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RETURN OF GENETIC RESEARCH RESULTS: THE JAPANESE EXPERIENCE AND ITS IMPLICATIONS FOR THE INTERNATIONAL DEBATE

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Abstract

In conducting medical and genetic research an ethical dilemma is faced as to whether individual genetic research results should be disclosed where such results may be relevant to the consideration of an individual's health and medical care. Japan's participation in this debate has yielded no consensus on policy as yet but has influenced the establishment of certain national guidelines. Japan established principles in 2000 that emphasized participants' rights to know their genetic research results, and incorporated this policy into governmental guidelines for genetic/genomic research in 2001, as the stance of "disclosure in principle". The newly-revised guidelines in 2013 retained the "disclosure in principle", and added stipulations regarding disclosure giving a greater role to researchers in creating disclosure policies of genetic research results. The process of their revisions was strongly influenced by the Act on the Protection of Personal Information 2003. This article considers the management of clinically significant findings in the context of the revision of the genetic/genomic research guidelines. We argue that the governmental guidelines based on the Act have the potential to give rise to practical and ethical challenges, which suggest the clear need for additional mechanisms for governing disclosure decisions. This method includes that the revised Guidelines can be interpreted to permit genomics researchers to adopt more active research disclosure policies with more participant-focused ethical consideration. This is consistent with researchers' ethical responsibilities to carefully consider the rights and interests of research participants to ensure the public's trust and confidence in research is maintained. The Japanese experience has implications for the international debate, as there is, as yet no

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clear and agreed guidance for researchers determining policies on the return of research results in other countries.

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1. Introduction

In recent years, there has been vigorous debate on the ethics and law of disclosure of individual genetic and genomic results in the setting of clinical care and research. This intensification of the debate is mainly due to rapid technological advancement in human genome research, as represented by "next-generation" sequencers and improved information-analysis techniques.[1] Genome analysis using these techniques enables the identification of several clinically significant loci in the course of clinical care and research. In response to this situation, some recommendations have already been made by professional organisations such as the American College of Medical Genetics and Genomics (ACMG) and the European Society of Human Genetics (ESHG) in clinical settings.[2] Notably, the ACMG recommended that patients undergoing clinical genome sequencing be tested for a specified set of 56 genes with established pathogenic or high risk variants as the most likely source of "incidental" findings. This recommendation has resulted in a great deal of controversy since its release,[3] not least since it proposed that patient consent should not be a requirement and feedback of these results should be mandatory. Indeed, the ACMG recently shifted their position to allow patient opt-out of incidental findings.[4] On the other hand, in research settings, this type of guidance seems to be less clear.

For this reason, one of the most controversial debates of disclosure is on the creation of specific guidance in genome research. In addition to many attempts to develop specific guidelines from ethical perspectives,[5] several legal experts have presented thorough and informative arguments, concerning the legal basis of research participant's access rights and researcher's obligations of disclosure to research participants.[6] Moreover, Kaye et al and Jarvik et al have recently reported several areas of consensus, regarding the extent of researchers' duty to disclose clinically significant findings and the identification of appropriate management pathways for such findings, within particular large scale research projects in the UK and US respectively.[7] However, these series of

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[1] ER Mardis, "A decade's perspective on DNA sequencing technology" (2011) 470 *Nature* 198-203; J Shendure and EL Aiden, "The expanding scope of DNA sequencing" (2012) 30 *Nature Biotechnology* 1084-1094.

[2] RC Green et al, "ACMG recommendations for reporting of incidental findings in clinical exome and genome sequencing" (2013) 15 *Genetics in Medicine* 565-574; CG van El et al, "Whole-genome sequencing in health care" (2013) 21 *European Journal of Human Genetics* 580-584.

[3] W Burke et al, "Recommendations for returning genomic incidental findings? We need to talk!" (2013) 15 *Genetics in Medicine* 854-859; E Vayena and J Tasioulas, "Genetic incidental findings: autonomy regained?" (2013) 15 *Genetics in Medicine* 868-870.

