RESEARCH ARTICLE

Recommendations for the development of Egyptian human biobanking ethical guidelines [version 1; peer review: 1 approved, 1 approved with reservations]

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v1 **First published:** 13 Jan 2021, **6**:4
https://doi.org/10.12688/wellcomeopenres.16556.1
Latest published: 19 Mar 2021, **6**:4
https://doi.org/10.12688/wellcomeopenres.16556.2

Abstract

Background: The development of biobanks is associated with the emergence of new ethical challenges. In Egypt, several biobanks have been established, but there are no specific local ethical guidelines to guide their work. The aim of this study is to develop recommendations for the Egyptian human biobanking ethical guidelines, which take into consideration the specific cultural and legal framework in Egypt.
Methods: We searched the literature for available biobanking ethical guidelines. Six themes were the concern of search, namely; informed consent, data protection, return of results, sharing of samples and data, community engagement, and stakeholder engagement. If a document refers to another guideline, the new source is identified and the previous step is repeated.
Results: Ten documents were identified, which were analyzed for the themes mentioned above. Guidelines and best practices were identified, and then compared with the published documents about ethical, legal and social issues (ELSI) related to biomedical research in Egypt to reach best recommendations.
Conclusions: We have proposed, by way of recommendations, key characteristics that a national ethics framework in Egypt could have. On informed consent, the practice of broad consent may be harmonized among biobanks in Egypt. Clear policies on return of research results, training requirements and availability of genetic counseling could also be instituted through the national framework. Additionally, such a framework should facilitate community and stakeholders engagement, which is important to secure trust and build consensus on contentious issues arising from sample and data sharing across borders and commercialization, among other concerns.

Open Peer Review

Reviewer Status ? ✓

	Invited Reviewers	
	1	**2**
version 2 (update) 19 Mar 2021		
version 1 13 Jan 2021	? report	✓ report

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Keywords
Biobanking, Ethical guidelines, Egypt, Informed consent, data sharing

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Author roles: Samir Abdelhafiz A: Conceptualization, Formal Analysis, Funding Acquisition, Methodology, Writing – Original Draft Preparation; **W. L. Ho C**: Supervision, Writing – Review & Editing; **Chuan Voo T**: Supervision, Writing – Review & Editing

Competing interests: No competing interests were disclosed.

Grant information: This work was supported by the Wellcome Trust through funding to the Global Forum on Bioethics in Research (GFBR) [216284]. GFBR funding is provided by the Wellcome Trust, the Bill & Melinda Gates Foundation, the National Institutes of Health and the UK Medical Research Council.
The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

How to cite this article: Samir Abdelhafiz A, W. L. Ho C and Chuan Voo T. **Recommendations for the development of Egyptian human biobanking ethical guidelines [version 1; peer review: 1 approved, 1 approved with reservations]** Wellcome Open Research 2021, **6**:4 https://doi.org/10.12688/wellcomeopenres.16556.1

First published: 13 Jan 2021, **6**:4 https://doi.org/10.12688/wellcomeopenres.16556.1

Introduction

In Egypt, eight human disease based biobanks have been established over the past few years[1]. These biobanks are distributed across six governorates (from the north to the south of Egypt), where they collect samples from different categories of patients, including cancer patients, liver patients, and heart disease patients (Table 1). While these biobanks have their own ethics policies and operating procedures, the divergent standards, expectations and practices that have emerged present a number of challenges to appropriate stewardship of valuable biological resources, including more effective management and sharing of these materials and related data. At present, Egypt does not have research ethical guidelines specific to medical research or biobanking and related databases; only documents containing a short chapter about clinical research[2]. The absence of specific guidelines has been identified as a major challenge by members of research ethics committees (RECs) in Egypt[3].

The development and growth of increasingly diverse pool of biobanks and complex biobanking practices are associated with aggravating well-recognized ethical concerns (such as informed consent and privacy) and the emergence of a range of new ethical challenges, including issues related to unfair discrimination arising from sharing of different types of samples and data[4,5]. First, it is not always clear which approach to consent-taking is ethically most appropriate for the type of biological material and data being collected for the purposes of primary and secondary research uses. Second, it is increasingly challenging to assure donors that their privacy and confidential information will be always secure. Third, there is growing complexity in the management of incidental and secondary findings, even while there is greater expectation on the part of potential donors that certain results should be returned to them[6,7]. Fourth, sample and data sharing across borders, ownership of tissue, and commercialization continue to raise concerns about equity and public trust[5,6].

These concerns and challenges have contributed to the development of a number of international and professional ethical guidelines and best practices over the past 20 years[6,7]. These include, among others, different versions of NCI Best Practices for Biospecimen Resources (NCI Best Practices), the International Society for Biological and Environmental Repositories (ISBER) best practices, the Organization for Economic Cooperation and Development (OECD) Guidelines for Human Biobanks and Human Genetic Databases[6]. These documents provide general technical and ethical guidance that are widely accepted, but differences in social, cultural, political and institutional conditions have resulted in divergent interpretations and practices. A major concern is the lack of uniform ethical standards and safeguards, which could impede appropriate sharing of materials and data and might have legitimized different turfs that have been formed. Moreover, many guidelines may be too general and do not provide adequate guidance in low resource research environments, with limited or no supportive legal, social and cultural infrastructure.

At an institutional level, biobanks attempt to address these issues through the establishment of an effective governance system which ensures protection of participants, integrity, accountability, transparency, and trust while being dynamic and flexible at the same time[8–11]. A clear governance structure that is consistent with local and international guidelines and/or regulations has been recognized to be important[8,10,12]. Like biobanks elsewhere, the biobanks in Egypt have established governance structures that provide guidance on technical and ethical issues encountered and policies on related committees, including RECs. While these institutional initiatives are important, they cannot adequately address the growing number of ethical concerns or provide public assurance. Health-related research that biobanks enable and support is as much a social concern, as it is a scientific endeavour[13]. Certain concerns that arise from the biobanking enterprise itself or from research

Table 1. A list of biobanks in Egypt.

Affiliation of the biobank	Organization hosting the biobank	Governorate	Patient categories
National Liver Institute, Menoufia University	University	Menoufia	Cancer and non-cancer
Children's Cancer Hospital 57357	NGO	Cairo	Cancer
National Cancer Institute, Cairo University	University	Cairo	Cancer
Faculty of Medicine Ain Shams Research Institute	University	Cairo	Cancer
South Egypt Cancer Institute	University	Assiut	Cancer
Shefaa Al Orman Oncology Hospital	NGO	Luxor	Cancer
MagdiYacoub heart foundation	NGO	Aswan	Non-cancer
Alexandria University	University	Alexandria	Cancer and non-cancer

* All biobanks are disease based, and all of them are non profit.

that a biobank supports require societal level engagement, deliberation and resolution. A national ethics framework for biobanking could be a means of harmonizing divergent standards and practices among different biobanks operating within a jurisdiction, and drawing participation from a broader range of interested stakeholders into dialogue and deliberation. In this paper, we argue for the establishment of such a national ethics framework for biobanks in Egypt, and suggest the themes that should be addressed therein.

