GENOMICS IN THE GULF REGION AND ISLAMIC ETHICS

A Special Report in Collaboration with the Research Center for Islamic Legislation and Ethics

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FOREWORD

Both Qatar and Saudi Arabia currently lead initiatives in the Gulf region with a view toward joining the genomic revolution. Given the foreseeable scientific leap in genomics in the region, the need for a solid knowledge base pairing scientific research with cutting-edge research in Islamic ethics is more urgent than ever. Managing these pioneering initiatives is not just a scientific venture but also an ethical challenge, one that requires acknowledging and understanding the religio-cultural fabric of this region and the wider Muslim world to which it belongs.

On the other hand, genomics and Islamic ethics is still a new field of study that has yet to mature. This study is an attempt to spark discussions and make a pioneering contribution to this promising field by focusing on the thorny ethical questions triggered by incidental findings. To put the Islamic ethical deliberations in their broader context, a variety of expert perspectives were incorporated which address relevant aspects, including the status quo of genomic research in the Gulf region and international ethical discourse on incidental findings.

Bearing in mind the target audience of this study hails from diverse backgrounds, extensive explanatory notes about Islamic bioethics are included in order to make this study accessible for those without a specialized background in Islamic studies. We hope this multidisciplinary approach will assist policy-makers, among others, to make informed decisions that take into consideration the socio-cultural and religio-ethical uniqueness of the Islamic tradition, which plays a key public role in the region and in the Muslim world at large.

EXECUTIVE SUMMARY

In much the same way that genomic technologies are changing the landscape of biomedical research, the ethical issues these technologies generate are setting today's agenda of ethics research. The distinct ethical issues concerning the management of incidental findings represent a serious challenge that has occupied the minds of Western bioethicists for a while, but has yet to capture due attention from specialists in the Muslim world. Incidental findings are generally defined as results that arise although they were not part of the original purpose of the research project or clinical test. Ethical management of these findings is not a simple matter, because while they can be lifesaving, they can also lead to harmful consequences for the individual and community at large, and at other times lack any clear significance.

This study is an attempt to fill the current lacuna in Islamic literature by addressing some aspects of the ethical management of incidental findings from an Islamic perspective. The study is divided into three main chapters. The first chapter offers an overview of recent genomic initiatives in the Gulf region, with a focus on ongoing initiatives by two nations: Qatar and Saudi Arabia. After this firsthand information about these primary initiatives in the Gulf region, the second chapter broadens the scope by reviewing international deliberations on the ethical management of incidental findings. By including these two chapters, we want to emphasize that Islamic bioethics should be interdisciplinary in nature, and informed as well by deliberations and discussions beyond the Islamic tradition. We hope that this interdisciplinary character will become more evident and better integrated in follow-up studies. The third chapter is dedicated to the core purpose of this study, namely delineating Islamic bioethical discussions related to incidental findings. In order to make the study accessible for non-specialists in Islamic studies, introductory notes are included about the field of Islamic bioethics in addition to an overview of previous ethical deliberations on genomics in general.

Recommendations / Conclusions

The ethical management of incidental findings in the context of the Muslim world, including the Gulf region, is still in its infancy. As it matures, ongoing genomic initiatives in the Gulf region are poised to further benefit. The recommendations and overall conclusions below are intended to improve discussions on the issue, propel them towards maturity, and develop culturally sensitive policy guidelines and jurisdictions. Because Islamic ethical deliberations on the management of incidental findings are part of the wider field of Islamic bioethics, some of the recommendations/conclusions will touch upon this broader field. Our recommendations and overall conclusions are:

- **Potential recipients of incidental findings should be properly informed.** Regardless of whether incidental findings will eventually be disclosed or not, potential recipients of these findings, in whatever context, should be informed that such findings might arise. Without this information, consent obtained from these people cannot be called "informed."

- **Incidental findings that can lead to actionable lifesaving procedures should be disclosed.** During the process of obtaining informed consent, it should be made clear that such findings will be communicated to the research participant. This condition can be included as part of the eligibility criteria for inclusion in the research project.

- **Incidental findings related to (misattributed) paternity should not be disclosed.** From the outset, it should be made clear that findings related to (misattributed) paternity will not be shared with those who participate in research projects or undergo clinical tests. This point should be part of standard policies adopted by research and healthcare institutions. To the extent possible, research projects and clinical tests should be designed in a way that minimizes the possibility of discovering these findings.

- **The one-size-fits-all approach does not work with many incidental findings.** Disclosing certain incidental findings can be categorized as ethically obligatory or forbidden in a few limited cases. In most cases, there are a lot of nuances and particular contexts in which the variables will affect the best practice in the ethical management of incidental findings. The main recommendation here is to involve various stakeholders, including experts from the health and Islamic bioethics sectors, to develop rigorous policies and guidelines tailored to the needs and concerns of each institution.

- **Rigorous research on Islamic ethics is needed in order to properly indigenize genomics in the Gulf region.** New forms of science and technology such as genomics cannot transfer from one geographical setting to another in a contextual void. Religio-ethical, socio-cultural, economic and political factors (broadly termed as the "moral world") definitively shape—and sometimes curtail—the way biomedical scientific technologies are introduced or received. Islamic ethics are integral to the dominant moral world of Muslim-majority countries and should therefore be the subject of rigorous studies whose results can be appropriately integrated into the healthcare policies of these countries.

- **Islamic bioethics should not only be rooted in the Islamic tradition but also engage with global bioethical discussions.** Islamic bioethical discourse needs to be rooted in Islamic tradition so that it can remain faithful to the dominant moral world of Muslim-majority countries. On the other hand, the global character of large-scale biomedical projects, as is the case with genomics, necessitates creating constructive dialogue with relevant bioethical discourses worldwide. This is also in line with the conviction that certain aspects of Islamic ethics are perceived as universal and part of a common human heritage, whereas other aspects are open for contextual adaptations.

SECTION 1: GENOMICS INITIATIVES IN THE GULF REGION:INFRASTRUCTURE, PROGRESS AND ETHICAL CHALLENGES

The term "genomics" is relatively recent, and its increasing use is symptomatic of the rapidly growing production of data in genetics. This growth owes itself to fast-evolving sequencing technologies that have made the assessment of whole genomes in health and disease routine, as opposed to studying one gene at a time. Genomics, therefore, is an appealing approach to any healthcare system that aims to unlock the role of DNA in medical care, and if implemented on a larger scale, to any nation interested in understanding heritable risk factors for common and rare diseases in its population, and in the development of long-term public health policies. Of particular interest today are possible applications in precision medicine, such as establishing sequencing in clinical settings, as well as the implementation of preventive programs such as premarital genetic screening, pre-implantation genetic diagnosis and neonatal screening for genetic metabolic disorders.

While a number of genomics initiatives are beginning to gain traction around the world, few are as organized or as comprehensive in their scope as those adopted by Arab countries in the Gulf Cooperation Council (GCC). Several countries have made it a central mandate to invest in establishing national genomics research infrastructure in order to study, and possibly treat, some of the genetic disorders affecting their societies.

One of the main advantages to fast adoption in the GCC is nationalized (free) healthcare, which is capable of casting its net over virtually the entire local population. Coupled with recent and substantial investment in research infrastructure, there is great potential in building nationwide genomics enterprises. Additionally, most GCC nations have already established genetic research efforts, though most efforts were fragmented, most likely because of funding mechanisms that tended to distribute available resources among specific academic or medical institutions to support small-scale research programs. The centralization of this process through national mandates means these initiatives can shift under the umbrella leadership of a "national genome program."

Perhaps the most significant force behind the national introduction of genomic medicine has been an increasing awareness of the acute need to tackle the high prevalence of genetic diseases in the GCC countries. Second, as local scientific knowledge and infrastructure grows in each country, there has been an increased emphasis on nationwide capacity building as a model of sustained economic growth. This is in stark contrast to the previous model of samples collected locally and then shipped overseas to teams of international investigators whose expertise and academic output were perceived as far superior to local capacities. Thus, local capacity building has become a key factor in national programs that enable local researchers to

investigate local health problems. Highly trained personnel with advanced degrees in genomics from world-renowned institutions continue to lead these programs, providing a much-needed mix of local talent and international experience.

Against this backdrop, the remaining part of this chapter will review (a) the main genomics initiatives in the Gulf region, (b) key ethical questions these initiatives are expected to face in the near future and, finally, (c) a number of case studies that are based on the practical experience of genomics experts working in the Gulf region.

A) Main Initiatives

Notably, the scale and progress of genomics initiatives in GCC countries vary widely by country and are dependent on a number of factors, including pre-existing research infrastructure, the engagement of institutional stakeholders and the size of the population. As a result, the prospective timelines for the maturity of each project vary.

While no centralized genome program has been announced in the United Arab Emirates, Oman or Kuwait, there have been several centers working on aspects of human genetics and genomics. The Dubai-based Center for Arab Genetic Studies (CAGS), for example, has functioned as a nexus of geneticists operating in the Middle East. It hosts the Catalogue for Transmission Genetics in Arabs (CTGA) database, which tallies all mutations and syndromes discovered in genetic studies of Arab populations. In Kuwait, the private genetic testing lab Genatak has been a central point for genetic and genomic studies of the population. In Oman, the National Genetic Center (NGC), equipped with modern diagnostic and educational facilities, was established in 2013, and several studies indicate the Ministry of Health plans to develop policies for translating genomic knowledge into public healthcare.* In personal communication with Khalid Al-Thihli (Genetic and Developmental Medicine Clinic, Sultan Qaboos University Hospital), we came to know that there is no nationwide ongoing genome project in Oman. However, massive parallel sequencing technologies are being applied at the College of Medicine and Health Sciences and Sultan Qaboos University Hospital, in addition to the NGC. The applications of these in Oman are presently geared towards gene discovery, assisting clinical genetics diagnostics, and estimating allele frequency or carrier frequency for variants detected in relation to specific disorders.

The Bahrain genome program deserves a special note. At the time of writing, the program was still in its nascent phase. It was officially announced on November 28, 2015 at a conference titled, "Towards Bahrain Genome Project: Building on International Experiences", organized by the Al-Jawhara Centre for Molecular Medicine at Bahrain's Arabian Gulf University. The conference featured several keynotes from high-profile international experts on large-scale genome projects, both population and disease-based, followed by a closed-door discussion between the speakers and the organizers to generate recommendations for moving the project forward.

* Rajab A, Al Rashdi I, Al Salmi Q. Genetic services and testing in the Sultanate of Oman. Sultanate of Oman steps into modern genetics. *Journal of Community Genetics.* 2013; 4:391–7.

The following six recommendations were subsequently issued to the Minister of Health and the Supreme Council of Health for approval and implementation:

1. An urgent need for the launch of the National Genome Project, which will contribute to the welfare and development of society, particularly in the provision of appropriate and effective treatment in the early stages of life to avoid the emergence of genetic and complex diseases later in life.