[4] https://www.acmg.net/docs/Release_ACMGUpdatesRecommendations_final.pdf

[5] AL Bredenoord et al, "Disclosure of individual genetic data to research participants: the debate reconsidered" (2011) 27 *Trends in Genetics* 41-47.

[6] EW Clayton and AL McGuire, "The legal risks of returning results of genomics research" (2012) 14 *Genetics in Medicine* 473-477; J Kaye et al, "Can I access my personal genome? The current legal position in the UK" (2014) 22 *Medical Law Review* 64-86; AL McGuire et al, "Can I be sued for that? Liability risk and the disclosure of clinically significant genetic research findings" (2014) 24 *Genome Research* 719-723.

[7] J Kaye et al, "Managing clinically significant findings in research: the UK10K example" (2014) *European Journal of Human Genetics* (doi: 10.1038/ejhg.2013.290); GP Jarvik et al, "Return of genomic

discussions have been centred mainly in Europe and North America, and there has been less discussion regarding disclosure in other countries/regions of the world.

It is becoming imperative to consider international harmonization in disclosure policy, as a growing number of international research projects, involving broad sharing of data and samples, have been carried out across the world. One major approach to addressing this is to compare the disclosure policies of different countries. In this regard, Knoppers et al and others have proactively contributed a wide-ranging comparison of existing disclosure policies regarding primary results, secondary results via biobanks, and incidental findings.[8] In addition, in-depth examination and analysis of specific national disclosure policies can be extremely valuable in reaching a deeper understanding of the historical and cultural context within which policies are developed in a particular region or country. In line with this approach, this study will focus on the current policies relating to disclosure of findings from genetic and genomic research in Japan.

In this article, we explore the character of the disclosure policy in ethical regulations of human genome research in Japan. In particular, we focus on the disclosure policy outlined in the newly revised government ethical guidelines for human genetic research, *Ethical Guidelines for Human Genome/Gene Analysis Research* (*Ethical Guidelines*). "Disclosure" here is taken to cover the issue of so called incidental findings in research settings, including biobank research. We analyse the revision process and resultant policies of the *Ethical Guidelines* on disclosure, based on the ethical principles related to researchers and research participants, and the provisions of the *Act on the Protection of Personal Information* (*APPI*), 2003. We show some of the key challenges of the revised *Ethical Guidelines* associated with policy design of disclosure in Japan. Furthermore, we propose as a means to achieve the potential benefits of personal genome research, the favouring of the disclosure of clinically significant findings, including incidental findings, to research participants as an ethical (if not necessarily legal) imperative. This study could be useful to similar debates in other countries and could contribute to efforts to establish an internationally harmonised disclosure policy where understanding different policies and national contexts internationally is a first step and a necessary precursor to harmonization.

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results to research participants: the floor, the ceiling, and the choices in between" (2014) 94 *American Journal of Human Genetics* 818-826.

[8] BM Knoppers et al, "The emergence of an ethical duty to disclose genetic research results: international perspectives" (2006) *European Journal of Human Genetics* 14, 1170-1178; Renegar G et al, "Returning genetic research results to individuals: points-to-consider" (2006) 20 *Bioethics* 24-36; E Levesque, Y Joly and J Simard, "Return of research results: general principles and international perspectives" (2011) 39 *The Journal of Law, Medicine and Ethics* 583-592; MH Zawati, B Van Ness and BM Knoppers, "Incidental findings in genomic research: a review of international norms" (2011) 9 *GenEdit* 1-8; Knoppers BM and Zawati MH, "International normative perspectives on the return of individual research results and incidental findings in genomic biobanks" (2012) 14 *Genetics in Medicine* 484-489.

