I.

Dilemmas of informed consent process in clinical research from a multireligious perspective[1]

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ABSTRACT

Improving the health literacy of patients in relation to medical practices and research is essential for upholding the principle of respect for autonomy – that is, respecting the patient's ability to make self-governed choices regarding medical interventions or research participation that reflects the patient's beliefs and values. This paper considers the challenges of informed consent (i.e. ethical gaps, barriers, and priority needs) that are unique to certain vulnerable groups, namely preadolescents, adolescents, and pregnant women, with a specific emphasis on how multicultural and interreligious variables should be considered when assessing the appropriateness of the current documents relying on the notion of informed consent. In exploring how we are to improve the process of obtain informed consent, this contribution pays particular attention to the relevance that different cultural and religious backgrounds can play a role in shaping the approach to clinical research by individuals, bringing forward valuable information on how we could improve our understanding and interaction with one another by knowing more about our different initial stands -for the benefit of the whole medical and civil community.

Keywords

Autonomy, Clinical research, Informed consent, Religion, Vulnerability.

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The UNESCO International Bioethics Committee stressed in more than one occasion that an individual has to be informed as much as possible on the outcomes of the procedure in which he/she is involved in: "The close connection between autonomy and responsibility supposes that consent be freely given by the person concerned, that the clearest possible information be provided, that his/her faculties of comprehension be intact, that he/she has been able to measure the consequences of the illness and its evolution, and that he/she understands the advantages and disadvantages of possible alternative treatment" (UNESCO IBC 2008: 15). In addition to these requirements, various cultural and social variables are to be considered when assessing the ethical validity of the informed consent process. Often, such considerations might impinge upon the monolithic, person-centered version of autonomy that we tend to give for granted in the Western contexts, creating a space for new versions of vulnerability -in which the vulnerable population is represented by those individual unable to see their attitude and perception of autonomy as sufficiently represented by current legislations. In some scenarios for example, "communal autonomy" or "relational autonomy", a version of autonomy that sees the deliberation and the legitimacy of a decision to belong not only to a single person, but rather the community to which one belongs (i.e. family). Often leaders of the community -nearly always family members- are those who make the decisions and their judgment is not questioned due to their age, expected wisdom and knowledge of the community's internal dynamics in place. In this work, we want to address some relevant aspects to be considered if we are to improve the informed consent process in clinical trials in the increasingly multicultural society we live in.

Individual and Relational Autonomy

In line with what just described, the words of Joseph Tham and Marie Letendre are particularly relevant to understand more accurately how some of our standard ways of conceptualizing the discussion around informed consent might not be as given as expected. "Cultural norms specify behavior. 'Honesty is an ideal value for most Americans, but it varies in strength as a real value for other cultures' (Spector R. 2000, Surbone A. 2006). Honor is highly prized in the Japanese culture as is female purity in the Islamic world. Direct eye contact is avoided in several cultures, notably Asian and the Middle Eastern culture; the Navaho use silence to formulate their thoughts in order to give the most complete answer. Trust is given only to family members in the Gypsy culture. Masculine and feminine pronouns do not exist in Asian languages, and 'yes' does not always mean the affirmative since many cultures use the 'yes' as a way of avoiding an embarrassing 'no'. This is just a short list of cultural variables that inform and form communication styles. A cross-cultural health care ethics combines the tenets of patient- family centered care with an understanding of the social and

cultural influences that affect the quality of medical services and treatment. Developing sensitivity to different cultures can make health care programs and activities attractive and interesting for a broader population base. In contrast, a lack of cultural sensitivity can deter people from using health care services" (Tham J.S., Letendre M.C. 2014). Hence, not all documents that assume that focusing on the individual might be sufficiently sensitive towards how one person with a cultural, religious or ethical background might want (or is capable) to express her views, values and desires if disconnected from her community. In accepting this reality, it is equally important to bear in mind that -though contemplated- relational autonomy has no effective role in the shaping of informed consent in official forms. As the notion of informed consent relies on a set value of individual autonomy that not all cultures and approaches to life share, a patient's cultural disposition and past experiences with medical health care professionals will have an impact on the amount of trust that they can have towards medical personnel (that they might see as more "external" to their tradition/heritage, and therefore also not included in that relational autonomy that connects them to their surrounding community) and "their" knowledge -seen as a way of "tricking" the person to the advantage of the "external entity". This could include a distrust in the actual efficacy of a vaccine for example. Although local culture may shape people's perception over time, people are more likely to trust experts that share a similar background, tradition, religion and culture with them (Kahan D.M., Braman D., Cohen G.L., Gastil J., Slovic P. 2010). When working with ethnic minority patients, it is important to note that comprehension may also transcend simply linguistic barriers.

