Reviewer's report

Title: Informed Consent and Registry-based Research - The Case of the Danish Circumcision Registry

Version: 0  Date: 28 Apr 2016

Reviewer: Allan Jacobs

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Ploug and Hølm (henceforth "Ploug" for stylistic reasons) address the tension between individual freedom and government power and provide an important contribution to the ethical literature. The manuscript highlights the intersection of two currently important and controversial topics in biomedical ethics - namely, the nature of consent required in archival research and the toleration of minority practices such as circumcision. Discussion of the former issue has chiefly focused on the tension between avoiding concrete and dignitary harms to the unembedded individual versus the imperative of obtaining new medical knowledge. Discussion of the latter has included the putative rights of the individual (with rights often tacitly regarded as benefits defined as important to a majority) versus benefits as perceived by a minority.

Ploug addresses the creation of a government registry in Denmark to follow all circumcised children. While we are sympathetic to his analysis, we feel that it could be extended further. Second, we discuss limitations regarding his proposed solution.

A project such as the Danish circumcision registry threatens people not merely as unembodied individuals, but as group members. Registry data is distilled from general medical data present in health and administrative records whose recording does not require specific consent. As Ploug notes, registered individuals are not anonymized, since the goal is to study their health longitudinally, and registrants' ethnicity usually can be readily ascertained by their names. Confidentiality of records such as these is a problem. Even if official Danish institutions are punctilious, data likely can be breached if they are useful or newsworthy. This has been demonstrated repeatedly by such events as Wikileaks, exposure of the Mossack Fonseca (Panama law firm) files, the hacking of the private email account of Hillary Clinton advisor Sidney Blumenthal, the Chinese hack of American government personnel records, and many hacks of commercial databases containing personal and financial information.

Presumably, someone interested in assembling a list of Muslims or Jews could hack circumcision data from the National Patient Registry even if there were no separate registry files. The SSI circumcision registry might facilitate this, but seemingly would not be essential. The privacy issue, then, is not one that would be resolved by tighter consent rules. Rather, it is due to the policy decision to make outpatient circumcision a reportable event, thereby incorporating all circumcisions into national medical files.
Ploug correctly identifies four problems. We would group them into two broader issues. One is the use of research to single out minority populations. The other, more general, issue is the use of data by the government and other institutions to use big data to provide information, and how to prevent abuses of such big data.

The Danish practices, taken as a whole, seem to single out minority populations, and we feel that Ploug could have placed more emphasis on this problem of discrimination. Denmark currently has a successful junior hockey program (ages 16 to 20), and this program is fed by children's programs. Concussions in hockey are common (1). Denmark similarly has a successful youth football (soccer) program. While concussions are less common than in hockey, they still occur in 0.18 per 1000 high school athletic exposures (1). Subconcussive injuries, caused by contact with balls or with other players, have also been linked to chronic traumatic encephalopathy and occur with greater frequency than frank concussion (2). If Denmark's concern were long-term serious effects to children of avoidable activities, it is at least as likely to find health hazards in these popular sports as in circumcision. To our knowledge, participation in these popular sports is not reportable to a national registry. Therefore, singling out minority cultural practices to quantify risks at a national level is problematic in light of the fact that cultural practices deemed acceptable by the majority such as youth sports are overlooked despite posing increased risks to children. We would have liked to see Ploug specifically address this issue of equity and possible discrimination.

Levin et al. (3), and Diekema (4) have suggested in the context of parental decision making that state intervention take into account the level of risk tolerated in standard practices. Levin et al suggest that "if society tolerates harms from comparable mainstream practices that imposes harms of a similar magnitude to the harms posed by the religious practice at issue, then it should not restrict that religious practice." Diekema suggests that "the pursuit of state intervention must be generalizable and impartial in the sense that all similar cases would also result in state intervention." If the Danish government were to observe this principle of fairness and equality, in addition to athletic injury, data regarding cosmetic procedures such as breast reduction (5), orthodontia (6), and rhinoplasty (7), among others, should also be reportable, and assembled in a national registry.

We also feel that the problems of stigmatization and medicalization are even more worrisome than Ploug discusses. The combination of these two effects could affect sexual health. If boys receive a consistent message from society that circumcision has an adverse effect on sexual health, and that they have been subjected to unwarranted mutilation, the result may well be a diminution of sexual capacity or enjoyment. In fact, it is unsettled in the academic literature as to what effects, if any, circumcision has on male sexual capacity and enjoyment (8). One also can speculate, that exposure to such characterization by the state and by state institutions could adversely affect the relationship between a circumcised boy and the parents who (according to circumcision critics) have abused him. Furthermore, there also is the possibility, that Ploug briefly alludes to, that circumcision will be driven underground by a combination of the registry and stigmatization.
Ploug discusses polarizing research. With this in mind, it is also important to note that studying the effect of circumcision on sexual health or function is extremely difficult and that a registry does little to advance this area of research. The parameters must be defined and measured. Measuring sexual health currently is subjective, and perception of one's sexual health may be influenced by expectations. Variation between circumcised and uncircumcised males might be influenced by the physical effects of the procedure, by cultural expectations, and (as previously stated) by adverse messages given to a circumcised minority. Of course, in a country where most people are circumcised, it is uncircumcised men who might be subjected to negative messages. Randomized trials of childhood circumcision will never be carried out. It is almost impossible to design a case-control or cohort study with appropriate controls, as there will be cultural and perhaps physical differences that will inevitably create selection bias. Unless reliable physical indicia of sexual health and satisfaction can be developed controversies in this area will continue.