2. Ethical regulations in Japan and the revised *Ethical Guidelines*

2.1 The background to government guidelines, the APPI and the Ethical Guidelines*:*

Biomedical research in Japan is primarily subject to soft regulation, through numerous subdivided government guidelines, without a binding legal framework.[9] Many of these government guidelines were created between 2000 and 2003, during which time seven government guidelines were issued. The government guidelines have since undergone a number of revisions, and in particular, several of them have been markedly revised in response to the enactment of the *APPI* in 2003,[10] which is legally binding legislation. As a result of the *APPI*, those guidelines now incorporate detailed stipulations concerning the protection and disclosure of personal information, but most of the guidelines do not address the disclosure of research results including incidental findings. The government guidelines for human genetic research, described as the *Ethical Guidelines* above, are a notable exception, covering a specific disclosure policy for research results.

The need for specific regulations in human genetic research was identified around the year 2000, in response to the rapid growth in that research field. This resulted in the establishment in 2000 of the Fundamental Principles of Research on the Human Genome (*Fundamental Principles*) by the Bioethics Committee of the Council for Science and Technology, Japan.[11] The *Fundamental Principles* describe the conceptual framework for human genome research and play a fundamental role in establishing relevant guidelines. With regard to disclosure in general, they stipulate that research participants have the right to be informed and the right not to be informed based on individual preference. Based on the concepts described in the *Fundamental Principles*, 2001 saw the publication of the *Ethical Guidelines*.[12] In particular, these Guidelines adopted "the policy of disclosure in principle", which emphasises the right of research participants to receive their research results when they so request. Although neither the *Fundamental Principles* nor the *Ethical Guidelines* are legally binding, they have been widely adopted, and are in general adhered to by the research community in Japan. As such, since their enactment in 2001 the *Ethical Guidelines* have set the disclosure policy, and have been subject to continued debate among stakeholders.[13]

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[9] BT Slingsby, N Nagao and A Akabayashi, "Administrative legislation in Japan: guidelines on scientific and ethical standards" (2004) 13 *Cambridge Quarterly of Healthcare Ethics* 245-253; S Tashiro, "Unintended consequences of "soft" regulations: the social control of human biomedical research in Japan" (2010) 19 *International Journal of Japanese Sociology* 4-17.

[10] *Act on the Protection of Personal Information 2003* (Act No. 57 of 2003, Japan) (hereafter *APPI*).

[11] Bioethics Committee, Council for Science and Technology, "Fundamental Principles of Research on the Human Genome" (2000).

[12] Ministry of Education, Culture, Sports, Science and Technology (MEXT), Ministry of Health, Labour and Welfare (MHLW), and Ministry of Economy Trade and Industry (METI), "Ethical Guidelines for Human Genome/Gene Analysis Research" (2001). Fully revised in 2004 and 2013, partially revised in 2005 and 2008.

[13] A Nomura and G Yoshizawa, "Critical discourse analysis of the revision of the Ethical Guidelines for Human Genome/Gene Analysis Research" (2013) 22 *Japanese Journal for Science, Technology and Society* 47-88.

2.2 The latest revision of the Ethical Guidelines*:*

Recently, during the full revision process of the *Ethical Guidelines*, there was significant debate of the disclosure policy. In response to government requests, the revision of the *Ethical Guidelines* started in 2011, with revised guidelines coming into effect in April 2013. The revision was conducted according to procedures set out by a Government Committee, with one of the most important discussions relating to whether "the policy of disclosure in principle" should be retained. A number of the Committee members strongly advocated against "the policy of disclosure in principle", and desired the alternative approach involving non-disclosure in principle (with appropriate measures for returning medically useful results). This was mainly due to the practical premise that, at present, most research results from genome analysis are still uncertain and not suitable to serve as clinical information for research participants. Nevertheless, this Committee ultimately decided to retain "the policy of disclosure in principle", meaning that research results are disclosed only in circumstances where researchers are requested to do so by research participants. The key reason for retention of the policy was to strictly follow Art 25 (Disclosure) of the *APPI*, which enshrines the disclosure principle.[14]