2. To provide effective treatment based on a patient's genetic makeup in order to reach positive conclusions. Early intervention for treatment through an accurate understanding of the genome of the person and the common diseases in the community will save time and save the costs associated with expensive therapies. It will also reduce the burden on state budgets through early detection of disease-related genome.

3. To develop professional competence in this important specialty, it is necessary to develop national occupational skills capable of building the National Genome Project and the continuity of the work, to scientifically consolidate these competencies.

4. The National Genome Project requires cooperation and coordination between relevant parties, especially between official bodies, to harmonize regulations.

5. To build and enhance international cooperation across research centers in order to develop and sustain the national genome project.

6. To create effective national participation and develop an integrated plan for awareness and education about the project because of its paramount importance to the health of the individual and society.

Below, two main initiatives will be highlighted, namely the Qatar Genome Programme and the Saudi Human Genome Program.

1) The Qatar Genome Programme

Compared with other initiatives in the region, the Qatar Genome Program (QGP) stands as one of the most ambitious national projects in the Gulf, and indeed the whole Middle East. The program was launched with a vision to position Qatar as a pioneer in the implementation of advanced precision medicine and personalized healthcare.

Her Highness Sheikha Moza Bint Nasser, Chairperson of Qatar Foundation, first announced QGP during the World Innovation Summit for Health (WISH) in December 2013. From its conception, the program was designed within the framework of a comprehensive national plan, based on seven building blocks required to build a unique model that placed Qatar as a lead nation in the implementation of precision medicine. These building blocks are: the national biobank; national genomics infrastructure; national

genomics research partnerships; national genome data network; qualified local human capacity; policies regulating genomics research and precision medicine; and finally, integration of genomics into the clinical setting.

The project is managed by the national QGP committee, which includes representation from all the key stakeholders in Qatar's medical, research and academic sectors. The program is currently incubated by Qatar Biobank (QBB) and relies on a strategic partnership with the Sidra Medical and Research Center.

In addition to forming an umbrella for QGP, QBB adds great value to the project with its extensive phenotyping, including a comprehensive list of biomarkers and various clinical measurements, which adds synergy in terms of the huge wealth of information that can be extracted from the genotype/phenotype association studies.

For whole genome sequencing and analysis, QGP utilizes Sidra's Clinical Genomics Lab (CGL) that houses state-of-the-art sequencing technology, as well as Sidra's biomedical informatics division, which is responsible for data analysis and houses a sophisticated data warehouse.

QGP envisages its role as a national platform, enabling all local stakeholders to collaborate and contribute to the program in a way that would maximize available resources and prevent the possible duplication of efforts.

The Pilot Phase and Beyond:

The pilot phase of QGP, which debuted in September 2015, is the initial period during which all national stakeholders commence coordinating efforts and embark on a well-planned national experiment to apply genomic research in Qatar. QGP differentiates itself from other disease-based research projects in the region in that it is a population-based initiative using DNA samples gathered by the QBB from apparently healthy individuals.

One of the main planned deliverables of the pilot phase is to establish the Qatari Reference Genome Map by sequencing 3,000 whole genomes (around 1% of the Qatari population) by June 2016. Establishing this reference map will help identify specific gene variants distinct to the local population, especially those related to various inherited genetic diseases. Such a map will also help policymakers start incorporating genome data into the healthcare system in order to better diagnose, treat and prevent many diseases.

The past few years have witnessed tremendous progress toward achieving the goals of QGP based on the seven building blocks of the national plan, aimed at creating solid and fertile ground for precision medicine in the healthcare system in Qatar. The following are some of these achievements and developments:

1. **Establishment of a national biobank:** QBB is now fully operational and follows the highest international standards. It has so far welcomed more than 5,000 predominantly Qatari volunteers, and has a wait list surpassing this number.

2. **Establishment of a national genomics infrastructure:** Sidra is now equipped with world-class, fully functional genome sequencing and bioinformatics facilities. Additional facilities exist at Weill Cornell Medicine Qatar (WCM-Q), Qatar University and Hamad Medical City (HMC).

   One of the main goals of QGP pilot phase, is the establishment of the Qatari reference genome map, which will be built with data generated by the sequencing of the first 3,000 genomes, which is anticipated to be completed around the end of 2016.

3. **Building national genomics research partnerships:** The Qatar National Research Fund (QNRF) and QGP are collaborating to create a research-funding program under the name "Pathway towards Personalized Medicine (PPM)". PPM was launched in 2016 to encourage local research on genomics. In parallel to the PPM projects, QGP has formed a publication steering committee to coordinate efforts by local researchers working on data generated by the first 3,000 genomes to publish their results in high-impact scientific journals.

4. **Building a national genome data network:** A plan has been put in place to build a national network that will eventually merge into a comprehensive effort to achieve this goal. One aspect includes ongoing efforts by the Sidra Biomedical Informatics team to build a data center capable of hosting and analyzing the huge amount of information coming out of the accelerated whole genome sequencing efforts. In close collaboration with QBB, the Sidra team is also involved in the development of a unique interface that will integrate phenotypic and genotypic data for each individual in a way that would empower researchers to perform their investigations in the most efficient and productive manner.

   Another aspect involves developing a nationwide system to incorporate genomic data into healthcare records in all main hospitals and clinics in the country. This will be one of the main goals of the next phase of the genome project, and will be discussed and reviewed in detail toward the end of the pilot phase.

5. **Building local human capacity:** On this front, QGP has initiated communication with local universities to launch two graduate programs, one in genetic counseling and another in genomic medicine. Such programs will support human capacity building in Qatar to enable a generation of healthcare professionals capable of moving the country into the age of precision medicine. In parallel, QGP also plans to develop short courses on the basics of genomic medicine to educate professionals unable to enroll in long-term courses.

6. **Development of policies regulating genomic research:** QGP and the Ministry of Public Health are collaborating to draft an ethico-legal policy document to provide guidelines that will govern genomic research in Qatar. The document will constitute a national umbrella for all related activities in genomics in Qatar.

7. **Integrating genomics into the clinical settings:** As a starting model project of immediate benefit, QGP is liaising with the HMC pathology department and other national stakeholders to develop comprehensive gene panels for use in neonatal screening and premarital testing. These are among the first examples of how genomics can add great value to diagnostic and preventive practices.

The pilot phase will create the foundation for a follow-up large-scale phase, which could involve the sequencing of the genomes of the whole Qatari population. This would potentially put QGP at the forefront of international programs integrating precision medicine into national healthcare systems.

However, the scope and timeline of this prospective phase will be decided after a critical review of the results of the pilot project, taking into account issues such as the ability to scale up sequencing and bioinformatics capacities, the possibility of increasing the number of samples processed by the biobank, and the level of coordination between all involved national stakeholders. This is in addition to other considerations, both financial and political.

One important factor that will also help shape the next phase is the national benchmarking surveys conducted on genomic medicine awareness in Qatar. In fact, QGP contracted the Social and Economic Survey Research Institute (SESRI) at Qatar University to conduct national surveys in June 2016 to assess public conceptions and attitudes towards genomics and precision medicine (http://sesri.qu.edu.qa/sites/default/files/QGPsurvey.pdf). Three separate surveys will be conducted on three different groups: the public, healthcare professionals and decision-makers. The results of these surveys will also help QGP design the next stage following the end of the pilot phase.

2) The Saudi Genome Program

The Kingdom of Saudi Arabia has a high burden of genetic diseases, both in the form of severe inherited diseases, which show up early in life and affect 8% of births in the Kingdom, and in the form of common genetic diseases that show up later in life (such as diabetes, which affects over 20% of the population).

These diseases have a considerable impact on the quality of life of those affected, and also place a huge burden on the national healthcare system in terms of cost, contributing in a large way to the kingdom's SAR100 billion annual healthcare expenditure. A substantial reduction in children born with genetic disabilities, through screening and prevention similar, to what has been achieved in regard to blood disorders, would save over SAR1 billion per year, and similar savings would be realized by achieving even a small delay in the age of onset of diabetes and other common disorders.

The first step to eliminating these burdens is to find the Saudi-specific genes and gene variants that cause these diseases—"solve the disease genetics"—so those at risk can be identified and given proper preventative counseling, and so that rational therapies can be devised—the core elements of personalized medicine (PMID: 25333061 and PMID: 23451714).

Program Structure:

The Saudi Human Genome Program (SHGP) is headquartered at King 'Abdulaziz City for Science and Technology (KACST), in close partnership with King Faisal Specialist Hospital and Research Center. In addition, satellite sites are expected to add variant information as they build up sequencing capacity. The key industry partner is Life Technologies/Thermo Fisher; others include Affymetrix, Dell, Illumina, Intel, Oracle and Samsung. In addition, the program has a panel of highly regarded international figures from the field of human genetics who serve as consultants and advisors, namely:

- James Watson (Nobel laureate), (USA)
- Takashi Gojobori, KACST (Saudi Arabia)
- Doug Wallace, Penn State University (USA)
- Giorgio Bernardi, CNRS (France)
- Christine Petit, Pasteur Institute (France)
- Sir John Bell, Oxford University (UK)

Unlike many other large genomics initiatives, SHGP has focused since its inception on sequencing individuals with suspected genetic disorders, rather than healthy individuals. Key to this decision is the Kingdom's commitment to making the results of SHGP as translational in nature as possible. While sequencing healthy individuals holds value in determining many interesting variables from a population genetics perspective, this benefit was felt to be secondary to the value of providing likely molecular diagnoses to research participants. Sequencing "healthy" individuals will be considered in subsequent phases of SHGP.

Milestones

As mentioned above, the early phase of SHGP has focused on identifying the etiology of genetic diseases in Saudi Arabia. This was achieved through a coordinated effort of genotyping and targeted sequencing with panels and whole exome sequencing. After establishing the world's first "Mendeliome assay", a multigene panel that covers more than 3,000 Mendelian genes, a robust workflow has been put in place where all samples undergo an initial screening by the Mendeliome assay first. Using this approach, the largest study on Mendelian disorders, involving more than 2,000 patients (PMID: 26112015), has been published. This has allowed for the provision of a likely molecular diagnosis in the case of 40% of participants. This also allowed the collation of an unprecedented amount of data on patterns of variations in Mendelian genes in Saudi Arabia. By using innovative data analysis methods, it was possible to extract from this data the first-ever map of founder mutations in Saudi Arabia, the carrier frequency and an estimate of the minimal disease burden for autosomal recessive diseases (PMID: 27124789).

As expected, many of the "negative" cases on the Mendeliome assay were subsequently found to harbor mutations in novel genes, as revealed by exome sequencing (PMID: 26112015). There have now been more than 1,500 exomes performed, and over 200 novel disease genes identified and published (reviewed in PMID: 27068822, PMID: 25333061 and Shamseldin et al, submitted).