The substance of this proposed framework is based on the existing body of international guidance and best practices. In the identification of these themes, we draw from the international and professional guidelines, while remaining sensitive to locally relevant issues and cultural differences. In other words, we have sought to identify ethical themes that apply to all biobanks in Egypt, with reference to international guidelines, and taking into consideration the specific cultural and legal framework in Egypt. It should be noted that although these themes apply mainly to Egypt, they are likely to be applicable to varying degrees to other developing countries in Africa and the Arab region due to similar infrastructure and/or cultural frameworks.

Methods

We searched the literature for available biobanking ethical policies and guidelines over the past ten years. he search, which was carried out from January to March 2020, included Google, Google Scholar and PubMed. The search terms included the words "Biobanking ethics", "Biobanking ethical guidelines", "Biobanking guidelines". The terms were searched on these websites without adding any parentheses or quotation marks. Six main themes have been the concern of search, namely; informed consent, data protection, privacy and confidentiality, return of results and incidental findings, access to and sharing of samples and data and commercialization issues, community engagement and stakeholders engagement. These themes have been highlighted to be important in recent literature on biobanking and related data use for research purposes. They also cover the key processes in the biobanks from the ethical point of view as they deal with different stakeholders starting from the establishment of a biobank, through sample and data collection and distribution, finally ending by return of results and incidental findings. Any international document discussing any of these themes and providing recommendations for them was included. Documents describing recommendations specific for a single country that can't be applied in Egypt were excluded. General documents about research ethics that are not applicable in the biobanking field were also excluded.

Potentially relevant papers and documents have been searched thoroughly for relevance to the subject. If a publication or a guideline refers to another guideline, the second source is identified and the previous step is repeated. To reach best recommendation, we also searched the literature for publications or regulations related to the ethical, legal, and social issues related to biomedical research or biobanking in Egypt. The search terms included "Research ethics in Egypt", "Clinical research law in Egypt" , "Research ethics guidelines in Egypt", and "Biobanking in Egypt". While specific and recent documents or regulations discussing these issues were included, general or old documents that have been updated were excluded.

Results

Ten relevant documents and six themes that relate to governance were identified. Each document was analyzed for the guidelines stated for each of the six titles mentioned above. A list of the guidelines, themes covered in each of them, and their relevance to the current work is listed in Table 2. Guidelines and best practices were identified, and then compared with the published documents about ELSI related to biomedical research in Egypt to reach best recommendations. In the section that follows, we consider how a national framework that encompasses these themes can advance ethical practices (inclusive of responsible sharing of biological materials and related data) in Egypt.

Discussion

The quality of research in Egypt needs to be improved through funding, international collaboration, capacity building and sharing of scientific data. Medical research should be done in accordance to local and international laws and regulations pertaining to human subject research[14]. In general, the laws in Egypt should not contradict the Qur'an and Islamic texts[15]. According to the Egyptian constitution ""Islam is the state religion, and that principles of Islamic Jurisprudence are the main source of legislation"[16]. Thus, it is important to consider religious issues while discussing the development of biobanking ethical guidelines in Egypt. Previous studies have shown that the establishment of research biobanks is allowed, and the issues of autonomy, confidentiality, beneficence and nonmaleficence are respected in Islam[15,17,18]. Interestingly, patients from the two main religions in Egypt, Islam and Christianity, who participated in a survey about biobanking did not think that there is a religious problem with donating samples for research in general[19]. Consistent with these empirical findings, religion should not present a barrier to most types of biobanking activities and related research, although the guidelines should emphasize the need to be respectful of religious beliefs and practices. Based on the themes that were identified from the literature review, we examine how they may be applied in the context of Egypt.

I. Informed consent

The aim of seeking consent is to inform potential participants about anticipated procedures, risks and benefits of participation and alternatives to participation so that they will be able to exercise voluntary choice on participation or contribution of biological material or related data to a biobank. As noted in the literature, this can be challenging if collected samples may be used for future and as yet unspecified research. This process may be even more challenging if future research use involves the generation and/or sharing of genomic data[20,21].

As the literature shows, several types of consent may be used by a biobank; each has its advantages and disadvantages. These include, among others, specific consent (which ties consent to

Table 2. Relevant document/guideline/best practice related to biobanking ethical guidelines.

Document/Guideline/Best practice	Year issued	Issued by	Themes covered	Relevance
OECD Guidelines on Human Biobanks and Genetic Research Databases[8].	2009	Organization for Economic Cooperation and Development.	Informed consent Privacy Access and sharing Return of results	An international document that provides guidance for the establishment, governance, access, use of human biobanks.
Common Minimum Technical Standards and Protocols for Biobanks Dedicated to Cancer Research[10].	2017	The International Agency for Research on Cancer (IARC)	Informed consent Privacy Access and sharing Return of results Community engagement Stakeholders engagement	An international document that includes guidelines and recommendations for biobanks. The based on evidence-based guidelines. The book includes sections on ELSI and sample sharing
WMA Declaration of Taipei on Ethical Considerations regarding Health Databases and Biobanks[11].	2016	World Medical Association	Informed consent Privacy Access and sharing	An international document that covers the collection, storage and use of samples and data for research. In agreement with the Declaration of Helsinki, this document provides ethical principles for their use in Biobanks
Ethics and Governance Framework for Best Practice in Genomic Research and Biobanking in Africa[12].	2017	H3Africa Working Group on Ethics.	Informed consent Privacy Access and sharing Return of results Community engagement	A regional document that provides a framework to provide an approach for best practice for biobanking in Africa
International Ethical Guidelines for Health-related Research Involving Humans[13].	2016	Council for International Organizations of Medical Sciences (CIOMS) in collaboration with the World Health Organization (WHO)	Informed consent Privacy Access and sharing Return of results Community engagement Stakeholders engagement	An international document that provides internationally accepted ethical principles and how ethical principles should be applied, with attention to research in low-resource settings.
NCI Best Practices for Biospecimen Resources[20].	2016	Biorepositories and Biospecimen Research Branch National Cancer Institute	Informed consent Privacy Access and sharing Return of results Community engagement Stakeholders engagement	A national document that provides guidelines for biospecimen best practices, and supports adherence to ethical and legal requirements.

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Document/Guideline/Best practice	Year issued	Issued by	Themes covered	Relevance
ISBER Best Practices: Recommendations for Repositories - 4th Edition[22].	2018	International Society for Biological and Environmental Repositories	Informed consent Privacy Access and sharing Return of results Community engagement	An international document that provides guidance in different aspects of biobanking base on the experience of different biobanking experts.
UK Biobank Ethics and Governance Framework[23].	2007	UK Biobank	Informed consent Privacy Access and sharing	A local document from a big biobank that outlines the ethics and governance framework of this biobank.
Recommendation CM/Rec(2016)6 of the Committee of Ministers to member States on research on biological materials of human origin – Explanatory Memorandum[24].	2016	Council of Europe.	Informed consent Privacy Access and sharing Return of results	A regional document on research on biological materials of human origin that aims to protect the rights of individuals whose samples could be used in research project after collection and storage, while benefiting researchers from the access to biological materials.
Framework for Responsible Sharing of Genomic and Health-Related Data[25].	2014	Global Alliance for Genomics and Health (GA4GH)	Informed consent Privacy Access and sharing Community engagement	An international document that provides a framework to accelerate progress in human health through effective and responsible sharing of genomic and clinical data.

a specific research project), broad consent, dynamic consent (using technology to give participants the choice between broad consent or to approve one study at a time), and tiered consent (also called multilayer consent, where the participant may allow some uses of the samples only and renewal of consent is needed for other studies)[6,7,10,22].