2.3 The influence of the APPI on the Ethical Guidelines*:*

It is not immediately clear why the Committee should have adopted the disclosure principle based on consistency with the *APPI* on the outcome of the *Ethical Guidelines* revision. The *APPI* was originally designed to deal with the regulation of personal information with significance in commerce or business, rather than in academic research. With consideration of "academic freedom", which is guaranteed in Art 23 of the Constitution of Japan, academic research was exempted from the provisions of the *APPI*, as indicated in Art 50 (Exclusion from Application). The exemption of the *APPI* itself, naturally, covers genome research, including the matter of disclosure. There are, however, other laws regarding personal information, which are closely related to the *APPI* but partly apply to academic research.[15] The mandate of the Committee on the *Ethical Guidelines* incorporated an imperative to ensure a consistent legal framework for the updated guidelines which necessitated redressing this discrepancy over academic research between the *APPI* and the other laws. As a result, in order to have clear legal guidance on personal information in the academic context, the *APPI*, as well as other

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[14] *APPI*, Art 25(1). "When a business operator handling personal information is requested by a person to disclose such retained personal data as may lead to the identification of the person (such disclosure includes notifying the person that the business operator has no such retained personal data as may lead to the identification of the person concerned. The same shall apply hereinafter.), the business operator shall disclose the retained personal data without delay by a method prescribed by a Cabinet Order. However, in falling under any of the following items, the business operator may keep all or part of the retained personal data undisclosed: (i) Cases in which disclosure is likely to harm the life, body, property, or other rights or interests of the person or a third party, (ii) Cases in which disclosure is likely to seriously impede the proper execution of the business of the business operator handling personal information, (iii) Cases in which disclosure violates other laws and regulations."

[15] *Act on the Protection of Personal Information Held by Administrative Organs 2003* (Act No. 58 of 2003, Japan); *Act on the Protection of Personal Information Held by Independent Administrative Agencies, etc. 2003* (Act No. 59 of 2003, Japan).

laws, were found to be applicable to the *Ethical Guidelines* despite the fact that the *APPI* was not originally designed for this purpose.

Another noteworthy influence of the APPI is seen in the exemption clause of the disclosure policy of the newly-revised *Ethical Guidelines.* Originally, the exemption clause of the disclosure policy was set alongside the policy of disclosure in principle in the enactment of the *Ethical Guidelines* in 2001, as follows: the policy of disclosure in principle "shall not, however, apply if there is no adequate significance in providing genetic information and informed consent to non-disclosure has been obtained from the donor".[16] This clause was immediately changed to precisely follow the description of the APPI in its enactment of 2003. Specifically, the condition of the exemption clause turned from "no adequate significance*"* to "likely to harm the life, body, property or other rights or interests of the donor or a third party".[17] In the current revision of 2013 another exemption from the *APPI* was added into the *Ethical Guidelines* where the disclosure is "likely to seriously impede the proper execution of the research study" (referred to here as "the research study exemption").[18] Both of these exemptions clauses, except for the requirements of informed consent for non-disclosure, are the result of the influence of the *APPI.* In this regard the addition of the second condition in this revision means that the *Ethical Guidelines* more strictly respect the *APPI* than before. This has the effect of making the *Ethical Guideline*s somewhat more complex, but also potentially offering researchers greater flexibility in interpreting the remit of terms such as "likely to seriously impede the proper execution of the research study".

2.4 The specific researcher disclosure policy in the revised Ethical Guidelines*:*

The revised *Ethical Guidelines* incorporate one further important clause on disclosure which provides researcher's with the discretion to create their own specific disclosure policy. This clause states that researchers should take the initiative in creating in advance a policy for the disclosure of research results.[19] Three points for researchers to consider in preparing this front-end disclosure policy for the project are emphasized in the clause: the accuracy and validity of genetic research results, the potential health benefits of their results for research participants, and the risk of impeding the research study. The clause further includes detailed rules concerning the management of incidental findings which are defined in the *Ethical Guidelines* as "originally unexpected research results that have significant impact on the lives of research participant's and their relative's". It specifies that researchers should make every effort to consider a disclosure policy relating to potential incidental findings in advance and facilitate research participants understanding of the disclosure policy as part of informed consent.