Future Plans:

- Building infrastructure
- Transfering training and knowledge
- Solving disease genetics
- Continuing to build the catalogue of disease-causing variants in the Saudi population
- Continuing to build the catalogue of normal variants in the Saudi population
- Sequencing of 5,000-10,000 whole genomes from random well-phenotyped "normal" individuals (representative of the Saudi population) over 3-4 years
- Next generation sequencing based on high-resolution HLA typing of several thousand Saudi samples
- Establishing a comprehensive pharmacogenetic gene panel, and cataloging associated variances in the Saudi population, by whole genome sequencing and whole exome sequencing of a substantial number of tumor samples, with a view to bringing forward personalized medicine in the diagnosis and treatment of cancer
- Transferring gene panel technology and knowledge databases to clinical diagnostic application
- Transferring the whole exome sequencing workflow to generate clinical exomes for solving rare disease cases and profiling selected clinical cancer cases
- Developing large-scale economic sequence-based procedures for premarital, prenatal and newborn screening
- Developing large-scale gene panel based assays for pharmacogenetic profiling of all patients.

B) Key Ethical Questions/Dilemmas

As with many disciplines of biomedical research, genomics carries its own set of potential ethical issues. Although many of these issues are global in their relevance, some are more pertinent to the local moral world of Arab and Muslim countries, especially in the Gulf region. As these nations pioneer the transformation of their healthcare systems toward personalized medicine, addressing certain major ethical issues becomes inevitable. Bearing in mind that this study is mainly concerned with the ethical issues that specifically relate to the broad theme of "Return of Results", the below list will attempt to focus on such issues:

1. **Incidental findings.** Whole exome sequencing (WES) has increasingly become a routine clinical test with a high diagnostic yield, particularly in Middle Eastern populations, because of high consanguinity rates, while whole genome sequencing (WGS) is primarily pursued in research settings. However, those genomic assays, by their very nature, are susceptible to revealing more information than originally intended. The ACMG working group estimates that approximately 1% of WES results will report an incidental finding in one of the 56 genes recommended by the ACMG to be reported on by clinical laboratories (Green et al.; 2013). Many of the genes recommended by the ACMG are adult-onset diseases, as well as genes involved with cancer or cardiac susceptibility syndromes that are amenable to preventive or treatment measures. A diagnosis of either one of these can drastically change an individual's day-to-day life. While this is a unique advantage in the research setting, it can pose vexing ethical questions when such information reveals or predicts important health risks, or touches on socially or culturally sensitive issues. In essence, the root of the ethical question surrounding incidental findings is in the balance between the principles of patient autonomy and "do no harm". In the absence of a clear ethical framework, each researcher may come to his or her own conclusion about how to balance these two principles. Such inconsistency risks dire consequences. In Western societies, offering a patient the option to receive incidental findings, or to opt out, is increasingly accepted. However, questions about the obligation to inform research participants of their incidental findings, i.e. in non-clinical settings, remains an area of hot debate. Although many of the ethical concerns around revealing incidental findings are global, the Middle East poses a unique set of concerns due to the specific cultural and religious beliefs of the population. Genetics and many diseases are highly stigmatized in the Middle East, and it is common for certain diagnoses to be hidden from immediate family members, extended family members and society. A family or tribe name still carries great importance and connotes respect in contemporary Muslim societies. Being associated with a hereditary condition can have dire social repercussions for an entire family or tribe. For such reasons, many individuals do not voluntarily choose to pursue genetic testing, believing the harm outweighs the good in a cultural sense. Although medically actionable, many of the diagnoses associated with incidental findings can affect familial relationships and social standing.

2. **Disclosure of actionable results to potentially affected relatives.** If one finds an actionable breast cancer mutation in one woman, should her sisters be tested preemptively? What if the affected sister doesn't want her other sisters to know about her breast cancer? This idea is applicable to many other forms of disease where disclosure to family members may be taboo for the affected individual, but the healthcare provider knows it could potentially save their lives if detected early. At the Medical Genetics Clinic at Hamad Medical Corporation (HMC) in Qatar, physicians have reviewed approximately 150 clinical exome, mainly in children with rare genetic disorders, from July 2012s to June 2014. Pathogenic variants were reported in the genes recommended by the ACMG for the proband and relatives, and four probands were found with reportable incidental findings (2 %), a rate comparable to that previously reported in literature (Yavarna et al 2015). Most incidental findings in WES that have been pursued in the Qatari population are related to cardiogenetics.

3. **Paternity.** Non-paternity can be unequivocally deduced from a single genomics scan. However, non-paternity can be inadvertently identified in the context of routine genomics research. In the West, it is customary to include a statement about this risk in the consent form. However, it has been difficult to include similar language in local consent forms due to the extremely sensitive nature of non-paternity.

4. **Ancestry.** Tribalism is a deeply rooted tradition in the local culture of some Arab communities, and extreme views on the marriage "compatibility" between tribes are common. In theory, a single genome scan can discern the ancestry of an individual to a great degree of precision. Although ancestry genomics is a thriving field globally, this line of research has been greatly limited locally by the taboo nature of the topic. This is despite many practical applications, not least of which is forensic. In Middle Eastern populations, many genetic disorders are due to founder mutations that could be traced back to identify an individual's ancestry and specific geographical origin. This disclosure may affect individuals' confidentiality and autonomy.

5. **Open discussion of evolutionary principles.** There is little doubt in scientific literature of the shared genetic ancestry between humans and non-human primates. Most recently, the discovery of numerous fossilized "older versions" of *homo* species that have been shown through DNA and genomic studies to be our recent cousins has shed more light on human evolution. Therefore, the field of genomics will undoubtedly create questions about the evolutionary origins of humans, which many laypeople may find in conflict with Islamic thought and cultural sensitivities.

6. **False negatives.** One of the major limitations in next-generation sequencing is errors caused by low coverage of genomic regions during sequencing. Due to the random nature of coverage distribution, this means certain genomic regions may not be covered at all, rendering the analysis blind to any variation in that region *within* the given individual. This issue rarely occurs when the method used is targeted (such as with first-generation Sanger sequencing), due to a region-specific amplification step required in preparing the samples. Most analysis pipelines currently do not notify scientists which regions are completely omitted, as they appear indistinguishable from regions where no mutations are found. These considerations need to be accounted for prior to returning results to the individual about a specific variant(s) they are interested in investigating. Otherwise, it may be a case where a variant or disease is not flagged (because it was not seen in the first place), yet the individual is surprised to discover they are indeed developing a certain disease. This issue would be especially difficult to deal with in a setting with socialized healthcare, where there is a public expectation that the health authority would have predicted and prevented those results in the first place.

C) Case Studies

1. **Case #1:** A Saudi family is enrolled in research testing, which reveals a mutation that explains their rhizomelic dysplasia. When it comes time to share the results with the parents, the father has already died and the maternal uncle is informed instead. He is shocked to learn that the mutation suggests the parents are distant relatives, and when asked to explain his reaction, he gives a long account of how he resisted the marriage of his sister to her late husband because their lineage was "incompatible". Emphasizing shared heritage is nothing new in Islam, but demonstrating this genetically seems to have a more profound impact. This case study also highlights the potential of genomics to demolish deeply held views about lineage superiority. Not only will fierce resistance to such an outcome be inevitable, it may also threaten the progress of genomics research in the region.

2. **Case #2:** In a counseling session, a religious father objects to the notion that his children's autosomal recessive disease was somehow related to the fact that he and his wife are consanguineous. He explains how the Prophet was related to his wife and how his daughter was married to her cousin. This is a very common argument, and one that needs to be addressed by highlighting the difference between claiming something is permissible through the actions of the Prophet and recommended by a specific statement attributed to him.

3. **Case #3:** The parents of a child with a recessive disorder are very upset to learn that their other children, who were tested as part of the segregation analysis to confirm the pathogenicity of a variant in their affected sibling, cannot be informed of their carrier status. Convincing parents that their children have the right not to know their carrier status until they are of legal age is particularly challenging in a culture where parents have a sense of ownership over their children and there is no clear religious direction on this important issue.

4. **Case #4:** A consanguineous Qatari family has two daughters who suffer from seizures and developmental delay. Their MRIs reveal abnormal brain MRI. They underwent whole genome sequencing (WES), which showed the causative gene that explains their phenotype. However, WES also reveals an incidental finding of a mutation associated with Long QT Syndrome (LQTS), a condition that can lead to sudden cardiac arrest. This incidental finding can not only impact the two young daughters of this family, but can also lead to a similar diagnoses in asymptomatic family members (parents, siblings, etc.) who may not want to know their risk status. Furthermore, LQTS shows reduced penetrance of signs and symptoms. Approximately 25% of individuals with a pathogenic mutation have a normal ECG, and up to 82% remain asymptomatic (Priori et al 2003). This leads to complicated genetic counseling and risk assessments of individuals. Furthermore, most clinical WES is on children, who are then at a risk of learning of adult onset conditions.

SECTION 2: RETURN OF RESULTS AND INCIDENTAL FINDINGS: INTERNATIONAL BIOETHICAL DELIBERATIONS

1) Evolution of the debate

The debate about the return of results and incidental findings started in the late 2000s and reached a peak in 2014 (Knoppers, Zawati and Sénécal 2015, 553). A number of prominent theoretical conflations have impeded the debate. Such confusion is even present in legislation and ethics guidelines (Zawati and Knoppers 2012, 484). This section will begin by describing some important sources of confusion, before examining their effects on the landscape of the debate.

In the research setting, a critical conflation occurs between research results and incidental findings. While research results are discovered within the course and objectives of a given research project, incidental findings occur outside of a research project's objectives (Zawati and Knoppers 2012, 484). Incidental findings, to clarify, are inadvertent, insofar as the findings were neither the intended nor the expected result of the research project (Presidential Commission for the Study of Bioethical Issues 2012). Both research results and incidental findings may have health implications for either an individual person or a population. Many early international norms failed to distinguish between research results and incidental findings. Consequently, the enumerated conditions for returning them were very similar. This was despite clear theoretical differences. Practical differences exist as well. While researchers undertaking an observational study are presumably able to interpret results, that fall within the objectives of such projects, incidental findings, because they are unexpected, may fall outside the field of the researcher's expertise. In other words, researchers are *looking for* research results and will thus probably know how to interpret them. In contrast, they are not looking for incidental findings and may therefore be unable to fully understand what they have found. This raises the risk that researchers, who may be incapable of properly interpreting the relevant results, will nevertheless return them simply for fear of liability (Zawati and Knoppers 2012, 484).