A broad informed consent allows the use of samples in multiple future research projects. Unlike blanket consent in which there are no restrictions on use of samples, broad consent allows for potential future use in specified areas of research indicated to participants[12,13]. Broad consent should contain details about the biobank, type of collected data, protection of participants' rights, use, storage, access, possibility of re-contact, property rights, sharing conditions and benefit sharing, as wells as commercialization of the samples[8,11,12,20,23]. Information on the right to withdraw, return of individual results, as well as risks especially if the uses include genome-wide association studies (GWAS) and gene sequencing studies, should also be provided[20]. A broad consent mechanism covering these aspects is considered adequate to meet the informational needs of a prospective donor/participant, and is recognized to be acceptable for use by biobanks in the guidelines that we analyzed. This should be complemented by a robust ethics governance system, which usually includes a REC or institutional review board (IRB) where ethical requirements are concerned[7,10,12,13,26]. RECs/IRBs oversee biobanking activities to ensure that the process meet these specifications[13]. Moreover, REC/IRB must revise and approve all research proposals that may involve use of samples and data stored in the biobanks[7,13,22]. If the scope of the submitted research proposals is beyond the scope of broad consent, new consent may be required by the REC/IRB, unless the requirement of consent is waived based on reasons such as minimal risk, necessity of using identifiable information, impracticability in obtaining consent, and public interest[8,10,22].

Research involving collection of biological samples from children should in general require heightened scrutiny due to their potential limited capacity to understand the concepts and implications of research[27]. A balance between the benefits and risks is especially important in this case. In general, risk of physical harm associated with biobanks participation is lower than risk associated with clinical trial participation. In addition to the informed consent which should be provided by the legal representative, an assent may also be asked for according to the level of maturity and understanding of the child[28]. Re-consent may be required when the child reaches adulthood[28]. Another issue is return of research results, in which a biobank has to determine whether results will be returned or not, and whether the parents have the right to receive these kinds of results[10,24]. If the biobank is going to collect samples from children, clear policies and procedures about these issues should be in place before sample and data collection take place.

Recommendation. The Egyptian Constitution states in Article 60 that: "It is not permissible to conduct any medical or scientific experiment on it (the human body) without the free and documented consent, in accordance with the established principles in the field of medical science, as regulated by law"[16]. Biobanks in Egypt generally recognize that informed consent is a critical prerequisite for human health related research. Currently, standard operating procedures (SOPs) in Egyptian biobanks give effect to these rights[19]. While there is no data on public preference fora model of informed consent for biobanking in Egypt, broad informed consent is already used in most biobanks in Egypt. Other approaches, such as dynamic consent, may allow participants/donors to actively manage their preferences over time but this may not be feasible in some areas in Egypt due to limited access to the internet and related technology; at time of writing, less than 50% of Egyptians have access to the internet[29]. The costs involved in establishing and maintaining a technological and data infrastructure to enable dynamic consent is likely to be a further obstacle. Apart from this, low literacy (especially among females and older people in Egypt) as shown in previous studies may limit the choice of consent models that may be effectively implemented in Egypt[30]. A previous study showed that among Egyptian patients who agreed to participate in research, many of them preferred a consent model that limits the use of their samples to the disease being studied[31]. This finding provides some support for the adoption of broad consent and tiered consent models in some settings, where participants can choose between allowing the use of their samples for research concerning a particular type of disease (e.g. cancer) in general or only to specified types of research (e.g. lung cancer and other smoking related diseases). While a national ethics framework could endorse the broad consent model, it will need to specify what basic information should be provided to prospective participants/donors and the means to promote understanding (such as the use of a simple Arabic glossary to explain the different terms that are commonly used in the informed consent), rights and interests of participants/donors that should be respected and promoted, and training and qualifications on ethics and communication that biobank operators and researchers must satisfy.

II. Data protection, confidentiality, and privacy issues

Protection of privacy and confidentiality is one of the core elements for trust in biobanks[11]. The whole process of sample collection, storage and distribution must respect the privacy and confidentiality of participants according to the local and international laws and regulations[22]. Egyptian patients participating in a survey about biobanking highlighted the importance of privacy issues, and considered it as an important element of trust[19]. Measures taken by the biobanks to protect privacy and confidentiality should be explained to potential donors during discussion of the informed consent[23].

Respecting privacy and maintaining confidentiality is generally recognized to be the duty of all staff members who have access to stored data. Biobank must have policies and appropriately designed information technology and data infrastructures for ensuring that personal data collected from participants are appropriately protected. Biobanks generally have SOPs to ensure that physical access, and access to personal data is restricted to persons in charge, and different levels of access are specified for operators[20]. Regular audits on the data management system should be carried out on a regular basis to ensure the efficiency of the procedures taken by the biobank[8].

The literature has highlighted the need for training of staff members about issues in privacy and confidentiality, and technical issues related to these concerns[24]. It is important to examine different means used to maintain privacy, to assess their effectiveness and to consider the possible need for re-identification for the purposes of re-contacting participants/contributors if they are agreeable to this[7,8,13]. Researchers getting access to participants' samples and data will also be required to ensure that privacy and confidentiality safeguards will be maintained[23], and potential identification of participants should be highlighted and explained during submission of research protocols[13].

There is broad recognition that access to samples should be done through transparent, ethical and fair governance policies that allow maximum benefits to be derived from these limited resources[20,24]. In general, biobanks should not share samples or data with third parties for non-research purposes except when required and regulated by law[8]. In the aforementioned survey about biobanking, about three quarters of Egyptian participants thought that law enforcement should have access to samples and data when necessary[19]. Another survey conducted with a diverse group of participants in Saudi Arabia showed that most of them agreed that control of infectious diseases and access granted by a court order can be a reasonable justification for access to personal data without the consent of the participants/contributors concerned[32]. There is at present a lack of clarity in Egypt over the probability and magnitude of potential harm or public interest that is necessary to justify a breach of privacy and/or confidentiality.

Protecting privacy and confidentiality may become more challenging with advancement in genome-sequencing technologies and advanced bioinformatics techniques. These include the risk of potential identification of the donor, as well as risks to their biological relatives if results show possibility of having a certain familial disease that may be stigmatizing[9,22]. In addition, even if the biobank takes appropriate measures to protect privacy and confidentiality, there is possibility that data repositories may be broken into or stolen. Where research on rare diseases is concerned, the risk of re-identification may be greater.