The conceptualization of illness and cultural bias both play a role in the ways that information is presented and understood. Thus, it is important to understand the role that culture plays in obtaining informed consent (Dein S., Bhui K. 2005). In particular, in multicultural societies, where a large portion of the society is made up of immigrants with varying cultural backgrounds, there may be differing attitudes regarding the role of physicians. Moreover, the quality of informed consent may be dependent on the relationship between a physician and their patient. To improve the physician-patient relationship, and for the consent gained to be effective, there has to be a partnership based on openness, trust, and good communication between the two parties (General Medical Council. 2008). Individual's religious beliefs or related cultural values can lead to questions and concerns that health professionals, unfamiliar with the religion or culture, have not encountered before. Not only does an immigrant have to trust the medical personnel, but also the attitude that the vaccinators display towards the immigrant has to be positive. It has been shown that culture (which can also include religious and spiritual backgrounds) can impact one's vulnerability to infectious diseases. Rejecting vaccination due to religious or cultural values is not a new phenomenon; there have been reports

of vaccines-preventable outbreaks in religious schools, congregations and religious communities (Thomas T.L. *et al.* 2013). As a case study, the World Health Organization reported that in a region in Nigeria 16% of the children were vaccinated against polio. The reason for the low vaccination rates is that the community is predominantly Muslim, and they believe that the polio drops are used as a tool to sterilize children. Likewise, a study from the Netherlands has shown that municipalities with high orthodox protestant domination have lower vaccination rates compared to municipalities without an orthodox protestant domination (Grabenstein J.D. 2013), with the refusal to vaccinate children among orthodox protestants being based on a combination of religious objections, family tradition, and fear of possible side-effects. A discussion of the views that every religion or culture has with regards to the link between informed consent and clinical research vaccination programs is outside the scope of this paper. Still, here the focus will concern six of the major religious and cultural traditions (Buddhism, Christianity, Confucianism, Hinduism, Islam and Judaism) with respect to immunization (i.e. vaccination programs). These specific religions and cultures have been selected due to their prominence in the Western context (above all, Europe), as well as the fact that, together, they represent an extremely high percentage of the world's population. Broadening the discussion back to the way informed consent notion interacts with biomedical research, some of the key questions that we want to address here are:

I. *How much of the notion of informed consent is applied in one's tradition? And in which way?*
II. *Can or should we have different informed consent forms for differently vulnerable populations?*
III. *Do all traditions agree with the general principles behind informed consent (i.e. the prioritization of individual autonomy)? If not, what alternative values/approach could support widespread vaccination for example?*

In the following sections different answers to these and other questions from the different traditions considered will be highlighted.

Considerations from Buddhism

The Buddhist tradition does not strictly rely on individual autonomy (hence, on informed consent), but it sees life as one, meaning that all forms of life are essentially related to one another and share a common essence. As a result, the involvement in clinical trials is seen as a duty towards the community that must be embraced. Ellen Zhang provides us with a very important reading of the practical value of the informed consent forms, and the role of duty in the Buddhist tradition. "While Buddhism challenges an individual-oriented approach to autonomy, it also challenges an individual-oriented approach to

rights. Buddhism would accept 'negative rights' as a protective means for the interests of the patient yet having problems with using the language of rights without qualification to grapple with every moral issue. In addition, Buddhism would also speak of the importance of duty along with the right-talk. For example, in the case of vaccination, Buddhism will use duty rather than right to argue for it. In other words, it is not someone's right (i.e., individual's autonomy) to have, or not have vaccination; instead, it is someone's duty to protect oneself and others in society through a proper prevention of the infection and its respective immunization. Since vaccination concerns public health, Buddhists today will generally use vaccines to make sure their health is protected" (Zhang E. 2018: 11). As shown already in the next section of the paper, a general attitude -from individuals and from the State- that will give priority to public health and duties towards the community might not be ideal and it might also restrict our individual autonomy, but it is an approach that is shared both by other traditions and the Western secular approach.

Considerations from Christianity

The Christian approach towards vaccination is favorable and based on the principle of solidarity -that sees, as in other traditions, a moral duty to protect the vulnerable (in this case immunodeficient people). Concerning clinical trials and informed consent instead, the approach is less all-encompassing: to an extent suffering is to be seen as a connection to God, so it should be tolerated to an extent. However, individual autonomy and informed consent are also seen as valuable tools to shape one's spiritual path (free will is necessary to discern right from wrong), so they need to be defended as well and the ultimate judges of a participation to a clinical trial are single individuals (that are to be defended from external pressures nonetheless). As highlighted by Laura Palazzani, in the Christian perspective in bioethics: "informed consent is inspired by Jesus, who cured the sick with compassion, generosity, and understanding. Christians believe that disease and suffering are trials from God to bring them closer to salvation through death and into His grace. Scientific research should be done for the purpose of serving those who are ill, not solely or primarily for the benefit of the researchers. Research should be conducted according to accepted scientific principles and it must always be deemed necessary and potentially useful for the patient. It must never subject an individual to unnecessary or disproportionate risks, which overshadow the expected benefit from the research. The researcher must never participate in projects that may involve the treatment of the human subject as an object of that interest. Studies which may involve immoral cooperation with evil must be avoided" (Palazzani L. 2018: 16). More specifically in relation to Roman Catholicism, the Vatican has produced a large number of documents and statements (Pontifical Academy for Life. 2017) in which it supports wide-