In this latest revision of the *Ethical Guidelines*, the revised disclosure policy for research has been essentially amended in a manner consistent with the commerce or business provisions of the *APPI,* which was not originally intended to apply to academic research.

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[16] See note 12 above. Part III, s 9(1) (2001 edition).
[17] See note 12 above. Part III, s 8(1).
[18] *Ibid.*
[19] See note 12 above. Part III, s 8(2).

3. Challenges and opportunities regarding the revised *Ethical Guidelines*

The fundamental question is whether the disclosure policy in the 2013 revised version of the *Ethical Guidelines* can provide appropriate guidance to researchers and adequately protect the interests of research participants. Based on the analysis of the revised *Ethical Guidelines* above, we here argue that there are both practical and ethical challenges in the revised disclosure policy, and propose some of suggestions to address those challenges.

3.1 Practical challenges of the revised disclosure policy:

One of the challenges in the current revision of the *Ethical Guidelines* is that the disclosure guidelines have not sufficiently described the practical requirements/issues. The new *Ethical Guidelines* present a broad description of the disclosure policy detailed in the *APPI* and refer to "the disclosure policy in principle" and its broad exceptions. However, this broad reference to the disclosure policy is not supported by specific and practical guidance on applying this disclosure policy in research practice. The revised disclosure policy could play a minor and limited role in influencing and changing researchers' practices in response to the development for their own specific disclosure policies. One factor causing this conservative approach is that, as shown in the current process, priority has been given to ensuring compliance with the existing legal framework on control of personal information rather than facilitating practical application in the creation of disclosure policies in the *Ethical Guidelines*. In order to reorient and achieve the purpose of the revised Guidelines towards more practical implementation a first step would be to separate, at least in part, the *Ethical Guidelines* from the *APPI*. Such an approach could focus both on the purpose and the revision process of the *Ethical Guidelines* themselves.

3.2 Ethical challenges of the revised disclosure policy:

The revised disclosure policy potentially raises two ethical challenges. First, "the disclosure policy in principle" may, in some cases, lead to a therapeutic misconception by research participants. Fundamentally, the concept of research is different from one of clinical care in at least two respects:

- Research primarily emphasizes the creation of new knowledge for the public, rather than for the of benefit individual patients
- Research findings can be held to appropriate scientific standards of data collection, analysis and application, but this is not a guarantee of clinical utility.

The blurring of this boundary in genomics could potentially lead to the therapeutic misconception which is said to occur "when a research participant mistakenly believes that the primary aim of the research project is therapeutic".[20] With regard to "the

[20] PS Appelbaum, LH Roth and C Lidz, "The therapeutic misconception: Informed consent in psychiatric research" (1982) 5 *International Journal of Law and Psychiatry* 319-329; AL Bredenoord et al, see note 5 above.

disclosure policy in principle", the term "in principle" is ambiguous, and therefore can be broadly interpreted by stakeholders. Consequently, research participants may assume that they can request researchers to disclose their research results for their own therapeutic benefits, and thus confuse the concept of research with one of clinical care. From this standpoint, it can be argued that "the disclosure policy in principle" may be legally valid but not necessarily ethical.

A second challenge arises from the newly-added exemption clause, "the research study exemption", allowing researchers considerable leeway to decide which circumstances might amount to a "serious impediment" to the research study. Potentially this exemption clause fails to carefully consider respect for persons or respect for autonomy. Respect for persons is referred to as "a basic ethical principle that gives rise to obligations regarding how competent adults should be treated".[21] This incorporates respect for participants' self-determination, and leads to the following ethical justification:

> "It would be disrespectful to treat research volunteers as conduits for generating scientific data without giving due consideration to their interest in receiving information about themselves derived from their participation in research".[22]

This is reinforced by the Declaration of Helsinki, which has enshrined that "[w]hile the primary purpose of medical research is to generate new knowledge, this goal can never take precedence over the rights and interests of individual research subjects".[23] With regard to "the research study exemption", the clause fully takes into account the interests of researchers but little of the interests of research participants. Any decision to restrict disclosure where the research study may be "impeded" is open to varying interpretation. This guideline would be undermined if stakeholders could interpret the "research study" exemption as allowing them not to disclose research results only for their own practical convenience. In short, this "research study" exemption has the potential to be used as an excuse not to disclose. Therefore, "the research study exemption" clause may not adequately respect the autonomy and interests of research participants rendering these principle-based approaches of the disclosure policy ethically undesirable.