Recommendations. In general, the Egyptian constitution, legal system, as well as professional regulations highlight the importance of safeguarding privacy and confidentiality in medical as well as personal life[2,33]. A personal data protection law has been recently enacted by the Egyptian parliament[34], and the privacy principles are broadly similar to international guidelines on personal data protection. Although personal data protection principles are mostly reflected in the SOPs of many biobanks in Egypt[19], there is currently no consistent approach among the biobanks in Egypt on addressing the risk of re-identification and how it can be explained during consent-taking.

While such a risk in genetics research is still low in Egypt as large scale genomic studies are still limited, it is likely to become a concern in the foreseeable future and should be addressed in a national ethics framework. There may also be a need for regulatory oversight that involves regular audits of biobanks to ensure that measures to protect privacy and confidentiality are implemented and observed.

III. Return of results and incidental findings

Biobanks usually use coding to link samples with associated data. This allows them to re-contact participants and to return individual or aggregate results, which should be carried out according to the wishes of the participants in the informed consent, where they should be informed about whether and how results will be returned[10,20,24].

Several types of results may be communicated with the individual and/or the community. General research results may be communicated with the public through websites or newsletters[10,22]. Individual test results may fall into two categories. First, there is initial general testing or retesting results (such as laboratory or radiological investigations). There are also research results which may be anticipated (within the goal of the study), or incidental findings (which may have potential health importance, but are not directly related to the original goal of research).

Return of results is associated with many challenges[6,12]. First, not every result should be returned to the participant. Returned results should be validated, clinically significant and could be associated with an action (e.g: The participant will have access to treatment)[13,25]. Second, individual counseling should be available for the participants and their families if the results include genetic findings, or if some family members don't want to know about results of familial diseases that may affect them[8,13,24].

Biobanks should have consistent and coherent policies and procedures for return of these results, and should have a mechanism to integrate them with the healthcare system if this is approved in their SOPs[8,10,22]. They should also be able to evaluate the validity of results, especially if they involve results of a complex (e.g. genetic) nature, and procedures to return results to participants based on agreed upon arrangements determined during consent-taking[10]. Special considerations and arrangements apply when biological samples are collected from children and young persons, which includes processes to determine whether results should be returned or not, and the role of parents, guardians or communities concerned[10,24].

Recommendations. In the above mentioned study about the attitude of Egyptian patients towards biobanking, about 55% of participants thought that individual results derived from their tissue and of potential therapeutic value should be added to their medical record[19]. In Egypt, return of genetic research results, including secondary and incidental findings is challenged by the difficulty in validating these results, and shortage of medical geneticists who can provide counseling for participants and their families. While return of results may not be a significant concern at the moment, a national ethics framework should address these concerns and to ensure that both the research and healthcare communities are adequately

equipped to meet these foreseeable challenges. Since Egypt is classified among low middle countries and biobanking practices are subject to similar resource constraints, the recommendations of Ethics and Governance Framework for Best Practice in Genomic Research and Biobanking in Africa may be the most suitable for Egypt[12]. A national framework should guide discussion between experts from the field of genetics, psychology and ethics to determine when and how return of genetic results, should take place. The need to train genetic counselors to communicate these findings to participants and their families should also be addressed in this framework. In the meantime, and until this happens, return of results should continue to be limited to general laboratory or radiological investigations.

IV. Access to and sharing of samples and data, benefit sharing and commercialization issues

Sharing of different types of samples and data is routine in international collaborative research. Biobanks play a central role in this process through being a custodian of these valuable resources. Results from research should be shared not only with the scientific community, but also with the biobanks as well. Such accumulation and dissemination of knowledge help to improve prevention, diagnosis and/or treatment of different diseases[13,23]. However, sharing of samples and associated data is associated with many challenges, including fair benefit sharing, intellectual property rights, as well as authorship over scientific publications. Ideally, these benefits should also be shared with the individual participants as well as the community concerned[8,25].

Researchers' access to biological samples and data in a biobank should be done through fair and transparent processes based on coherent scientific and ethical criteria such as scientific merit[20,24]. Biotechnology and pharmaceutical companies, which play an important role in healthcare research through development of new biomedical products, require access to samples and data. Although commercialization of specimens and data is important for financial sustainability of biobanks[35], it raises questions about fair sharing of benefits, and is considered as a critical factor that may affect trust and participation[36,37].

Biobanks need to have consistent and fair policies about access to samples and data, and about commercialization and intellectual property rights[8,10,11]. These policies should also indicate what provisions should be incorporated in material transfer agreements (MTA) and data transfer agreements (DTA), including the types and uses of samples and data that will be transferred, sharing of research results, citation or acknowledgment of the biobanks, patents and intellectual property rights[8,10].

Although there is some guidance on data sharing in general, collaboration between high income and low middle income countries (LMIC) raises a number of additional issues that require further deliberation and public engagement. LMIC play a growing role in research today. So, sample and data sharing should take into consideration the health needs of less developed countries, and the rights and interests of the communities participating in research should be protected[11].

Access to sample and data from these countries should be regulated by local committees (at the institution where the biobanks is based), or national committees, which must balance the potential benefits to science and humanity with fair benefits for the local community. This balance should be taken into consideration especially when commercialization issues and related benefits and burdens are discussed[12]. The benefits for developing countries may include different forms of capacity building (e.g. training and developing research infrastructure), sharing in authorship of scientific publications, patents and sharing of intellectual property rights with local researchers, and providing access to commercial products at affordable prices for the local community[12]. Achieving these goals is not easy, but a national ethics framework may help to support dialogue among the research community, international organizations, commercial entities, funders, sponsors and other interested stakeholders. In this respect, a recent Nuffield report on research in global health emergencies advocates authorship recognition for those who contribute data or samples for primary research, or whose data and samples are used for secondary research[38].

Recommendations. In Egypt, sample sharing across borders raises social and legal debates. A law for regulation of clinical research was discussed last year in the Egyptian Parliament. This law would have prohibited transfer of any human samples for research purposes from Egypt, except when necessary and only after the approval of the county's security authorities[39]. Although the law was approved by Parliament, it was rejected by the President, and the aforementioned prohibition was among the reasons for his objection[40]. The legislation would have prohibited any form of trading in human samples, which may put limits on access by, and collaboration with, commercial entities[39].

Egyptian patients have expressed concerns regarding sharing their samples with Western countries and pharmaceutical companies[19,41]. Egyptian physicians participating in a survey about biobanking were similarly concerned about commercialization, but data from this survey has not yet been published.

Due to sensitivity of the issues at the political and community levels, we recommend that sample and data sharing across Egyptian borders or with commercial entities should be governed by a legal framework and appropriate national-level ethical guidelines and processes. While this governance approach should protect public interests, it should not hinder research collaboration of scientific and social value. A national ethics framework may help to promote public discussion on how sample and data sharing and collaboration could support capacity building in Egypt. This framework could also help to inform provisions that should be included in MTA and DTA between biobanks with local and international researchers requiring access to samples and data, such as requirements relating to benefit sharing(e.g. who will be authors on publications, intellectual property rights, etc). Where commercialization is concerned, the national framework could provide guidance on when it should be allowed due to the novelty of biobanking and related data sharing in Egypt, and the need to build trust with stakeholders.

