*, cit.

[80] J. HUGHSON ET AL., *A review of approaches to improve participation of culturally and linguistically diverse populations in clinical trials*, in *Trials*, 2016, 17:263.

languages have no standard written form, translating documents into the local language and back translating into the national language is impractical[81]. In particular, illiterate participants may not understand research concepts and this fact could undermine their ability to give truly and effective informed consent.

A study on effectiveness of the multimedia tool in malaria treatment trial in the Gambia confirmed that use of a multimedia informed consent tool results in significantly better understanding of clinical trial information than the current standard method for obtaining consent. In the scientific study, the multimedia tool was tailored to the cultural and linguistic diversity of the Gambian population: the visual and verbal information presented through the DVD resulted clear and easy to understand in an area of the Gambia with low levels of literacy.

### 4.3. Ethical challenges related to the use of ICT and social media in clinical research: e-Consent in an intercultural setting

The expression 'e-Consent' refers to the use of any electronic media (such as text, graphics, audio, video, podcasts or websites) to convey information related to the study and to seek informed consent via an electronic device (such as smartphone, tablet or computer). These electronic methods are adopted by researchers either to supplement or substitute the traditional paper-based approach. E-consent may increase understanding of the study, particularly for people with a low educational level or limited literacy.

Most studies have shown that participants' recall of key facts about a study is better with the use of e-consent with these interactive features than with paper forms[82]. However, there are also challenges regarding electronic consent for researchers. First of all, when the consent documents are provided by electronic methods there is the problem to verify the participant's identity. Additionally, there is the problem of the high initial expense for infrastructure and technology to manage online documents and establish systems to validate electronic consent.

The use of multimedia informational aids in clinical research shows many advantages.

Ensuring participant comprehension continues to be a challenge in e-Consent. A study focused on assessment of a convenience sample of participant reaction to the e-Consent implementation (within the Parkinson mPower mobile study) using a mixed methods approach[83].

The starting point was that to fully capitalize on mobile technology we must develop companion self-administered electronic informed consent (e-Consent) processes. Incorporating novel informed consent approaches on a target study population diverse in terms of ethnicity, primary language and health literacy, demonstrating that the use of the electronic consent (e-Consent) not only increases the opportunity to recruit patients culturally isolated, but also has the potential to increase the trust.

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[81] M.O. Afolabi et al., *A multimedia consent tool for research participants in the Gambia: a randomized controlled trial,* cit., p. 320.

[82] J. Kaye, E.A.Whitley, D. Lund, M. Morrison, H. Teare, K. Melham, *Dynamic consent: a patient interface for twenty-first century research networks*, cit., 141-6; C.M. Simon, D.W. Klein, H.A. Schartz, *Interactive multimedia consent for biobanking: a randomized trial*, in *Genetics in Medicine*, 18 (1), 2016, pp. 57-64.

[83] M. Doerr, A. Maguire Truong, B.M. Bot, J. Wilbanks, C. Suver, L.M. Mangravite, *Formative evaluation of participant experience with mobile eConsent in the App-Mediated Parkinson mPower Study: a Mixed Methods Study, in Journal of Medical Internet Research Mhealth Uhealth*, 5 (2), 2016, pp. 42-47.



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A study underlines the advantages of use of technology in clinical trials[84]:

a) communication: technology tools improve communications not just with study staff, but also with patients and communities.
b) recruitment: using apps and social media could increase the number of participants contacted and enrolled.
c) retention: mobile phones/devices, apps, and social media offer the opportunity to connect with participants more often and potentially improve their involvement and retention. Smartphones, apps, and wearable body sensors can allow for large quantities of data to be collected automatically and not require face-to-face interactions with researchers.
d) e-technology-based interventions can reduce resource requirements related to staff training and ongoing supervision, maintain consistent delivery of an intervention.
e) data collection: use of registries can improve targeted recruitment and make standard clinical data available in real-time for study outcome purposes. Digitized forms have been shown to improve data quality.

The use of social media in research consent may improve the quality of the consent process by overcoming awareness issues about trials and in particular low understanding of the concept of research. Furthermore, the use of these methods may improve comprehension issues associated with medical and legal jargon. The influence of ICT and the Internet including social media was an important factor in how healthcare services in Thailand are being offered and practiced. In Thailand, the use of social media for Thai healthcare professionals is emphasized on Facebook and LINE Chat applications. Thailand has achieved an elevated level of access to e-health services and use of ICT[85]. The use of social media in research consent allows research participants can open up online dialogue and interaction with professionals and exchange information during the process from anywhere and at any time[86].