In research settings, an additional source of possible conflation exists in the range of health implications that may be the subject of genetic findings. Results concerning a population or group of people, for example, are typically returned through publication in newsletters or on websites. Results concerning a single individual, on the other hand, are typically returned in accordance with the policies of a biobank or in reflection of a research project's consent framework. Confusion between population and individual results remains despite the clear distinction between these concepts. The Italian Society of Human Genetics, for example, does not fully capture in its 2004 *Guidelines for Genetic Biobanks* the meaning of the word "results" (Italian Society of Human Genetics 2006). This fosters confusion about precisely the kinds of results that fall under its ambit. Such confusion matters particularly for research participants, who may, without warrant, expect both types of results to be returned. Consequently, research participants may misattribute therapeutic intent to projects for which researchers allude to the return of results (Zawati and Knoppers 2012, 484).

The expectation of return is closely associated with the duty to rescue, which exemplifies a third source of confusion. The duty to rescue is traditionally defined as a civil law obligation to assist identifiable individuals who are in immediate physical peril. While it is a source of tension in the literature, recent developments in international norms and ethics guidelines suggest the duty to rescue is not a tenable basis for the return of results. There are a number of reasons for this, but perhaps most prominent is the view that genetic information is often not urgent. Furthermore, research participants often prefer not to have results returned; it is not clear how the duty to rescue would interact with the threat of vitiating such consent (Zawati and Knoppers 2012, 484).

The confusions outlined above help explain some of the tensions within the return of results debate in the early 2010s. Ambiguity in terms, paired with the conflation of divergent concepts, produced an inconsistent international normative framework. In response, authors called for the creation and dissemination of a lexicon aimed at clarifying ambiguity and framing future guidelines. Similarly, others called for distinguishing research contexts. Without giving attention to the theoretical differences between, for example, biobanking and research in ethical frameworks, there is the threat that researchers' duties become many and undefined, while the expectations of participants similarly expand. Put another way, the confusions highlighted above promote both professional uncertainty and therapeutic misconception (Zawati and Knoppers 2012, 484).

With the development of whole genome sequencing, policy guidance specific to that practice has emerged. This time, focus shifted to the clinical setting. A survey of international approaches to return of results conducted in 2015 (both research and clinical) found four distinct measures currently in place. First, certain guidelines allow only targeted sequencing in an effort to reduce the frequency of incidental findings. Second, results are only returned if they meet a set of three criteria: analytical validity, clinical significance and actionability. Third, determinations about return are made on an essentially *ad hoc*, case-by-case basis. Finally, no return is made at all (Knoppers, Zawati and Sénécal 2015, 553). The following section will discuss these positions in more detail.

These novel approaches to whole genome sequencing respond to emerging issues raised by a developing practice. As the debate begins to recognize the need for a more nuanced approach to the kinds of results produced by increasingly powerful tools, so too is it recognizing that not all undertakings (whether clinical or research-related) can be subsumed under a singular approach. Indeed, it is probably not even tenable to present a uniform approach to whole genome sequencing, so diverse are the contexts in which it is used (Knoppers, Zawati and Sénécal 2015, 553). In general terms, the return of results debate is now beginning to incorporate complexity and context, based on a variety of settings. Uniform approaches to the ethics of result return are unlikely to be persuasive. Rather, ethical frameworks are beginning to account for various typologies.

2) Specifics of the debate

This section will describe some of the specific international normative approaches taken in relation to the return of results. A 2012 study by Zawati and Knoppers identified 15 laws, policies and guidelines relevant to the return of results. At the time of the study, binding legislation existed only in Spain, Taiwan and Estonia, with remaining jurisdictions having only non-binding ethics norms in place. The majority of documents reviewed referred to concerns with the kinds of conflation and therapeutic misconception previously described. Of particular note, five criteria for the return of results were found to dominate the debate. Results could be returned where (a) the findings were analytically valid, (b) returning them to the donor would accord to applicable law, (c) the donor consented to receive individual results, (d) the findings reveal an established and substantial risk of a serious health condition or a serious condition of reproductive importance, and (e) the findings were actionable (Zawati and Knoppers 2012, 484). As indicated above, the most pronounced trend revealed by this study was the lack of clarity and consistency in the international normative frameworks.

A 2015 study of whole genome sequencing return policies revealed similar inconsistencies. Traditionally, policies regarding genetic testing are developed by professional organizations, such as national geneticists' associations, and not by legislators. It is worth noting that the practice of genetic testing has nevertheless been indirectly influenced by biobanking legislation (Knoppers, Zawati and Sénécal 2015, 553). Estonia became the first country to legislate on the issue of genetic testing in 2000, with its *Human Genes Research Act* (Riigikogu 2000, 685). The Act sought to protect the right of withdrawal, the right to access personal health information and the right not to know genetic data. It took the better part of a decade for Spain to follow. In 2007, Spain introduced general legislation on biomedical research. The law creates a legal duty for researchers to communicate results with family members of subjects who had exercised the right not to know. The duty is specifically triggered when such information is necessary to avoid serious damage to the relatives in question. Other examples of legislation include Taiwan's 2010 law on biobanking, which emphasizes the importance of consent to genetic testing (Parliament of Taiwan 2010), and Finland's 2012 *Biobank Act*, which grants subjects the right to receive health information on request. Importantly, Taiwan's legislation creates a duty to return results with respect to the genetic information that could possibly affect the participant, their family or their ethnic group (Knoppers, Zawati and Sénécal 2015, 553). The Finnish legislation, on the other hand, does not provide guidance about the extent to which results may be returned to family members of research participants (Parliament of Finland 2012).

While the legislative response to returning results has been slow, policy guidelines have, in contrast, flourished. In the past five years, a variety of policy documents have emerged in an array of jurisdictional settings. While the legislative landscape considers general genetics research and biobanking, several policy documents have emerged that deal explicitly with problems presented by whole genome sequencing in both research and the clinic (Knoppers, Zawati and Sénécal 2015, 553). Their responses are varied on the issue of the return of results. For some policy organizations, such as the Foundation for Genomics and Population Health in the United Kingdom, the consent process should contemplate that disclosure of results to subject family members where incidental findings may be relevant to them (Hall, Finnegan and Alberg 2014).

In certain jurisdictions, physicians are permitted to contact family members in order to warn them of serious, heritable genetic conditions. Such permission is typically an exception to more fundamental rules of confidentiality (Zawati and Thorogood 2014, 21). Spain's *Law on Biomedical Research*, for example, allows physicians to share information to the extent necessary to "avoid serious damage to the health" of a subject's family (Law 14 2007, of 3 July, on Biomedical Research). Similarly, Quebec's *Code of ethics of physicians* allows physicians to "divulge facts or confidences...when there are compelling and just grounds related to the health or safety of the patient or of others" (CQLR, 3:20(5)). However, Quebec law does not recognize a *duty* for physicians to inform family members (Zawati and Thorogood 2014, 21). In the 2012 Quebec Court of Appeal case *Watters v. White*, a physician, Dr. Watters, was alleged to have failed in the duty to inform the family of a patient he had diagnosed with Pelizaeus-Merzbacher Disease of the risks associated with the disease's heritability. The Court of Appeals found that the duty of physicians to inform their patients did not extend to relatives. Rather, the Court found that the physician's duty of confidentiality, which is the "cornerstone of the doctor-patient relationship", precludes the creation of a strict duty to inform family members of persons diagnosed with genetic conditions (*Watters v White* 2012, 257).

As mentioned above, there are four distinct approaches to the return of results captured by international policy documents. First, the return of results can be avoided with targeted sequencing that attempts to avoid incidental findings in the first place. This approach, however, is imperfect. Despite filters and gene panels, incidental findings sometimes happen anyway (Knoppers, Zawati and Sénécal 2015, 553). Most guidelines that recommend filters also allow subjects to opt out of receiving inadvertent incidental findings. This position has been taken by the American College of Medical Genetics, though after significant debate (Richards et al 2015, 405-423). It is worth noting that the filtering approach applies in both research and clinical settings. Guidelines that promote this view typically stress that pre-test counseling is a central portion of the consent process (Knoppers, Zawati and Sénécal 2015, 553).

Second, results may be returned subject to certain conditions. This is the most prevalent approach in results return. Typically, a baseline set of three criteria support return. These criteria, sometimes called the ACA criteria, are (a) analytical validity, (b) clinical significance and (c) actionability (Knoppers, Zawati and Sénécal 2015, 553). This approach bears a striking similarity to the five circumstances for return described by Knoppers and Zawati in 2012 (484). According to this view, a return of results is justified only insofar as the finding has predictive value, is of scientific and clinical value or utility, and concerns a condition for which there is available prevention or treatment. Additional considerations are also often relevant, such as approval of a return-of-results plan by an ethics committee or a requirement of results confirmation in research settings (Knoppers, Zawati and Sénécal 2015, 553).

Third, a case-by-case approach, though less prevalent than ACA criteria, is more traditional. This contextual system is used in both clinical and research settings. A typical adoption of the approach would allow clinicians, based on their knowledge of the specific circumstances of the patient, including age, prognosis and personal circumstances, to communicate incidental findings to the extent that they see fit. This approach is highly flexible, and is thereby accompanied by certain attendant risks. For one, incidental findings may be added to a patient's medical record, thereafter it falls to a physician to communicate such results to the patient. Problematically, a physician may not be adequately prepared to interpret the findings, and thus be unable to fulfill this role. In research settings, moreover, a high degree of specialization may prevent researchers from properly interpreting whether a result is clinically significant (Knoppers, Zawati and Sénécal 2015, 553).

The final approach to the return of results and incidental findings present in international policy documents is the option in which incidental findings are not returned at all. This view is particularly popular in strictly research settings, where the offer to return results can be seen to create a therapeutic misconception (Knoppers, Zawati and Sénécal 2015, 553). Recently, some research projects have moved to providing participants with lay descriptions of the project in addition to the promise of aggregate results publication on media or online platforms. Some organizations, without expressing preference for any of the approaches described above, simply warn that the communication of incidental findings may cause unnecessary harm to a participant and their family (Ethical Advisory Group of the UK 10K Project 2010).

3) Return of results for children

Of course, the approach taken to the return of results will depend in no small measure on the age and vulnerability of the subject in question. Results that implicate the health of children are susceptible to specific considerations, in particular the principle of the best interest of the child. This organizing value is enshrined in the 1989 *Convention on the Rights of the Child* (UN General Assembly 1989, 3) and is incorporated into a number of policies about results return for children. A statement on the return of research results prepared for the Réseau de médecine génétique appliquée (Network of Applied Genetic Medicine), for example, underscores that the best interest principle is *essential* to decisions about the communication of findings (Sénécal et al 2013).

For some, the principle implies that findings that are actionable in childhood and for which effective treatment or prevention is available, should generally be returned. Indeed, where parents refuse the return of these kinds of results, they may be, from a legal perspective, acting neglectfully. On the other hand, this same argument maintains that, where the relevant finding concerns only the future adult health of the child, results should typically *not* be returned (Sénécal et al 2013). Policy and legislation in Europe and North America is trending toward making the return of results mandatory where supported by the best interests principle (Zawati et al 2014, 72). These questions arise predominantly in clinical settings, with findings typically emanating from a course of treatment or testing for disease.