Though not Ploug's burden to discuss background information regarding the registry, additional information would have been of interest and raises interesting ethical questions. The authors note that it was done at the request of the Ministry of Health, and required permission to collect the data from a government body called the Datatilsynet (Danish Data Protection Agency). What does this entail, and what criteria are used to grant or deny permission? Is there a body comparable to an IRB that judges the utility of the registry, the security of data, or its impact on vulnerable populations? Second, how is the integrity of the data protected? Are there procedures to ensure that (1) the data are maintained or audited in a manner that ensures its accuracy; (2) the data are open to qualified researchers; and (3) raw data from any publication would be subject to audit and re-analysis to the extent that is customary?

We now turn to Ploug's recommendations, with which we take issue. A requirement for informed consent would not address the problems that Ploug elaborates, and would interfere with important medical progress. Yet, if the purpose or effect of this research is to discriminate against members of a religion or ethnic group, or to facilitate identification of members of such groups on a large scale, the unethical nature of this research would not be rescued by consent of all of the subjects or, a fortiori, by the consent of some of them.

Conversely, the likely value of analyzing big data is so great as to overwhelm the magnitude of any dignitary injuries, at least from the standpoint of utility. In any event, it seems unlikely that many states would enact consent requirements that would significantly impede the possibility or ease of obtaining knowledge from retrospective data review, since such knowledge is highly likely to greatly improve health and control costs. The impetus for conducting such research is so strong that it must be taken as a given that limitations through consent are impractical. Analysis must therefore be centered on how concrete injury (as opposed to the dignitary harm of having one's data subject to group analysis) can be averted. Most big data research, whether involving tissue banks or clinical data repositories, is unlikely to harm patients beyond the possibility of lost privacy. Unlike collection of circumcision information, analysis of population data on (for example) coronary heart disease or myasthenia gravis is unlikely to induce the state to interfere
with the views or practices of specific religious or cultural groups. Furthermore, though controversially, there may be an ethical obligation to participate in research (9).

The authors cite several sorts of diseases in which privacy considerations may be a factor, including not only minority groups, but diseases that are socially stigmatized. The importance of such research, and the fact that there are alternative ways of obtaining data on individual patients from non-research records, suggest that the consent process is not an adequate safeguard. Rather, control of the use of data for medical research, must take place at the institutional level, and not the patient level. There must be both substantive limits on the power to use large-scale data and there must be procedural safeguards to ensure that deviation from the substantive standards is unlikely. The standards might begin with demonstration of a reasonable suspicion that there is a potential health problem, which Coleman (10), as well as Diekema (4) and Jacobs and Arora (11) regard as a requirement for government action. Whether the probe is discriminatory, as outlined above, should be a factor. Finally, research approval should follow the spirit of Dworkin's warning that

A state "may not curtail liberty, in order to protect an intrinsic value, when the effect on one group would be special and grave, when the community is seriously divided about what respect for that value requires, and when people's opinions about the nature of that value reflect essentially religious convictions that are fundamental to personality (12)."

Creation of a registry or data bank for research purposes should require review and approval from sources outside the agency. Such reviewing entities should be able to evaluate both the scientific validity of the proposed enterprise and its impact on individual rights. An institutional review board alone would be necessary but is not adequate; it is skewed toward a scientific viewpoint. Other bodies should review provisions for data security and for the impact of the project both on minorities and on society as a whole. As a hypothetical example, use of a large collection of photographs in the public domain to find ways for police to determine if people are lying would not have particular impact on minorities, but might threaten civil liberties generally. Members of impacted cultural and other groups, and organizations professing to represent those groups, should have adequate opportunity to present their views to agencies formulating the regulation establishing registries or similar research, as the American Administrative Procedures Act (APA) is supposed to provide (12). Perhaps lay interests should have a voice even stronger than the APA comment and review provision to ensure that projects that unreasonably threaten interests of citizens as a whole or minority groups should not be approved.

We do not maintain that government policies and procedures will provide perfect protection in these circumstances. Appropriate tolerance is, in the final analysis, dependent on respect for others and good will-- qualities that historically have served modern Denmark well.
And, regardless of its flaws, this manuscript presents a thorough and well-considered analysis of a topic that has received little attention.

REFERENCES


3. Levin HY, Jacobs AJ, Arora KS. To Accommodate or Not to Accommodate: (When) Should the State Regulate Religion to Protect the Rights of Children and Third Parties? Washington & Lee Law Rev. 2016; Forthcoming


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