V. Community engagement

The different processes of the biobank should be fully transparent, and showing respect is valuable for the successful conduct of research through ensuring acceptability and understanding the values of the proposed research[13]. It is important to engage individuals and communities that have an interest in the research process[12]. Engagement is a continuous process that should start from the development of the informed consent, through monitoring of the research process, till the dissemination of its results[12,13]. Research protocols and SOPs of biobanks should include plans for community engagement[10,12,22]. Such plans should clearly identify the goals and processes for community engagement, and should allow the community to find out more about the biobank and, when possible, provide means to participate in the discussions and research use of stored materials and data[13]. The plan should be implemented by the researchers and their sponsoring institutions, and should be reviewed at regular intervals[12,13,25].

Community engagement can take several forms; such as public forums, and inclusion of representatives from patient groups or the community[10,20]. This participation has mutual benefits to both parties: On one side, it will promote understanding on the part of community members and trust by providing the opportunity to talk about their needs and raise any concerns[12,13]. On the other side, this will inform biobank operators about the communities' cultures and perceptions about different biobanks policies and practices, including sensitive issues[12,25]. Failure to secure trust may threaten the long-term viability of biobanks as individuals and communities refuse to contribute their materials or data[13].

Recommendations. In Egypt, there are no clear models for public engagement in research. We believe that transparent and open public discussion about sensitive issues such as sample and data sharing and commercialization will help build public consensus on these issues. We recommend using social media as one of the platforms for community engagement as these platforms have shown effectiveness for communication about biobanking and health issues with different stakeholders[1,42]. Interestingly, growth of interest in health and medical research in Egypt accompanied the emergence of COVID-19 pandemic. We think that this could be a good time to start new initiatives of community engagement in research.

VI. Stakeholders engagement

Meaningful engagement of different stakeholders is important to ensure the long-term viability of biobanks[10,22]. Biobank stakeholders include patients, researchers, community leaders and representatives, regulatory authorities, government agencies, funders, as well as the general community. Transparency, effective communication and trust should also be promoted among these different stakeholders before the initiation of sample collection processes[22].

A biobank governance framework should support communication among the different stakeholders. This framework should include different institutional leaders to whom the biobanks manager reports[22], as well as oversight committees which oversee the process and support transparency and accountability[10,22].

Researchers, as users of the biological materials and related data, should know about the existence of biobanks, and the resources that are maintained by them. Cost recovery models and service fees should be developed by biobanks in consultation with key stakeholders, reviewed regularly and adjusted as needed[22].

Recommendations. In a study about their knowledge, perceptions, and attitude of about biobanking, Egyptian physicians reported limited knowledge about the existence of biobanks in Egypt. They also had concerns regarding broad consent and use of user fees by biobanks (Data not published). Taken together, we believe that these results represent limited engagement with these stakeholders. A national framework can help to promote engagement between biobanks and stakeholders (other than participants or contributors). Conferences, workshops, as well as social media could also be used for these purposes.

Development and implementation of biobanking ethics guidelines cannot proceed without the help and support of national and local RECs. It should be noted that although number and distribution of RECs is improving in Egypt[14], many of them suffer from administrative and financial limitations. Adoption of any guidelines should be done in parallel with improvement of RECs, through financial and administrative support and continuous training of their members[3,14].

Conclusions

We have identified some recommendations on themes that should be addressed in a national ethics framework on biobanking in Egypt. For informed consent, broad consent could be the most appropriate approach for biobanks in Egypt, although another possible option is tiered consent. In either cases, a national ethics framework can help to promote consistency among all the biobanks in Egypt and to set out the key governance requirements that are needed to support autonomous decision-making among donors/contributors, as well as public trust. This framework should also address current and anticipated challenges to safeguards on privacy and confidentiality, and to provide guidance on return of research results, which requires selection of the types of results to be returned, training for genetic of counselors and researchers, and better integration of the research and healthcare systems. Sample and data sharing across borders, and commercialization and intellectual property rights, draw a variety of issues that will require public engagement. More efforts are needed by the biobanking community to engage with different stakeholders, including the public. The proposed national ethics framework may help to enable public deliberation on the types of interests that should be protected by law, on benefit sharing and appropriate ethical and regulatory mechanisms that need to be established, including appropriate use of material and data transfer agreements.

Data availability

Underlying data

All data underlying the results are available as part of the article and no additional source data are required.

Acknowledgements

We would like to thank all members of Centre for Biomedical Ethics, Yong Loo Lin School of Medicine, National University of Singapore, for their help and support during this work.

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Open Peer Review

Current Peer Review Status: ? ✓

Version 1

Reviewer Report 15 February 2021

https://doi.org/10.21956/wellcomeopenres.18243.r42427

✓ **Lana Shaiba**
Department of Pediatrics, Medical City King Saud University, Riyadh, Saudi Arabia
Ahmed El-Malky
King Saud University Medical City, King Saud University, Riyadh, Saudi Arabia

The work is clearly and accurately presented and does cite the current literature. Grammatical work, of developing argument and counter argument, and essay expression is accepted.

The study design appropriate and the is work technically sound. I am very glad the authors wrote this essay. It is a well-written, needed, and useful summary of the current status of “data publication” from a certain perspective. The authors, however, need to be bolder and more analytical. This is an opinion piece, yet I see little opinion. A certain view is implied by the organization of the paper and the references chosen, but they could be more explicit.

Sufficient details of methods and analysis provided to allow replication by others. The statistical analysis and its interpretation appropriate. The source data underlying the results available to ensure full reproducibility. The conclusions drawn adequately supported by the results

I think this paper excellent and is an important addition to the literature. I really like the conceptualization of Recommendations for the development of Egyptian human biobanking ethical guidelines.

There are minor corrections that do not affect the final decision:

1. The methods chapter need some details about research question formulation. What is the problem are you trying to address by conducting this review? The research problem should be a structured and unambiguous question.

2. Define inclusion and exclusion criteria. Clearly state the criteria you will use to determine whether or not a study will be included in your search. Consider study populations, study design, intervention types, comparison groups, measured outcomes.

3. Add a more detailed spreadsheet to describe all relevant data from each included study. It is recommended that you pilot your data extraction tool, to determine if other fields should be included or existing fields clarified.

4. Evaluate the risk of bias of included studies. Use a Risk of Bias tool (such as the Cochrane RoB Tool) to assess the potential biases of studies in regards to study design and other factors. Read the Cochrane training materials to learn about the topic of assessing risk of bias in included studies.

Is the work clearly and accurately presented and does it cite the current literature?
Yes

Is the study design appropriate and is the work technically sound?
Yes

Are sufficient details of methods and analysis provided to allow replication by others?
Yes

If applicable, is the statistical analysis and its interpretation appropriate?
Yes

Are all the source data underlying the results available to ensure full reproducibility?
Yes

Are the conclusions drawn adequately supported by the results?
Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Public health and community medicine/ international health policies and healthcare CPGs.