4) Return of results for the deceased

The death of a research subject creates an ethical challenge for the return of results to family members of the deceased, asking for balance between the rights of family members to information about their health and the theoretical right to privacy of the deceased. This problem has become especially relevant in recent years as genomics research becomes increasingly long-term and longitudinal (Tassé, *Human Genetics*, 2011, 415). The WHO's 2003 report on genetic databases stresses that ethical duties owed by genetics researchers should not end when a research participant dies WHO's 2003. International policy and legislation, however, lacks specific guidance on the issue (Tassé, *Human Genetics*, 2011, 415). Despite this, some authors maintain that the balancing of justifications in consideration of post mortem disclosure will rarely favor protecting the privacy interests of the deceased. Of note, while this brief discussion has focused on the return of results in a research setting, these worries may be equally pronounced in the clinic, though with perhaps greater legislative guidance (Tassé, *Journal of Law, Medicine* & Ethics, 2011, 621).

5) Return of paternity results

One issue that has not received much treatment in international return of results policies is the acceptability of returning parentage results. Of course, as Susan Wolf et al point out, "misattributed parentage or other misattributed lineage may be discovered" in the course of performing family studies. Some studies suggest that parentage is misreported at a rate of nearly 10%. That figure, however, is not well supported and requires further study (Wolf et al 2008, 219). The standard clinical practice with respect to incidental findings of misattributed parentage is nondisclosure. Some authors have shown that the central argument favoring this position is that disclosure would threaten to throw the family dynamic into disarray (Cho 2008). Disclosure could have a range of psychological and emotional effects on children, as well as on both genetic and non-genetic social parents (Palmor and Fiester 2014, 163).

There are, nevertheless, several arguments in the literature that favor disclosure. First is the view that parents have a moral right to know about their genetic relationship to their children (Cho 2008). This stems from the proposition that non-genetic parents are often victims of some ostensible wrong. For example, they are made to believe they are the parent of a child when, genetically speaking, they are not. A second prominent argument that favors disclosure holds that children have a right to know their genetic identity. Palmor and Fiester argue that, while this view may be compelling when it is applied to adult children, it is somewhat less convincing in cases of young children, who are still highly dependent on a familial social structure. A third and final argument in the literature considers an attitude of nondisclosure to be paternalistic. Refraining from providing parents with genetic information is a value judgment a researcher is not morally entitled to make. When a researcher decides not to return incidentally discovered parentage information, they are tacitly expressing a determination about what they believe is best for the social family. According to some authors, genetics researchers have no right to make such decisions. It is, however, worth noting that there are important moral differences between genetic information sought by a research subject and information that has been discovered *inadvertently* (Palmor and Fiester 2014, 163).

6) Religion and the ethics of result return

Though religion plays a central role in the lives of many, its effects on the ethics of genetic results return have not yet been studied in the literature.

SECTION 3: ISLAMIC ETHICAL PERSPECTIVES

By the second half of the twentieth century, roughly speaking, the Islamic tradition started to face, and increasingly began to address, an unstoppable flow of bioethical questions triggered by biomedical advances and the ensuing flux of new information.* These questions usually posed a twofold challenge for contemporary Islamic deliberations on bioethical issues. First, religious scholars needed to understand these advances and related ethical questions. A second challenge was that the advances often originated outside the Muslim world, in a socio-political and cultural setting unfamiliar to the scholars. On the other hand, it was necessary to provide answers for these questions in order to demonstrate the contemporaneity of Islam and its inherent ability to continue providing guidance for Muslims in the modern world. This has been inseparably linked to the premise that the functionality of Islam and its overarching religio-ethical system (Sharia) is timeless. That is why producing an Islamic bioethical discourse necessitated not just generating answers and positions conducive for the modern (biomedical) reality, but also making sure these answers and positions comply with the Islamic tradition and its religio-ethical system in order to justify their legitimacy from a religious perspective.

In order to tackle this twofold challenge, contemporary Muslim religious scholars approached the modern bioethical questions through the prism of *nawāzil* (literally 'predicaments'), a technical term in Islamic jurisprudence that refers to the novel issues that likely have rarely been addressed. Thus, *nawāzil* is a recurrent phenomenon throughout Islamic history, because each generation of Muslim jurists have had their own novel issues that their predecessors did not address, perhaps because they never thought such issues would exist. Novel issues and their relevant ethical questions triggered by modern biomedical technologies are par excellence part of the *nawāzil* of the modern (biomedical) reality. The very term *nawāzil* also figures in the titles of various contemporary works on Islam and biomedical ethics. Other authors sometimes use the modern equivalent of *nawāzil*, namely *qadāyā mustajadda*, which literally means 'novel issues' (Ghaly 2015, 287).

* The fatwa of the Saudi Religious scholar 'Abd al-Rahmān al-Sa'dī (d. 1955) on organ transplantation can be counted as a pioneer example in this regard (Qaradāwī 2010, 67). It seems that the need to address such questions was also felt by physicians, maybe even earlier than some religious scholars, as it was reflected in the work written by the well-known Egyptian physician 'Abd al-'Azīz Ismā'īl, whose first edition appeared in 1939, followed by later editions published in 1954 and 1959. The book was prefaced by the grand imam of al-Azhar Muhammad Mustafā al-Marāghī, who died in 1945 (Ismāghīl 1959).

The twofold challenge could be addressed through the approach of *nawāzil*. According to this approach, examining novel issues from an Islamic juristic perspective has always been dependent upon two main elements. The first element, the informative element, involves devising the right and precise perception (*tasawwur sahīh*) of the question or issue at hand. Muslim religious scholars agree that information related to this element should not necessarily be part of the jurists' already existing knowledge, but it can be gained by consulting experts in specific disciplines of knowledge, e.g. medicine, veterinary science, architecture, astronomy, economics and finance. The second element, the normative element, involves approaching the question or issue that has been correctly perceived through the lens of relevant scriptural texts and juristic interpretative methods. This element usually ends by adopting a certain position that assumes the form of a religious ruling (*hukm shar'ī*). This normative element is typically seen as the exclusive task of competent Muslim religious scholars (Ghaly 2015, 287-88).

Because of these two core elements of the *nawāzil* approach, communication between Muslim religious scholars and experts in other fields of knowledge, including medicine, almost never waned, but instead usually remained on a case-by-case basis (e.g. Shaham 2010). From the second half of the twentieth century onwards, the spectacular changes that our modern world has witnessed resulted not just in novel individual issues, but even produced a novel reality *in toto*, as noted by some contemporary religious scholars (Jum'a 2007 35-36). This shift from novel *individual issues* to novel *total reality* dictated changing the case-by-case communication between religious scholars and experts in other disciplines of knowledge into intensive, systematic and finally institutionalized collaboration. By the beginning of the 1980s, deliberations on Islam and biomedical ethics—together with other novel issues such as economics and finance—started to assume a collective form through collaboration between Muslim religious scholars and specialists in other fields of knowledge, especially biomedical sciences. This mode of collaboration is known in Islamic studies as "collective *ijtihad*" (independent legal reasoning); in Arabic, "*ijtihād jamā'ī*". Within this framework of collaboration, biomedical scientists will, in principle, be responsible for the aforementioned informative element and the religious scholars will work on the normative element.

Bearing in mind that the target audience of this study will not necessarily come from an Islamic studies background, we will use the more common term "interdisciplinarity" besides the more specialized term collective *ijtihād*. Interdisciplinarity is not only used here for the sake of convenience, but because it rightly expresses the internal mechanism of collective *ijtihad*, where at least two disciplines of knowledge, (religious studies and biomedical sciences) are at play. Also, specialists in other disciplines can sometimes be involved.

Typology of contemporary Islamic bioethical deliberations

Three main transnational institutions, all headquartered in the Gulf region, played a seminal role in employing the mechanism of collective *ijtihād* or interdisciplinarity for developing positions on a long list of bioethical questions. The Islamic Organization for Medical Sciences (IOMS), based in Kuwait and officially established in 1984, has been the most productive in this field, and their symposia are exclusively dedicated to studying bioethical issues. IOMS coordinates with two other institutions that pay occasional, but not exclusive, attention to bioethics. One is the Islamic Fiqh Academy (IFA), established in 1977, which is affiliated with the Muslim World League and based in Mecca, Saudi Arabia. The other is the International Islamic Fiqh Academy (IIFA), established in 1981, based in Jeddah, Saudi Arabia, and affiliated with the Organization of Islamic Cooperation (Ghaly 2010, 2). Keeping in mind the frequent and systematic character of the work produced by these three institutions, it is discussed below as "continual deliberations".

Besides these three institutions, the conveners of a large number of conferences and symposia on bioethical issues in the Muslim world adopted the same interdisciplinary approach by combining religious scholars and biomedical scientists. Two good examples in this regard are the seminar, "Ethical Implications of Modern Researches in Genetics", organized by the Faculty of Science, University of Qatar from 13 to 15 February, 1993, and the conference "Genetic Engineering between Sharia and Law" held by the Faculty of Sharia and Law, United Arab Emirates University, from 5 to 7 May, 2002. Unlike the three influential institutions mentioned above, the organizers of such events are interested in a specific bioethical topic rather than in working systematically on developing Islamic bioethical discourse. Keeping in mind the infrequent and seasoned character of the work produced by these events, it will be discussed below as "occasional deliberations".

It should be noted that the popularity of both institutionalized and occasional deliberations that adopted the mechanism of collective *ijtihād* was not necessarily at the cost of the conventional individual *ijtihād*, which is done by one individual religious scholar. Both forms of *ijtihād* continue to exist and function in parallel to each other, as clearly shown by a number of individual scholars who regularly participate in the aforementioned collective endeavors but still write their monographs and defend their individual bioethical positions ('Uthmān 2009; Ghaly 2015, 294). As we shall see below, the discussions on the ethical questions related to genomics have assumed all these three forms, namely the continual and occasional types of collective *ijtihād* in addition to the individual *ijtihād*.

Deliberations on genomics: Main contributors

Islamic ethical deliberations on genomics started in 1993 as part of discussions regarding the possible implications of the then in-progress Human Genome Project (HGP). The overview sketched in this section will follow the typology outlined in the previous section and thus will start with the two types of collective or interdisciplinary bioethical deliberations, namely the continual and occasional forms, and end with the individual constitutions.