App-based research has the advantage that all or most of the research study can be conducted through the smartphone, from obtaining informed consent to collecting data[87]. Conducting health research and obtaining informed consent on smartphones raise several unique challenges and limitations. The most important limitation is that there is no face-to-face confirmation of identity. Another challenge with respect to app-based research is data security and privacy.

Despite multimedia tools in clinical research have certainly important advantages, some ethical challenges to the use of digital technologies in informed consent remain.

a) First of all, Information Technologies could involve risks related to the processing and protection of privacy and personal data and misuse of these. A fundamental challenge lies in ensuring that patient data remain confidential and secure in order to build trust in the use of ICT[88].

[84] C. ROSA ET AL., *Using e-technologies in clinical trials,* in *Contemporary Clinical Trials,* 45, 2015, pp. 41-54.
[85] S. JANTAVONGSO, *Ethics, social media and e-health in Thailand,* in *Journal of the Thai Medical Informatics Association*, 1, 2015, pp. 25-37.
[86] D. O'CONNOR, *The apomediated world: regulating research when social media has changed research*, in *The Journal of Law, Medicine & Ethics*, 41 (2), 2013, pp. 470-83.
[87] C. GRADY, *The changing face of informed consent*, in *The New England Journal of Medicine*, 2017, pp. 856-867.
[88] EGE, *The ethical implications of new health technologies and citizen participation*. *Opinion n. 29*, 2015, available at https://publications.europa.eu/en/publication-detail/-/publication/e86c21fa-ef2f-11e5-8529-01aa75ed71a1/language-en/format-PDF/source-77404221.

b) The Guideline n° 23 (CIOMS, 2009) provides for that the investigator must ensure that an appropriate informed consent procedure is applied and that data confidentiality is maintained[89]. Subjects' privacy, confidentiality and security are at stake when data are conveyed to others electronically. In this regard, CIOMS, 2016, Guideline n. 22 (Use of data obtained from the online environment and digital tools in health related research) highlights the need for privacy protection in combination with technological capabilities[90]. When researchers use the online environment and digital tools to obtain data for health related research they should assess the privacy risks of their research, mitigate these risks as much as possible and describe the remaining risks in the research protocol. The development of regulations and codes to allow for the widespread, lawful, ethical and secure use of IT in research consent should be supported[91].

c) Furthermore, technology evolves constantly and available tools change continuously and keeping track of progress and available tools is challenging. Although smartphone use and familiarity with mobile technology are growing, they are certainly not evenly distributed across populations[92]. Scientific literature shows that in the African context, experiences with integrating ICT in action-oriented and cross-cultural communication projects have been developed later and more slowly than in high-income countries[93]. A digital divide means that unequal access to digital technologies as well as highly divergent levels of online literacy persist[94].

d) Even more of an ethical challenge is the inability of a part of population to participate in smartphone-based research studies because of issues related to access or cost of smartphones or data connectivity. Another issue concerns access to technologies. There is, today, a "digital divide" because of many factors, such as a socio-economic gap and the network coverage for the Internet in the area under consideration[95]. Equal access should be guaranteed, allowing everyone to acquire tools, knowledge, skills to use new information technologies, according to the principle of equality, equal opportunities and non-discrimination[96].

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[89] CIOMS, *International Ethical Guidelines for Epidemiological Studies*, 2009, available at https://cioms.ch/wp-content/uploads/2017/01/International_Ethical_Guidelines_LR.pdf

[90] CIOMS, *International Ethical Guidelines for Health-Related Research Involving Humans*, Geneva, 2016, https://cioms.ch/wp-content/uploads/2017/01/WEB-CIOMS-EthicalGuidelines.pdf.

[91] C. TABER ET AL., *Improving the Quality of Informed Consent in Clinical Research with Information Technology*, in *Studies in Health Technology and Informatics*, 2016, pp. 135-142.

[92] C.R.N. GRADY, *The changing face of informed consent*, cit., p. 856.

[93] N. LARSEN, *ICT-based, cross-cultural communication: A methodological perspective,* in *International Journal of Education and Development using Information and Communication Technology* (IJEDICT), Vol. 10, Issue 1, 2014, pp. 107-120.

[94] EGE, *The ethical implications of new health technologies and citizen participation. Opinion n. 29*, 2015, cit.; ITALIAN COMMITTEE FOR BIOETHICS (NBC), *Opinion on Ethics, Health and New Information Technologies*, 2006.

[95] ITALIAN COMMITTEE FOR BIOETHICS (NBC), *Opinion on Mobile Health Apps: bioethical aspects*, 2015.

[96] ITALIAN COMMITTEE FOR BIOETHICS (NBC), *Opinion on Information and Communication Technologies and Big Data: Bioethical Issues*, 2016.