We confirm that we have read this submission and believe that we have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Author Response 10 Mar 2021

Samir Abdelhafiz, National Cancer Institute, Cairo University, Cairo, Egypt

Dear Dr El-Malky, and Dr Shaiba,

We are grateful for the instructive comments we received from you, which have helped to improve our manuscript. In addition, we also took the opportunity to update our manuscript on two recent developments. First, a clinical research law has been approved in Egypt. The law applies mainly to clinical research but is not specific to pre-clinical research. It provides guidance by setting out principles and standards for protection of participants

and highlights the importance of consistency with generally accepted international ethical standards. We have referred to applicable provisions of this law. Second, a national biobank network has been established to harmonize the activities of biobanks in Egypt. We have also highlighted this development in our manuscript. Kindly find our response to your comments below.

- The methods chapter needs some details about research question formulation. What is the problem are you trying to address by conducting this review? The research problem should be a structured and unambiguous question.

Thank you for this helpful observation. We have clarified that the goal of our review is to identify key ethical norms or standards that are set out in generally accepted transnational guidance documents on biobanking and related data practices, and to further consider which of these norms or standards apply to the context of Egypt. We have clarified our research questions in the methodology section of the revised manuscript.

- Define inclusion and exclusion criteria. Clearly state the criteria you will use to determine whether or not a study will be included in your search. Consider study populations, study design, intervention types, comparison groups, measured outcomes.

Thank you for this helpful observation as well. We have clarified the inclusion and exclusion criteria, following from the research questions and goals the steered our project. As our research is not an intervention study, the conventional features of a research design (e.g. study population, intervention types, comparison groups, and outcome measures) do not apply to our study. Instead, a list of relevant policies is set out in Table 2.

- Add a more detailed spreadsheet to describe all relevant data from each included study. It is recommended that you pilot your data extraction tool, to determine if other fields should be included or existing fields clarified.

A spreadsheet that includes data and quotations from different sources has been prepared.

- Evaluate the risk of bias of included studies. Use a Risk of Bias tool (such as the Cochrane RoB Tool) to assess the potential biases of studies in regards to study design and other factors. Read the Cochrane training materials to learn about the topic of assessing risk of bias in included studies.

Thank you for this recommendation, in response to which we have included in the manuscript a limitation of our review. We have explained that the determination of ethical or normative themes that are relevant to the context of Egypt is based on the experience of one of the authors (ASA), as well as our understanding of the relevant laws and policies in Egypt. As our study does not involve the assessment of fixed result from randomized clinical trials, the Cochrane Risk of Bias Tool is not applicable. However, we hope that in explicitly specifying the analytical vantage point that we have adopted as limitation, we acknowledge that there may be inherent bias in our interpretation and/or understanding of the Egyptian context, which should in turn be critically evaluated by the reader.

Competing Interests: No competing interests were disclosed.

Reviewer Report 29 January 2021

https://doi.org/10.21956/wellcomeopenres.18243.r42134

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Ciara Staunton
[1] Department of Law, Middlesex University, London, UK
[2] Institute for Biomedicine, Eurac Research, Bolzano, Italy

I would like to thank the authors for the opportunity to review this paper. In the absence of a national framework for Egypt, the recommendations contained in this paper will be of the utmost importance.

I do have a few points the authors may want to consider in revising this paper.

I would suggest including much more background about the regulation of medical research more broadly in Egypt, research ethics review, any regulation of human tissues, and biobanks more specifically in the background. The new Data Protection Act is likely to have a great impact on biobanks and should be discussed here e.g. how will it impact research, are there special provisions for research, are the provisions unclear as they apply to research, etc. In South Africa, due to the uncertainty in the application of some of the principles of the Protection of Personal Information Act, the South African Academy of Sciences is developing a Code of Conduct for the use of health data in research. Is a similar Code needed in Egypt?

The particular ELSI issues that arise in Egypt should be mentioned in the introduction also. Consider the literature in the region as it currently is very focused on these discussions in HICs. I think this discussion of the legal framework (or lack of) in Egypt and the ELSI issues that arise would be important in contextualising the paper. This is probably necessary as if you want to "to identify ethical themes that apply to all biobanks in Egypt, with reference to international guidelines, and taking into consideration the specific cultural and legal framework in Egypt" you do need to explain what these are.

I would absolutely agree that there is a need for a national framework, but the justification could be stronger. You have alluded to these i.e. there are biobanks in Egypt that need governance, but make the case for public deliberation and engagement stronger. Perhaps link it to accountability and transparency. Many appear to be public bodies – are they biobanks in public institutions? If they are, perhaps you could reflect on that.

Linked to this, the discussion on the policies of the governance of current biobanks needs to be a bit more robust. There are no links to the policies of these biobanks, their governance structures, and policies on related committees that you mention. How do you know what these policies contain and what are the differences in them? The differences in these frameworks could then provide a stronger justification for why you think there is a need for a national framework as there is currently no evidential basis for a lack of a harmonised process. Have you identified any gaps in them?

There are some points in the methodology that would be good to clarify:

- In the methods section it seems to suggest that the themes guided the literature search, but in the results it seems that the themes came out of the search. Methods also initially seem to suggest that you were looking for policies only, but then seems to be that the process included getting other secondary sources.

- Related to that: “These themes have been highlighted to be important in recent literature on biobanking and related data use for research purposes.” – If the 6 themes to be looked at are coming from the literature, then the selection of these themes need to have a justification and link to the sources. Or is it the themes came from the guidelines?

- If you are comparing the guidelines with published ELSI related to biomedical research in Egypt then you probably should state what these papers are, how they were obtained and also provide a list of sources.

- When referring to the documents reviewed make it clear what are the guidelines and what is ELSI literature. Sometimes I wasn’t very sure.

In the results section it would be good to get clarity or further discussion on the following:

- What particular consent model will be affected by level levels of education?

- If previous research stated that Egyptians would like to limit their samples to the disease being studied, this would suggest that a very limited form of broad consent is acceptable and not in line with the definition of broad consent as you’ve presented. In reality, is it not tiered consent that would be best? What are the challenges with a tiered consent model in this context?

- Return of results: are medical geneticists considered to be able to provide counselling? Are there genetic counsellors in Egypt? The Ethics WG and other groups within H3Africa have also considered this issues in detail and this literature should be considered.

- Rather than saying what guideline may be more suitable, it would be of more benefit to have explicit recommendations for the national guideline.

- What impact does the Data Protection Act have on collection, access to and sharing (both within Egypt) and outside of Egypt’s borders?

Is the work clearly and accurately presented and does it cite the current literature?
Partly

Is the study design appropriate and is the work technically sound?
Yes

Are sufficient details of methods and analysis provided to allow replication by others?
Partly

If applicable, is the statistical analysis and its interpretation appropriate?
Not applicable

Are all the source data underlying the results available to ensure full reproducibility?

Partly

Are the conclusions drawn adequately supported by the results?
Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Legal and ethical issues associated with biobank research, genomic research and the use of health data.