As for the influential institutions involved in the continual and systematic bioethical deliberations, the IOMS, IIFA and IFA have intensively deliberated on the ethical questions related to genomics (see Table 1). The IOMS initiated these discussions by convening the symposium "Genetics, Genetic Engineering, Human Genome and Gene Therapy: An Islamic Perspective" held from 13 to 15 October, 1998. The final recommendations of that symposium remain the most influential document until now, and all subsequent collective deliberations either commented on these recommendations or produced a slightly revised version of them. In its eleventh session, held from 14 to 19 November, 1998, the IIFA discussed these recommendations. Resolution on this topic was deferred to a future meeting because participants felt the need to conduct further study and research. From 5 to 10 January, 2002, the IFA held its sixteenth session, which discussed, among other issues, the possible fields in which DNA fingerprinting can be employed. The seventh resolution of this session made a cursory reference to the human genome, stressing that it should not be commodified in any way. From 6 to 9 February, 2006, the IOMS organized an international seminar on "Human Genetic and Reproductive Technologies: Comparing Religious and Secular Perspectives". The recommendations of this seminar included a section entitled "Declaration of Principles", which paraphrased specific segments of the recommendations adopted during the IOMS symposium held in 1998. The attempt here was to augment support for these principles by engaging religious and secular voices from outside the Islamic tradition (Awadi and Gendy 2008, 1173-75). A few years later, and during its twentieth session held from 13 to 18 September, 2012, the IIFA rekindled the discussions on the IOMS recommendations, which dated back to 1998, but again the resolution was deferred to another future meeting. However, participants recommended holding a specialized symposium dedicated to discussing the IOMS recommendations. This symposium took place in Jeddah from 23 to 25 February, 2013, and was jointly organized by the IIFA and IOMS. Finally, the IIFA endorsed the IOMS recommendations, issued about 15 years ago with few additional points. This was during the IIFA twenty-first session, held from 18 to 22 November, 2013.

Concerning the occasional bioethical deliberations that adopted the mechanism of collective *ijtihād*, we refer to some representative examples. The first example is the international seminar "Ethical Implications of Modern Researches in Genetics" held from 13 to 15 February, 1993, in Doha, Qatar. The seminar was jointly organized by the Islamic Educational, Scientific and Cultural Organization (ISESCO), the World Islamic Call Society, and the Faculty of Science at Qatar University. The seminar issued twelve recommendations, the fifth of which was dedicated to the HGP. The HGP was described as "one of the most ambitious scientific projects in the history of mankind". A forceful call was issued to Islamic countries urging them to generously fund research in this field so that Muslims may not lag behind in this domain of knowledge, which has potential far-reaching results (Islamic Educational, Scientific and Cultural Organization 1993, 263). The second example is the international conference on "Genetic Engineering between Sharia and Law". The conference was convened by the Faculty of Sharia and Law, United Arab Emirates University, and was held from 5 to 7 May, 2002. The first session of the conference was dedicated to "Human genome: its essence and future", during which papers addressed a number of genomics-related issues. Combining contributions from Muslim religious scholars and specialists in codified laws was one of the elements of this conference that was understudied in other deliberations. The published proceedings of the conference did not include final recommendations (Faculty of Sharia and Law 2002; Qashqüsh 2002, 207-214). The third example is the conference series "Pan Arab Human Genetics", organized by the Dubai-based Centre for Arab Genomic Studies (CAGS). The second edition of this series included a public forum on "The Ethical Perspectives of Human Genetic Applications in the Arab World", which was held on 20 November, 2007. The speakers in the forum, including scientists, legal advisors and religious scholars, discussed issues related to the religious and legal controls of genome research and genetic testing. Besides the submitted papers, the forum issued the "Dubai Declaration" that, among other things, recommended developing jurisdictions for regulating genome research and stressed that any scientific research in the field should not be at the expense of respecting firmly established religious principles.

In collaboration with other Qatar-based institutions, the research Center for Islamic Legislation & Ethics (CILE) also convened two activities, both of which focused on genomics and Islamic ethics. On 2 October 2014, a public seminar entitled "Islamic Ethics in the Era of Genomics" was organized in collaboration with the Qatar Supreme Council of Health (SCH).* As part of its 2015 edition, the Doha-based World Innovation Summit for Health (WISH) collaborated with CILE to organize a public panel on "Healthcare and Ethics: Genomics".** Both events convened various experts including religious scholars and biomedical scientists.***

* More information is available via http://www.cilecenter.org/en/press-release/cile-hosts-public-seminar-on-islamics-ethics-in-the-era-of-genomics/ (accessed 15 July 2015).

** More information is available via http://www.cilecenter.org/en/area-of-research/medicine-bioethics/activities/seminar/) (accessed 15 July 2015).

*** After exploring the discussions with the public, CILE has plans to involve academics in conducting research on this topic. In 2015, CILE received a prestigious award from the Qatar National Research Fund (QNRF) for the research project "Indigenizing Genomics in the Gulf Region (IGGR): The Missing Islamic Bioethical Discourse". This three-year project will start in September 2016.

Table 1: Islamic Ethical Deliberations on Genomics (1998-2013)

No.	Meeting	Place	Period	Organizers
	(A) Continual Deliberations			
1	• *Al-wirātha wa al-handasa al-wirāthiyya wa al-jīnüm al-basharī wa al-ʿilāj al-jīnī* (Genetics, Genetic Engineering, Human Genome and Gene Therapy: An Islamic Perspective)	• Kuwait	• 13-15 October 1998	• Islamic Organization for Medical Sciences (IOMS)
2	• Eleventh session	• Manama, Bahrain	• 14-19 November 1998	• The International Islamic Fiqh Academy (IIFA)
3	• Sixteenth	• Mecca, Saudi Arabia	• 5-10 January 2002	• Islamic Fiqh Academy (IFA)
4	• Human Genetic and Reproductive Technologies: Comparing Religious and Secular Perspectives	• Cairo, Egypt	• 6-9 February 2006	• Islamic Organization for Medical Sciences (IOMS)
5	• Twentieth session	• Oran, Algeria	• 13-18 September 2012	• International Islamic Fiqh Academy (IIFA)
6	• Specialized symposium	• Jeddah, Saudi Arabia	• 23-25 February 2013	• International Islamic Fiqh Academy (IIFA) • Islamic Organization for Medical Sciences (IOMS)
7	• Twenty-first session	• Riyadh, Saudi Arabia	• 18-22 November 2013	• International Islamic Fiqh Academy (IIFA)

No.	Meeting	Place	Period	Organizers
	(B) Occasional Deliberations			
8	• Ethical Implications of Modern Researches in Genetics	• Doha, Qatar	• 13-15 February 1993	• Islamic Educational, Scientific and Cultural Organization (ISESCO) • World Islamic Call Society • Faculty of Science at Qatar University
9	• Genetic Engineering between Sharia and Law	• Al Ain, United Arab Emirates	• 5-7 May 2002	• Faculty of Sharia and Law, United Arab Emirates University
10	• The Ethical Perspectives of Human Genetic Applications in the Arab World	• Dubai, United Arab Emirates	• 20 November 2007	• Dubai-based Centre for Arab Genomic Studies (CAGS)
11	• Islamic Ethics in the Era of Genomics	• Doha, Qatar	• 2 October 2014	• Center for Islamic Legislation & Ethics (CILE) • Supreme Council of Health
12	• Healthcare and Ethics: Genomics	• Doha, Qatar	• 17 February 2015	• Center for Islamic Legislation & Ethics (CILE) • World Innovation Summit for Health (WISH)

As mentioned earlier, studying the interplay of genomics and Islamic ethics is not restricted to the collective *ijtihad*, which brings together both religious scholars and biomedical scientists in a face-to-face setting. Some Muslim religious scholars made their own individual contributions on this topic as well. A few illustrative examples should be sufficient in this regard. Tunisian Nūr al-Dīn al-Khādimī is one of the active religious scholars who wrote on genomics and Islamic ethics. Besides his participation in some of the aforementioned collective meetings (e.g. the conference held in 2002 by the Faculty of Sharia and Law and the forum organized in 2007 by the CAGS, both in the UAE), al-Khādimī also published on this topic in his capacity as an individual Muslim scholar (Khādimī 2003, 7-48; Khādimī 2004, 59-76). Egyptian Muhammad Ra'fat 'Uthmān is another important religious scholar in this respect. He participated in the 2002 conference held by the Faculty of Sharia and Law in the UAE, but he also published a book whose title can be translated as *Genetic Material: Genome* ('Uthmān 2009). Also, Jordanian Muhammad Na'īm Yāsīn participated in the two activities organized by CILE in collaboration with other Qatar-based institutions in 2014 and 2015. He presented two papers, both of which are now available online on the CILE website (Yāsīn 2014; Yāsīn 2015). Besides these three examples, other religious scholars have published their views on ethical issues related to genomics (Kan'ān 2003, 68-101; Idrīs 2003, 22-25).

These individual contributions are smaller in volume, and usually present a less rigorous reasoning, compared to the work produced through the mechanism of collective *ijtihād*. However, the individual and collective contributions are linked in different ways. As mentioned above, some of these individual scholars already participate in expert meetings that bring them together with biomedical scientists. At the minimum level, these individual scholars show awareness of these expert meetings and their published proceedings, e.g. the 1993 conference held in Doha (Idrīs 2003, 25; 'Uthmān 2009, 537), the 1998 symposium organized by the IOMS in Kuwait (Uthmān 2009, 536) and the 2002 deliberations of the IFA during its sixteenth session held in Mecca (Khādimī 2004, 67). Despite missing the advantage of having face-to-face encounters with biomedical scientists, the works of these individual religious scholars did not completely miss the interdisciplinary character. It is to be noted in this regard that Muslim biomedical scientists also sometimes consult religious scholars and ask for their feedback prior to publication. The main example here is Mūsā al-Khalaf, who solicited feedback from, among other specialists and religious scholars 'Ajīl al-Nashmī and Muhammad Qal'a Jī on the draft of his book on genomics (Khalaf 2003, 15).

Ethical Management of Incidental Findings

Previous Contributions

Despite the abundance and richness of the aforementioned collective and individual deliberations, the ethical questions triggered by incidental findings did not receive their due share in the discussions. This has to do, among possible other reasons, with the fact that the core and seminal discussions on genomics took place during the IOMS seminar held in 1998. At that time, the ethical questions generated by incidental findings did not make standard part of the bioethical literature on genomics worldwide.* As stated above, it seems that subsequent, especially collective, deliberations within the Muslim world were just tightening and fine-tuning the discussions of the 1998 seminar, without responding to the new updates and pertinent ethical questions in this field. It should be noted that a recent study, authored by a number of Qatar-based biomedical scientists, stressed the significance of addressing the ethical questions raised by the incidental findings in the context of Muslim-majority countries (Shanti et al 2015). However, the study did not elaborate on how this issue should be approached from an Islamic perspective.

The Saudi-based epidemiologist Omar Kasule, who frequently writes on Islam and bioethics, also touched briefly upon this issue in his presentation during the First Annual Saudi Society of Medical Genetics Conference, held at King 'Abdulaziz City for Science and Technology on 30 April, 2015. In the bullet-point presentation available on his website, Kasule argues that the genetic researcher "must avoid the complications of incidental findings by not looking for them or even noticing them". He added that the ethical dilemmas that may arise from incidental findings could be resolved in advance through the consent process (Kasule 2015).