3.3 Ethical challenges of the **Ethical Guidelines** *in general:*

There is more general ethical challenge in the disclosure policy in the *Ethical Guidelines.* Arguably, they do not adequately consider certain aspects of research participants' choices in research. In the *Ethical Guidelines,* the disclosure policy sets out

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[21] DI Shalowitz and FG Miller, "Disclosing Individual Results of Clinical Research" (2005) 294 *JAMA* 737-740.

[22] DI Shalowitz and FG Miller, see note 21 above; SM Wolf, J Paradise and C Caga-anan, "The law of incidental findings in human subjects research: establishing researchers' duties" (2008) 36 *The Journal of Law, Medicine and Ethics* 361-383.

[23] World Medical Association of Helsinki, Declaration of Helsinki, "Ethical Principles for Medical Research Involving Human Subjects" (1964).

"the disclosure policy in principle" regarding the right to know, and also referred to the right not to know.[24] In this regard, the disclosure policy considers a research participant's rights. However, the disclosure policy does not clearly encourage researchers to offer opportunities for participants to express and incorporate their wishes and opinions into a disclosure decision. It may be more ethically considered for researchers to create a disclosure policy relying not only on their own perspective, but also taking in to account the views of participants in line with the principle of respect for persons, as mentioned above. Furthermore, the 2003 UNESCO declarations formally stipulate research participants' right to choose in advance whether or not they are informed of the results in Article 10 (the right to decide whether or not to be informed about research results).[25] In fact, there has been an absence of discussion among researchers in Japan on the ethical need to incorporate the opinions of research participants into research design.[26] In addition, researchers have formulated previous policies for return of genetic research results without external input, though in some cases the researchers consult experts in ethics and/or law. In such circumstances there is a possibility that researchers fail to give sufficient ethical consideration to research participants. Therefore, at least, as stated in the 2003 UNESCO declarations, the disclosure policy of the *Ethical Guidelines* would have to positively value those research participants' informed choice.

3.4 Opportunities in the Ethical Guidelines*:*

Despite the practical and ethical challenges outlined above, the revised *Ethical Guidelines* do have the potential to provide opportunities for the research community. These opportunities could be achieved through the provision of additional mechanisms for governing disclosure decisions in relation to the identified challenges, in three proactive approaches of the research collective, individual researchers and individual research participants, respectively.

First, as a research collective approach, academic societies and research projects could create their own policies for disclosure of research results to research participants. In this approach, the compliance with such a policy is a requirement of project participation, whilst in others the policy is provided as a recommendation only. Such policies might take the form of a flowchart describing the passage of results from researchers to research participants, and describe the decision processes involved. They can provide further guidance of how to treat findings in different circumstances, including the types of research methods, research findings and researchers and they could provide an *a priori* list of clinically significant findings, based upon the genomes of the population in the relevant country/countries. In research collective approaches, it may be valuable to consider the disclosure models of previous activities, such as the UK 10K project, ACMG and Clinical Sequencing Exploratory Research (CSER)

[24] See note 12 above. Part III, s 8(4) With regard to human genome/gene analysis research through which the genetic information of individual donors is revealed, when a donor has not requested disclosure of his/her own genetic information, the research director shall not disclose the requested information.
[25] UNESCO International Declaration on Human Genetic Data (2003).
[26] Research Unit for the ELSI of Genomics, "Report of a meeting to consider research ethical review in human genome research" (2014).

consortium,[27] and use these approaches to inform new policies specific to the research endeavour. While, in Japan, there is still a difficulty regarding the lack of a common certification for clinical sequencing in laboratories, like the Clinical Laboratory Improvement Amendments (CLIA) in the US and Clinical Pathology Accreditation (CPA) in the UK, the development of those policies in Japan through a "bottom-up" approach would provide more guidance to researchers, who could create a practical disclosure policy, and be valuable in particular, when research is integrated with clinical care.