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Author Response 10 Mar 2021

Samir Abdelhafiz, National Cancer Institute, Cairo University, Cairo, Egypt

Dear Dr Staunton,

We are grateful for the instructive comments we received from you, which have helped to improve our manuscript. In addition, we also took the opportunity to update our manuscript on two recent developments. First, a clinical research law has been approved in Egypt. The law applies mainly to clinical research but is not specific to pre-clinical research. It provides guidance by setting out principles and standards for protection of participants and highlights the importance of consistency with generally accepted international ethical standards. We have referred to applicable provisions of this law. Second, a national biobank network has been established to harmonize the activities of biobanks in Egypt. We have also highlighted this development in our manuscript. Kindly find our response to the reviewers' comments below.

Reviewer 1

- I would suggest including much more background about the regulation of medical research more broadly in Egypt, research ethics review, any regulation of human tissues, and biobanks more specifically in the background.

A recent clinical research law has been approved by the Egyptian president (after the manuscript was submitted). We added a brief introduction about the law in the introduction as follows: "Recently, a Clinical Research Law was enacted by the Egyptian parliament and approved by the Egyptian president to regulate clinical research conducted on humans. The law endorsed the establishment of a supreme council to review the ethics of clinical research. This council is entrusted with following up the implementation of the provisions of the law and taking the necessary actions if violation of any provisions occurs. The absence of specific guidelines has been identified in the past as a major challenge by members of research ethics committees (RECs) in Egypt. Although the aforementioned law applies mainly to clinical research and clinical trials and is not specific to pre-clinical research, it forests out principles and standards for protection of participants and highlights the importance of consistency with generally accepted international ethical standards. Where applicable, relevant provisions of this law will be referred to."

Concerning regulation of biobanks and the ethics review in Egypt, we added the following about this point " It is important to note that most RECs in Egypt use international research ethics guidelines, such as the Declaration of Helsinki, the Islamic Organization for Medical Sciences (IOMS), and guidelines of the Council for International Organizations of Medical Sciences (CIOMS) to review research protocols" And the following reference was added :Sleem, H., El-Kamary, S.S. & Silverman, H.J. Identifying structures, processes, resources and needs of research ethics committees in Egypt. BMC Med Ethics 11, 12 (2010). https://doi.org/10.1186/1472-6939-11-12).

We also added this paragraph about the recently established Egyptian biobank network. The corresponding author of this manuscript is a member in this network " Recently, a national biobank network has been established to harmonize biobanking activities in Egypt. Several committees including ethics, quality, and accreditation are being established for this purpose. One important role of this network is to enhance communication, transparency and trust among the different stakeholders, including patients/participants and researchers in the institutions, hospitals, or organizations where biobanks are located, and with policymakers at the national level. ."

- The new Data Protection Act is likely to have a great impact on biobanks and should be discussed here e.g., how will it impact research, are there special provisions for research, are the provisions unclear as they apply to research, etc. In South Africa, due to the uncertainty in the application of some of the principles of the Protection of Personal Information Act, the South African Academy of Sciences is developing a Code of Conduct for the use of health data in research. Is a similar Code needed in Egypt?

The law is not directly related to medical research. However, we mentioned it in the context of our work since it is related to the general issue of data protection. The Clinical Research Law is more concerned with protection of privacy and confidentiality in the context of medical research. We mentioned that in the following paragraph "In addition, article 12 of the Clinical Research Law sets out specific requirements on the rights of research subjects or participants, including the right to getting a copy of the informed consent document, the right to withdraw at any time, and an obligation on the part of the principal investigator to protect the confidentiality of personal data used in research." We also added some details about data protection from the recently approved clinical research law " Article 15 of the Clinical Research Law sets out the roles of the principal investigator and the study sponsor, if any, who are obliged not to publish any information, data or reports about the research except after its completion and getting a written approval for this purpose from the institutional committee, the Supreme Council, and after getting the written consent of the research participants if any specific information related to them is disclosed".
We also added more details about the data protection law as follows "Although the law does not relate to clinical practice, some provisions relate to the protection of medical data. For example, Article 1 of identifies sensitive personal data as: "Data that disclose mental, physical or genetic health, biometric data, financial data, religious beliefs, political opinions, or security status. In all cases, children's data are considered sensitive personal data.", and Chapter 6 of the law is concerned with protection of such data and comprise provisions that highlight the importance of fulfilling the necessary data protection policies and procedures

to avoid any breach or violation of personal data privacy."

- The ELSI issues that arise in Egypt should be mentioned in the introduction also. Consider the literature in the region as it currently is very focused on these discussions in HICs. I think this discussion of the legal framework (or lack of) in Egypt and the ELSI issues that arise would be important in contextualising the paper. This is probably necessary as if you want to “to identify ethical themes that apply to all biobanks in Egypt, with reference to international guidelines, and taking into consideration the specific cultural and legal framework in Egypt” you do need to explain what these are.

We think that the issue of trust is the major issues facing the growing biobanking field in Egypt. We added the following statement in the introduction " As biobanking grows in Egypt, mutual trust must be strengthened and sustained among different stakeholders”
We already mentioned the issue about religion and how it could impact biobanks. This is an important issue in Arab/Islamic countries.
Concerning the legal framework, we included some articles of the newly approved clinical research law, and how it applies in some points to biobanking.
Otherwise, challenges faced by biobanks are quite similar to other parts in the world. We added the following statement to clarify this point " In general, Egyptian biobanks face the same challenges as other biobanks, but some are especially onerous in low resource settings like Egypt, such as issues relating to sharing of samples or data and fair distribution of benefits.”

- I would absolutely agree that there is a need for a national framework, but the justification could be stronger. You have alluded to these i.e., there are biobanks in Egypt that need governance, but make the case for public deliberation and engagement stronger. Perhaps link it to accountability and transparency. Many appear to be public bodies – are they biobanks in public institutions? If they are, perhaps you could reflect on that.

Based on the previous point, where we stated that a major issue with biobanking in Egypt is trust, we think that these recommendations can help resolve this issue through the recently developed biobank network as we explained earlier in the following paragraph " Recently, a national biobank network has been established to harmonize biobanking activities in Egypt. Several committees including ethics, quality, and accreditation are being established for this purpose. One important role of this network is to enhance communication, transparency and trust among the different stakeholders, including patients/participants and researchers in the institutions, hospitals, or organizations where biobanks are located, and with policymakers at the national level.

In this work, we argue for the establishment of a national ethics framework for biobanks in Egypt and suggest the themes that should be addressed therein. This framework could be of importance for the new biobank network, where it could be used for the development of local guidelines and best practices for biobanks and related practices at the national level. "

- Linked to this, the discussion on the policies of the governance of current biobanks needs to be a bit more robust. There are no links to the policies of these biobanks, their governance structures, and policies on related committees that you mention. How do you know what these policies contain and what are the differences in them? The differences in these frameworks could then provide a stronger justification for

why you think there is a need for a national framework as there is currently no evidential basis for a lack of a harmonized process. Have you identified any gaps in them?