Framing the Discussion: Methodological Remarks

Normally speaking, full and consistent bioethical analysis should take note of four main levels of moral discourse. At the first and most abstract level (metaethics), one addresses the basic questions of ethics and their ultimate grounding, e.g. 'What are the sources of ethics?' 'How do we deal with these sources and make sure that the answers we provide are possibly the right ones?' Religious traditions usually have a particular interest in this level and most of them, including the Islamic tradition, have developed standard approaches towards such metaethical questions. At the second level of moral discourse (normative ethics), one examines the broad norms of behavior and character. Within this level, lists of moral principles and values are articulated and used as ethical criteria for judging actions besides other lists concerned with the character traits that are to be judged as morally praiseworthy. At the third level (rules and maxims), one moves to the general rules, rights and maxims

* According to the report released by the Presidential Commission for the Study of Bioethical Issues in December 2013, the earliest (indirect) recommendations related to incidental and secondary findings were issued in 1998 by the US National Human Genome Research Institute and, outside the United Sates, in 2001 by the Japanese Ministry of Health, Labour and Welfare (Presidential Commission for the Study of Bioethical Issues 2013, 139, 144).

that apply to several cases. Sometimes certain groups of these rules and maxims are put together as codes of ethics. At the bottom and fourth level (casuistry), one deals with concrete and individual case problems where one tries to look for the morally appropriate behavior in a particular situation. It is sometimes possible to come to an agreement on the morally acceptable course of action in a particular situation (fourth level) without having the same degree of agreement at other levels, especially the first one. However, it becomes sometimes indispensable to develop a full and consistent ethical analysis that includes all four levels when the bioethical issues at hand are multi-layered and intricate, as is the case with genetic engineering and new reproductive technologies (Veatch 2012, 2-9).

Against this background, and for the sake of presenting a rigorous bioethical analysis rooted in Islamic tradition and open for constructive dialogue with other traditions, we believe that Islamic ethical discourse on genomics in general needs to touch upon the above-mentioned levels and bring them into equilibrium to the greatest extent possible.* One ideally starts with the level of metaethics and then moves down to the remaining levels, ending with the bottom level of casuistry. It is usually not of great importance where one starts: either from the top level of metaethics and then moving down to the point, which tells us how to act in particular cases, or the other way around. However, some theorists believe that the ideal way is the only right way (Veatch 2012, 9). For the sake of convenience, we will group the first three levels (metaethics, normative ethics and rules) together under the heading "Theoretical Framework", whereas the fourth level (casuistry) will be discussed separately under the heading "Towards Practical Guidelines".

Theoretical Framework

The basic metaethical questions about the sources of ethics and how to employ them properly in ethical reasoning have been an integral part of Islamic tradition throughout history. Muslim scholars consensually agree that the Quran, believed to be the literal word of God, is the fundamental source of knowledge about ethics, among many other things. Immediately after the Quran, and according to some scholars even parallel to it, comes the Sunna, which includes the statements, deeds and approvals attributed to the Prophet of Islam. All other sources of knowledge, including human intellect, rationality and people's customs, derive their legitimacy from these two main sources: the Quran and the Sunna.

The Quran introduces a detailed vision about the universe, the position of humans therein, and how man should act and behave in an ethical way. According to the macro-narrative portrayed in the Quran and also further delineated in the Sunna, man is presented as God's noble creature who was created to accomplish three main tasks: cultivation of the earth (*'imārat al-ard*), worshipping God through performing certain religious obligations and rituals (*'ibāda*), and behaving in the capacity of God's trustee and vicegerent on earth (*khilāfa*) (see the Quranic verses 11:61; 51:56; 07:129).

* This approach also goes in line with recent calls made by some academics to develop a comprehensive discourse in contemporary Islamic bioethics which goes beyond the strict legal boundaries (Sachedina 2008, 244).

According to Muslim scholars, these tasks represent the main objectives for which humans were created (*maqāsid al-khalq*) and they express the purport of the divine universal will (*al-irāda al-takwīniyya*). The more one gets closer to these objectives, the more moral this individual becomes. Thus, one's status and degree of nobility, according to the Creator's scale, is inherently linked to the degree of success in fulfilling these tasks or achieving these objectives. (Asfahānī 2007, 82-83). In order to help human beings lead their lives in a way which does the best service to these objectives, a religio-ethical system (Sharia), including much more detailed and practical guidelines, was revealed to every human nation, as clearly stated in the Quran (05:48). When Muslim scholars surveyed the religio-ethical system of Islam, they concluded that Sharia has five main objectives, sometimes called the higher objectives of Sharia (*maqāsid al-Sharī'a*) that reflect the broad lines of the divine legislative will (*al-irāda al-tashrī'iyya*). These objectives consist of safeguarding religion, life, wealth, intellect and offspring. Thus, actions that lead to achieving one of these five objectives is to be considered a benefit and deserves to be promoted from an ethical perspective, whereas actions that contradict these objectives are to be categorized as harm and thus should be morally condemned.* Striving towards achieving these objectives is introduced in the Quran as the way to gain happiness and prosperity in this life and salvation in the hereafter. As for the question about what makes a certain individual a morally good physician or biomedical scientist, various works throughout the history of Islamic tradition tried to outline the praiseworthy character traits of such a person. Besides being well-versed in the medical profession, authors of this genre spoke about the need to master various virtues mentioned in and promoted by the Quran and Sunna. Some authors also spoke about the need to have some basic knowledge about the relevance of religious precepts and rulings for his/her professional work (Ruhāwī 1992, Abu Ghudda 1981, 145-165; Bār and Sibā'ī 2009). The discourse on the objectives of creation would fall within the first level (metaethics) and that on the objectives of Sharia and the physician's praiseworthy character traits within the second level (normative ethics), although an overlap can sometimes happen between the two levels.

What do these two levels of moral discourse mean for the ethical questions relevant to incidental findings? We give just a few concise illustrative examples, leaving the detailed explanation for the following section when we speak about the practical aspects related to the fourth level (casuistry). First, the divine will, in its both universal and legislative forms, has higher authority than the will of the human individual. The concept of submission to God's will (*imtithāl*) is central to both the objectives of creation and those of Sharia ('Atiyya 2003, 109). Thus, if it is known that revealing a specific incidental finding will result in preventing an individual from achieving one of the abovementioned objectives (e.g. performing religious duties or rituals [*'ibāda*] because of the distress resulting from receiving bad news), then this finding should not be communicated to this individual even if he/she gave consent to do so. The abovementioned two levels of moral discourse also have a bearing on grasping the two key concepts of benefit and harm and how to demarcate their boundaries. In mainstream bioethical literature, it is usually argued that revealing incidental

* The relevance of the objectives of *maqāsid al-Sharī'a* to bioethics was explored in various studies published in both Arabic and English (Zuzu 2002, 167-201; Raf' 2012; Ghaly 2016).

findings can be defended on ethical grounds whenever there is clinical utility. Some bioethicists tried to broaden this concept by speaking about personal utility, which may include the possibility of arranging one's plans for reproduction or career development and retirement (Daack-Hirscha et al 2013, 11-18). However, in an Islamic moral discourse that takes these two levels of moral discourse into consideration, the concept of utility cannot remain confined within the boundaries of health-related or social well-being in this life. Other religious dimensions, including spiritual well-being and the impact of one's actions on his/her salvation in the hereafter, must also be part of the benefit-harm assessment within the context of incidental findings. Similarly, incidental findings with implications for human reproduction should be approached with extreme cautiousness, because protecting offspring is one of the higher objectives of Sharia. In addition, the Islamic discourse on the ideal character traits of a physician or biomedical scientist can also be of help for the ethical management of incidental findings. Besides the requirement of having a high standard of professional skills, healthcare providers should also be aware of the pertinent religious aspects, or should at least communicate and consult with advisory bodies that have this type of knowledge.

The third level of moral discourse (rules and maxims) is complementary to the abovementioned two levels. This level helps the process of specification: when we move from the abstract and general levels to the more specific level of casuistry. This level is typically represented in the Islamic tradition by the vast genre of juristic maxims (*al-qawā'id al-fiqhiyya*). By examining various references in the Quran and Sunna and reviewing a great number of individual juristic rulings, Muslim jurists formulated concise and precise maxims that can be employed to judge a great number of similar new cases (Zakariyah 2015, 24-79). Various contemporary writings have explored the possible contribution of this genre to the field of bioethics and more particularly principle-based bioethics (Ghaly 2015, 28-29, 32-33). As for the relevance of this level to the moral discourse on incidental findings, we refer to the legal maxim that reads, "Nobody is allowed to dispose of another's property without their consent". We have explained above that the primary factor, which guarantees the moral character of actions is their conformity with God's will. However, when certain actions are declared as permissible or morally praiseworthy from a religious perspective, it does not mean that they can be unconditionally practiced. When these actions are performed on another person's body, this legal maxim demonstrates, obtaining the consent of this person becomes mandatory in order to legitimize the action from a religio-ethical perspective. This is because managing affairs related to the human body necessitates considering two main rights or claims, the first of which relates to God in the capacity of the Creator of the body and the second claim relates to the person in the capacity of the body's trustee (Abu Ghudda 1982, 789). This means that the ethical management of incidental findings cannot be properly done without closely consulting with research participants or patients and getting their consent for the management process.

Towards Practical Guidelines

The fourth level of moral discourse (casuistry) is the most practical one, in which concrete actions are to be judged from an ethical perspective. In moral philosophy, the standard threefold scheme for the classification of actions entails that actions would normally fall into one of three main categories, namely (a) obligatory, (b) prohibited, and (c) permissible or morally neutral. Actions which are morally right and required fall into the first category, those which are morally wrong and condemned fall into the second category, and the actions which do not fit into one of the first two categories would be considered neutral and make part of the third category. In his article "Saints and Heroes", published in 1958, J. O. Urmson was the first in modern non-religious moral philosophy* to argue for the need of a fourth category, namely (d) supererogatory. This fourth category would include heroic or saintly self-sacrifices that go beyond the bounds of duty, like the doctor who volunteers to help in a foreign, plague-ridden city. Despite Urmson's critique, some moral philosophers continued defending the veracity of the traditional tripartite classification scheme of actions. However, the new fourfold categorization of moral acts (obligatory, forbidden, supererogatory and permissible) proved to be more appealing to the extent that some moral philosophers now describe it as "near dogma" (Guevara 1999, 593-624; Hedberg 2014, 3623- 24), which could find its way to standard works on bioethics (Beauchamp and Childress 2013, 45). However, the traditional tripartite classification is not obsolete, and some bioethicists suggested using it within the context of the ethical management of incidental findings (Presidential Commission for the Study of Bioethical Issues 2013, 84-85).