spread vaccination, establishing clearly that the balance between risks and benefits for both the individual (the primary concern of biomedical research) and the community is not put at risk by the practice, and clarifying once and for all that the previous reticence against *some* vaccination that was using cell lines derived from a voluntary aborted fetus is not a real problem as vaccines are not produced in this way anymore.

Considerations from Confucianism

In the Confucian tradition, the link between the medical and political sphere is even more evident, with the latter having priority in the ethical assessment of a practice -including clinical research. Ruiping Fan expresses some of the peculiarity of this way of seeing the world and processing what the best way of behaving between and towards society is. Medicine is subordinated to politics as a way of benefiting society, hence the last call for any medical decision that concerns public health is given to politics. "Confucianism sees medicine as 'the art of *ren*'[2] (*renshu*), in contrast of seeing politics as 'the governance of *ren*' (*renzheng*). This indicates that both medicine and politics are taken to be the virtuous causes of humanity, but politics is more important than medicine perhaps because it can benefit people more than medicine in the proper context. […] Both traditional Confucian politics and medicine have a meritocratic and paternalistic tendency: only virtuous persons should become politicians or physicians, and they should make decisions to promote people's welfare in light of their own professional knowledge and judgements. In medicine, Confucian physician ethics has been similar to the Hippocratic Oath ethics in terms of medical professional obligations. It is the health and well-being of people that constitute the end of the art of medicine, but the judgment of such health and well-being lies in the hands of the physician. Throughout the history of Chinese medicine, the emphasis has always been placed on the physician's virtue and obligation in performing the art of *ren* for assisting people, rather than on providing adequate information to patients and their families. In reality, Chinese physicians must have gained consent, either explicitly or implicitly, from patients and their families in order to conduct medical treatment, but it is also clear that obtaining such consent before treatment has never been formally and clearly required in the tradition" (Fan R. 2018: 24). The settle aspect that must be considered is the balance between the inclusion of the family and the preservation of individual autonomy as the final, decisive notion of reference when deciding what to do with the patient or subject. There is room for a more sensitive attitude towards familiar networks and that is another linking ring with other traditions -not last the next one considered.

[2] « Ren » could mean : 'humanity', 'humaneness', 'goodness', 'benevolence', or 'love'.

Considerations from Hinduism

In the Hindu tradition, as for other Asian ones, the centrality of the individual is less relevant than in the West. Hence the moral acceptance of the clinical trials as legitimate does not derive from an acceptance of informed consent as the decisive factor, but rather from a conceptualization of relational autonomy both in legal and moral terms. In relation to this, John Lunstroth tells us: "the peoples of the subcontinent all share a concern for life and genuine friendliness and compassion for the other. This is their *dharma*[3], a central feature of their way of life. But it would be a mistake to think of *dharma* as meaning just that. *Dharma* also means law/right, in its broadest sense, and through this set of meanings it reads for government[4]" (Lunstroth J. 2018). Hence, it becomes evident that India represents a context in which people feel at the same time a duty and to act in accordance to the law -that prescribes them to care about the others- but this very "imposition" overlaps with a genuine, altruistic tendency to want to benefit and help the other. The bi-dimensional use of *dharma* in this sense, shows the richness that can be derived (also by other religious and non-religious traditions) from the consideration of other points of view on matter of informed consent. This is also evident in the next tradition considered.