There are no published data about the governance of these biobanks. However, the corresponding author of this manuscript participated in interviews with different biobank managers in Egypt as a part of another research project that aimed at evaluating stakeholders' views in the Arab region, including Egypt, about biobanking (Data not published). These interviews showed that there is lack of harmonization about policies related to some issues such as collaboration with pharmaceutical companies and commercialization. We mentioned in the current manuscript that biobanks in Egypt are are in different stages of maturity, so some of them still don't have clear policies for access and sharing. We clarified this in the introduction as follows " While established biobanks are at different stages of maturity, still others are being established. Some of these biobanks are affiliated to university hospitals or governmental research centers, and others are affiliated to non-governmental organizations (NGOs). The stage of development or maturity, affiliation of the biobank and its position in the hierarchy of the organization affect the policies and procedures of the biobank. For example, biobanks that are still building their inventory of samples and data repositories may not have clear policies on access and sharing. Biobanks affiliated with public universities and governmental organizations could also have issues with commercialization and collaboration with pharmaceutical companies, which may not be the case with biobanks affiliated with NGOs. As biobanking grows in Egypt, mutual trust must be strengthened and sustained among different stakeholders " Another point that indicates the need of harmonization is the development of the Egyptian biobank network. The network which includes all biobank managers as well as other stakeholders aims mainly at harmonization of biobanking activities in Egypt.

- There are some points in the methodology that would be good to clarify: In the methods section it seems to suggest that the themes guided the literature search, but in the results it seems that the themes came out of the search. Methods also initially seem to suggest that you were looking for policies only, but then seems to be that the process included getting other secondary sources.

Thank you for these helpful observations on the methodology. Our literature review focused on transnational policies that apply to biobanking and related data practices, but we did also include some secondary sources that helped to clarify or explain the applicability of these policy provisions to biobanking in Egypt. From the review, common themes were identified, and out of these themes, we focused on those that are relevant in guiding policy development in Egypt. We have clarified our methodology in the manuscript.

- Related to that: "These themes have been highlighted to be important in recent literature on biobanking and related data use for research purposes." – If the 6 themes to be looked at are coming from the literature, then the selection of these themes need to have a justification and link to the sources. Or is it the themes came from the guidelines?

Thank you for observation, which is helpful. We have clarified that our review focused on transnational policies that are set out in Table 2, and on themes that are applicable to biobanking and related data practices in the Egyptian context.

- If you are comparing the guidelines with published ELSI related to biomedical research in Egypt then you probably should state what these papers are, how they were obtained and also provide a list of sources.

We described how these sources were obtained in the methods as follows " we also searched the literature for publications or regulations related to the ethical, legal, and social issues related to biomedical research or biobanking in Egypt. The search terms included "Research ethics in Egypt", "Clinical research law in Egypt", "Research ethics guidelines in Egypt", and "Biobanking in Egypt". Search results that did not apply to biobanking and related practices in Egypt were excluded. While specific and recent documents or regulations discussing these issues were included, general or older versions of documents that have been updated were excluded."
A list of these documents was added in table 3.

- When referring to the documents reviewed make it clear what are the guidelines and what is ELSI literature. Sometimes I wasn't very sure in the results section it would be good to get clarity or further discussion on the following.

We added a column about the document type to table 2.

- What particular consent model will be affected by level levels of education?

There is no published data about this, and we stated that in the discussion "While there is no data on public preference for a model of informed consent for biobanking in Egypt, broad informed consent is already used in most biobanks in Egypt. Other approaches, such as dynamic consent, may allow participants/donors to actively manage their preferences over time but this may not be feasible in some areas in Egypt due to limited access to the internet and related technology; at time of writing, less than 50% of Egyptians have access to the internet" And later on " Apart from this, low literacy (especially among females and older people in Egypt) as shown in previous studies may limit the choice of consent models that may be effectively implemented in Egypt."

- If previous research stated that Egyptians would like to limit their samples to the disease being studied, this would suggest that a very limited form of broad consent is acceptable and not in line with the definition of broad consent as you've presented. In reality, is it not tiered consent that would be best? What are the challenges with a tiered consent model in this context?

Although the study by Abou-Zeid et al. stated that consent model that limits the use of their samples to the disease being studied, other studies show the acceptability of participants to broad consent. We added a reference for this as follows" A study by Labib et al. showed that most parents of children with cancer provide broad consent to biobanks for the research use of their children's biological materials and data". Another clue for the acceptability of broad consent is the fact that it is already adopted by most biobanks in Egypt, with no reported problems.

However, we agree that each type of consent has its own advantages. We added a reference about the value of tiered consent and discussed challenges associated with its use as

follows " Although broad consent is generally an acceptable option, this model may not fully account for the preferences of individuals. Tiered consent may overcome these problems by providing potential participants with greater control over the future use of donated samples and data. Through responding to specific questions, these sample donors can specify acceptable levels of sample and data sharing.33 On the other hand, tiered consent may be time consuming and difficult to apply in some settings. For example, cancer patients usually suffer from psychological stress, especially during the first few visits to the hospital, where the biobank coordinators usually meet them and ask them to participate. Psychological stress could interfere with their ability to consider and discuss the different options. Significant illiteracy among certain individuals in Egypt may be another challenge, as they could have difficulty in understanding research terms and options."

- Return of results: are medical geneticists considered to be able to provide counselling? Are there genetic counsellors in Egypt? The Ethics WG and other groups within H3Africa have also considered this issue in detail and this literature should be considered.

Yes, there are genetic counselors in Egypt, but their number is limited, and they work in a few centers. We added a reference about the experience of genetic counseling in Cairo University as follows "Although genetic counseling services are provided in Egypt, such services are still limited to a few centers all over the country. For example, El Hawary et al. described their experience in genetic counseling for families with children suffering from primary immunodeficiency disorders. Counseling included family education about the mode of inheritance of the disease, possibility of having an affected child, explanation of the available options for treatment, as well as the availability of prenatal diagnosis and preimplantation genetic diagnosis."
We have also included H3Africa Guideline for the Return of Individual Genetic Research Findings as a reference as follows" In other words, the findings should have high analytical validity, high clinical validity, and medical actionability. For example, if a genetic test is strongly predictive of an adverse clinical outcome, and has been validated through a second sample using a different or reference method, and possible intervention is available for participants in their particular contexts, these results should be returned"

- Rather than saying what guideline may be more suitable, it would be of more benefit to have explicit recommendations for the national guideline.

Thank you for this recommendation. We have indeed argued that it will be helpful to have a consistent set of ethical guidance for all biobanks, although such a guideline need not be 'national', in that it could be collaboratively developed and adopted by the Biobanks' Network. Such a bottom-up approach could complement the top-down regime established under the newly enacted Clinical Research Law.

- What impact does the Data Protection Act have on collection, access to and sharing (both within Egypt) and outside of Egypt's borders?

Since the law is not directly related to medical data, we do not know if the law will affect the process of collection, access or sharing. However, we included the chapters/articles that could be related to medical data as follows "Although the law does not relate to clinical practice, some provisions relate to the protection of medical data. For example, Article 1 of identifies sensitive personal data as: "Data that disclose mental, physical or genetic health, biometric data, financial data, religious beliefs, political opinions, or security status. In all cases, children's data are considered sensitive personal data.", and Chapter 6 of the law is concerned with protection of such data and comprise provisions that highlight the

importance of fulfilling the necessary data protection policies and procedures to avoid any breach or violation of personal data privacy."

Competing Interests: No competing interests were disclosed.