In the Islamic tradition, similar discussions took place, but neither the traditional tripartite classification nor the new fourfold categorization was adopted. Besides the abovementioned four categories (obligatory, forbidden, supererogatory and permissible), the standard Islamic classification of actions included a fifth one, namely (e) reprehensible. The fifth category includes actions that are discouraged from a religio-ethical perspective although they are not strictly forbidden. This fivefold categorization for actions is called *al-ahkām al-khamsa*, which literally means "the five rulings" and usually translates into English as "five values", "five categories" or "five principles" (Firmage, Weiss and Welsh 1990, 204; Kamali 2003, 413). Besides the difference in the number of categories between the categorization of actions in moral philosophy and the one adopted in the Islamic tradition, especially within the discipline of Islamic jurisprudence (*fiqh*), two other differences should be kept in mind. As explained above, the religious dimension represented in conformity with God's will plays a key role in judging the moral worth of actions. For instance, obligatory actions were defined as the actions whose omission would incur God's wrath and punishment in this life or in the hereafter. The other four categories were also defined through the same lines (Kamali 2003, 413-431). In addition, this fivefold categorization remained almost exclusive to the discipline of Islamic jurisprudence (*fiqh*) in which the legal and ethical aspects are sometimes conflated. Thus, one should be aware of this issue because the "ethical" and "legal" aspects of an action are not always identical.

* It is to be noted that some ethical traditions, including the Roman Catholic, did not embrace the traditional tripartite classification of actions (Hedberg 2014, 3623). Although the Roman Catholic tradition adopted the concept of supererogation, it was strongly attacked by Lutherans and Calvinists.

We argue that this fivefold categorization is the most fitting tool through which actions related to the ethical management of incidental findings should be classified based on their moral worth. This categorization is deeply rooted in Islamic tradition and makes up part of the moral philosophical discourse that is not exclusive to Islamic tradition. Additionally, it can be easily linked to the previously mentioned three levels of moral discourse, and thus enhance the possibility of developing a consistent and coherent discourse. In order to remain within the standard size allocated for this study, we will just give examples of two main categories only, namely (a) obligatory and (b) forbidden. These two categories represent the two borderlines that distinguish the ethical action from the unethical one. Discussions on further nuances will be left for a follow-up study and/or policy guidelines tailored for specific contexts.

(A) Obligatory

The minimum ethical obligation to the potential recipients of incidental findings, including patients and research participants, is to adequately inform them beforehand that such findings may arise. This obligation emanates from the principle of fidelity, which is one of the key values promoted by the foundational scriptures of Islam, namely the Quran and Sunna. This principle becomes incumbent when there is a relationship between two parties with unequal power, for example the relationship between the patient and the physician, or the research participant and researcher. The more powerful party (in this case the physician and researcher) are bound by the fiduciary duty. The aforementioned legal maxim "Nobody is allowed to dispose of others' property without their consent" is also relevant. As explained above, this maxim dictates obtaining consent from people whenever their body will be the subject of specific interventions. Such consent cannot be obtained in an ethical way without informing the concerned person about the likelihood of incidental findings. This information will empower the potential recipient of incidental findings and enable him/her to take informed decisions.

The disclosure of some incidental findings can also be obligatory in certain cases, such as a probable life-threatening condition which could be avoided though preventive measures. The US Presidential Commission gave the example of the genetic predisposition to malignant hyperthermia. It is a condition associated with severe and life-threatening reactions to certain kinds of anesthesia. Disclosing this information can be lifesaving (Presidential Commission for the Study of Bioethical Issues 2013, 139, V). One of the co-authors of this study had personal experience with a specific mutation that put him at risk of sudden death due to heart arrest and he had to undergo a six-hour surgery. Now, he plans to screen his (future) children to see if any of them has this mutation so that the necessary preventive measures can be taken. Whenever such information is contained within the incidental findings, then it is an ethical requirement to communicate it to the people concerned.

The ethical obligation of disclosing this type of information to the recipient of incidental findings relates to the previously noted higher objective of Sharia, protecting life (*hifz al-nafs*) and all its ramifications found throughout the Islamic tradition. Muslim scholars consensually agree that providing lifesaving support for someone in danger (*ighāthat al-mudarr*) is a religio-ethical obligation, and not doing so is considered a sin from an Islamic perspective. Although this obligation is indiscriminately applicable to all members of society, Muslim scholars state that it is more stringent for those who have the knowledge or the capacity to provide this lifesaving support than other members of society who cannot do so (Wizārat al-Awqāf wa al-Shu'ūn al-Islāmiyya 1984-2005, 5/195-96). This means that physicians and researchers will be more bound by the ethical duty to warn people about life-threatening conditions than anyone else. The same line of reasoning is more or less applicable to some communicable conditions that represent danger for those infected and for others in society as well. The ethical duty of disclosing such information may even be more stringent about life-threatening diseases because it would involve the possibility of avoiding public harm and not just individual harm.

We argue that concerned institutions, including biobanks, research centers and hospitals, should make their own list of obligatory actions related to incidental findings. This list should be thoroughly discussed with the potential recipients of incidental findings during the process of obtaining consent. Rejecting some of the items included in this list can be an exclusion criterion of the research study. In the clinical context, the Institutional Review Board (IRB) or similar consultative bodies should be involved to decide the best course of actions to be followed with such patients, depending on the particularity of each case.

(B) Forbidden

Some of the incidental findings are now relatively common to the extent that they are quite anticipatable, and thus a rigorous prior plan for their ethical management is indispensable. As explained in the first two chapters of this study, misattributed paternity is one of the typical examples in this regard. Because of its highly sensitive nature, especially within the context of Muslim culture, this example will be addressed with some details below. The main thesis here is that it is ethically objectionable and prohibited to disclose such incidental findings.*

As mentioned above, protecting offspring is one of the higher objectives of Sharia. The package of procedures developed in Islamic tradition for the sake of achieving this objective is considerably vast and wide in scope, and many of its details already exist in the Quran. Part of this package has to do with the preservation of the unblemished lineage (*nasab*) of future generations, which can be secured through children born from a legitimate marital relationship between a man and a woman. Preservation of *nasab* through marriage is not only the obligation of future parents, but also the inalienable right of future children. Having children through legitimate marital relationships is crucial for effecting a great number of rights and duties accruing from the *nasab* between parents and their children. Thus, the child's lineage, which produces

* It is to be noted that the discussions here exclusively relate to paternity and thus not to ancestry. For instance, disclosing incidental findings related to one's tribe or clan can be problematic because of the sensitivity of these issues for (some segments of) society in the Gulf region (GhidhāmÏ2009). However, disclosing this information does not necessarily always fall within the category of forbidden actions. Instances related to ancestry should be based on a case-by-cases basis and within their particular context.

such rights and duties in Sharia, is not exclusively biological, but it is also essentially tied with the existence of a legitimate marital relationship between the parents when they conceived the child (Quradāghī and Muhammadī 2008, 342-345).

This is not only a matter of normative religious theorization, but it also has considerable potential impact on the life of many Muslims. In Muslim culture, the institution of marriage is conditional for guaranteeing proper lineage and the ensuing dignity for the procured children. Children born out of marital wedlock can lose this dignity in society and end up suffering serious stigmatization. The codified laws adopted by many Muslim majority countries also reflect this dominant culture. The existence of recognized marital relationships is usually a condition for the children's entitlement to many rights, including inheriting property from biological parents (Welchman 2007, 142-150; Sachedina 2009, 103, 107).

Within this broad framework, the lineage of children born between a married couple is automatically and firmly established. The way to negate this established lineage is via a spouse's request to engage into a specific legal procedure known as mutual oaths of condemnation (*liān*). This procedure entails a public confirmation, assuming the form of pronouncing strict oaths, from the side of the husband that his wife has engaged in illicit sexual relations and that the resulting child is not his. On her side, the wife has the right to deny her husband's accusation through pronouncing counter oaths that her husband is telling lies. Upon pronouncing the oaths of condemnation from both sides, not only is the blood relationship between the husband and the child negated, but also the marital relationship is irrevocably terminated. However, the truth about the paternal lineage of the child remains indeterminable (Shabana 2013, 159).

With the introduction of the modern technology of DNA fingerprinting, the question was raised about the possibility of using this technology to settle paternity disputes instead of mutual oaths of condemnation (*liān*). The question was addressed by many individual religious scholars and by the institutions that employed the mechanism of collective *ijtihād* or interdisciplinarity. The position adopted in 2002 by the Islamic Fiqh Academy (IFA) in Mecca fairly represents the mainstream voice in contemporary Islamic bioethics.

The IFA did not question the scientific reliability of the DNA fingerprinting, but clearly stated that this new technology cannot replace *liān* and also cannot be used for negating an established lineage. The IFA statement also stressed that this new technology must not be used for checking or verifying an already-established lineage from the perspective of Sharia, and that deterring penalties should be imposed on those who use it for this purpose (Quradāghī and Muhammadī 2008, 367-369). In line with this position, some Muslim countries, such as Saudi Arabia, have already outlawed conducting DNA paternity testing among married couples. These recent discussions show resistance from the side of Muslim religious scholars to integrate the technology of DNA fingerprinting into the Islamic religio-ethical discourse on paternity disputes between married couples even if it is requested by one spouse. It is clear that their main concern here is not the (un)reliability of the DNA test but the Islamic ethical principles that will be sacrificed, e.g. safeguarding individuals' privacy (*satr*) and dignity, and also maintaining public order in society.

These deliberations show the broad ethical framework that guided the discussions of Muslim religious scholars on paternity disputes between married couples, and their position: that modern technology plays hardly any role in settling such disputes. Within this ethical framework, paternity is automatically and inseparably linked to marital relations. This established paternity cannot be negated except through specific channels recognized by Sharia. The incidental findings that reveal information about misattributed paternity do not fall within any of these channels. Additionally, negating an established paternity falls outside the scope of biomedical research projects and clinical tests. Thus, these incidental findings should not be disclosed. Furthermore, both research analysis and clinical tests should be targeted as much as possible in order to avoid, or at least minimize, resulting in this type of sensitive finding. Such a targeted approach is the one recommended by various international institutions, including the European Society of Human Genetics and the UK-based PHG Foundation (Presidential Commission for the Study of Bioethical Issues 2013, 140). Some of the religious scholars we have personally approached about this issue suggested differentiating between disclosing this information to individuals—that should be strictly forbidden—and to state authorities. According to some, sharing the overall statistics about the cases of misattributed paternity with state authorities does not entail direct harm to individuals' privacy because their identities will remain unidentifiable. However, the main benefit here is to have an overall indication about the actual role of Islamic normative ethics in the living realities of Muslim societies. This will help authorities in Muslim-majority countries to develop their plans for promoting Islamic ethics accordingly. However, we argue that this suggestion may also have detrimental effects upon public order and thus should be taken with caution.

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