Considerations from Islam

The Islamic tradition shares with the others considered here a general assessment of clinical trials as morally sound if and when done respecting the individual and with the intention to help the community. Yet, the specific geopolitical specificity of Islamic majority represents a specific global input that can stress the relevance of this dimension for the mission of our work. In an approach that might be defined as a way of decolonizing the debate also in respect to terminology, Aasim Padela tells us that: "as medicine has globalized so has bioethics. Just as medical technology and curricula are patterned after Western academies, bioethics teaching around the world also draws upon ethical principles and moral frameworks first worked out in the "West." (De Vries R., Rott L. 2011) It should come as no surprise then that four-principle Georgetown model of medical ethics is widely-taught in Muslim lands, and that research and medical practice guidelines in these countries are borrowed from American and European institutions. While there has been increased attention given to formulating

[3] The eternal law of the cosmos, inherent in the very nature of things.
[4] Swami Rama relates a remarkable story of how, when he was a young renunciate, he was walking in a mountain wilderness when he slipped and was severely injured. Pilgrims and others would simply walk by him as he suffered, secure in the knowledge that as a spiritually advanced being he would be fine (Rama S. 1978).

medical ethics guidelines based on indigenous Muslim cultural values or based on Islamic law, these efforts are in their infancy and not as yet widespread (Suleman M. 2017). Given the scant literature that is available on informed consent practices in Muslim contexts, these trends suggest that informed consent processes and structures likely mimic implementation models within the US and Europe. [I want to] draw attention to a couple of features of Muslim culture that problematize such consent processes and thereby necessitate a re-imagining of these procedures to suit Muslim sensibilities and culture" (Padela A. 2018: 35-36). Those features include the fact that Muslim societies operate out of a communitarian ethos and shared decision-making processes and that, for such societies, there is a need to ground ethics regulations within Islamic law -including during the implementation of informed consent processes. In other words, Padela is interestingly stressing that, within Muslim contexts, we might reach the same medical results we would in a context revolving more directly around that notion of individual autonomy (and informed consent), but it might sensitive to -at least consider to- adapt the language (e.g. terminology) to the audience to make the process of understanding and agreement smoother.

Considerations from Judaism

Judaism is extremely supportive of implementing biomedical advancements -especially when deemed to save lives of human beings- and hence, while giving importance to the autonomy of the individual, it generally supports immunization programs. Yet, as other traditions it sees small religious minorities that reject some "communitarian obligations" such as vaccinations for instance. David Heyd writes: "Indeed, there were a few cases in which leading rabbis instructed their communities to avoid immunization, but this occurred on the occasion of some medical controversy about the effectiveness of particular immunization (which led also some non-religious sectors to refuse to immunize their children). There is some general suspicion on part of these communities in the instructions of the State [of Israel],[5] but this suspicion is not derived from any formal religious argument against the idea of immunization as such. Living in small and relatively isolated communities, this sector in the population may feel that the 'herd effect' of most people getting immunized is sufficient to protect them from the disease without them taking the inoculation. Furthermore, some immunizations are thought of as conveying a negative moral message, such as the inoculation against papillomavirus, which prevents cervical cancer in young women. […] I should emphasize that the leading religious authorities do not oppose immunization and many of them

[5] Added for a clarification of context by the authors.

strongly encourage their followers to take them, including children and some of them consider them and clinical trials even as 'a holy war' against the threat of fatal illness, a war which calls for a universal draft" (Heyd D. 2018: 44). Here, a number of interesting, universally applicable, considerations are to be made. First, the fact that there might be connection between the proximity of risk and the rate of acceptance towards a certain treatment underlines how this way of processing information does represent a problem when we think of the globe. It is additionally difficult to sensitize Westerners towards malaria if this is not present in north America and Europe. Second, the role of religious leaders can help but is not guarantee of success. Third, the "spiritual damage" (i.e. the increase risk of pre-marital sex) of a practice might be considered more important than the actual medical damage in some instances.

Conclusions

As the main objective of this paper is to identify the ethical gaps, barriers and challenges currently present in obtaining informed consent from patients in different, challenging multicultural contexts and address the issues with some practical suggestions for future policies, two main conclusions can be extracted from the inputs here analyzed. They should be further expanded and taken into consideration when developing new models and forms that aim at providing convincing guidelines for the informed consent process. The first aspect to consider is the role of culturally sensitive and locally adapted (taking into consideration religious mindset, local peculiarities and geopolitical dinamycs in place) keywords. Implementation of some key terms directly referring to some religious traditions. For example, *kosher* or *halal* in vaccines, or reference to *xiaodao* and *dadao* as notions helpful to conceptualize better why we, as single individuals, should behave in a certain way in relation to society. Not only ensuring the "religious approval" from different traditions will increase the trust towards doctors and researchers, but it will also make more evident and immediate in the eyes of the believer terms that will help him filling up required forms and documents with more conviction, speeding up the process of sharing scientific information. The second point is that international accepted notions and values such as human duties, (UNESCO. 1998) should be considered when discussing informed consent, not only human rights. Where possible, use the specific tradition to reinforce the duties towards society as a whole. For example, the principle of the public interest (*maslahat al-ummah*) that sees vaccines as a way to protect *others* in Islam. Or the idea of *dharma* in the Hindu tradition in relation to laws and duties towards society (stressed by many other traditions through different concepts, notions and approaches, but still very similar in practice).

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