In our second approach, individual researchers could create their own disclosure policies, particularly by flexible interpretation of the *Ethical Guidelines*. This approach requires that the "principles" and "exceptions" of the disclosure policy in the *Ethical Guidelines* are broadly and flexibly interpreted, which includes that stakeholders do not necessarily regard "principles" and "exceptions" to apply to "most cases" and "some cases", respectively. The approach is also particularly desirable when considering "the research study exemption" which will require careful consideration of the research participants' interests. In these cases, researchers have an opportunity to offer useful results to research participants within their capability, while avoiding therapeutic misconceptions, and decision making based solely on their own practical convenience. This approach by researchers can be ethically justified by the beneficence principle, simply stated as "doing good for the sake of others".[28] In this approach, it would be important for members of ethics review committees to support these interpretations of the disclosure policy. For this, it could be effective to hold meetings/workshops for members of ethics review committees across the country on an ongoing basis, which would facilitate knowledge sharing and policy discussion of basic rules for the ethical review and state-of-the-art research between research ethics committees.[29]

For the third individual research participants approach, researchers could assign the decision process of disclosure to individual participants. For example, in the process of obtaining consent, researchers can proactively offer identifiable research participants a choice regarding disclosure. In some research projects, there may be several options depending on research results with different characteristics.[30] There may be primary research results and incidental findings in the course of original research, or secondary research results obtained through biobanks and databases. In this approach, it would be important for researchers to anticipate, in advance, the potential of clinically significant findings in their own research. Equally, it may be necessary for research participants to understand the potential implications of those findings before giving consent. This approach requires a thorough consideration by the research team of the findings before

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[27] RC Green et al and J Kaye et al, see note 2 and 7 above, respectively; JS Berg et al, "Processes and preliminary outputs for identification of actionable genes as incidental findings in genomic sequence data in the Clinical Sequencing Exploratory Research Consortium" (2013) 15 *Genetics in Medicine* 860-867.

[28] AL Bredenoord et al, see note 5 above.

[29] J Minari, T Shirai and K Kato, "Ethical considerations of research policy for personal genome analysis: the approach of the Genome Science Project in Japan" (2014) 10:4 *Life Sciences, Society and Policy*; G Yoshizawa et al, "ELSI practices in genomic research in East Asia: implications for research collaboration and public participation" (2014) 6:39 *Genome Medicine*.

[30] LM Beskow and W Burke, "Offering individual genetic research results: context matters" 2010 2 *Science Translational Medicine* 38cm20.

creating any consent form, and detailed project information, for the participants. This approach, however, may be limited and constrained in a static, one-time consent in advance,[31] where there may often be difficulty in adapting to changes in research progress and research participants' preference. This difficulty has received considerable attention, more recently, in the light of the introduction of information and communication technologies for decision making on disclosure. Technologies can be used for the selection of options such as My46[32] but also for on-going consent such as dynamic consent.[33] Dynamic consent is a flexible and continuously personalized consent, and allows participants to choose from a range of consent preferences and to change their mind over time. These approaches enable both researcher and research participants to manage the decision making on disclosure by working in partnership. This opportunity involving research participants could ensure further research advancements and research participants' trust and better understanding of research fields.

4. Conclusion

The disclosure policy in the revised Japanese *Ethical Guidelines* gives priority to adherence to related legal regulations, with easing the limitation of non-disclosure, and to granting researchers greater discretion to create their own disclosure policy. In particular, the revised disclosure policy has been significantly influenced by the personal information privacy protection law, despite its original design exempting academic research. We argue that there are several challenges regarding the revised disclosure policy, and propose interpretive ways to address these challenges, specifically the necessity for additional governance systems shaped by three distinct approaches of the research collective, individual researchers and individual research participants. We do not advocate disclosing all potentially beneficial research results to the research participants. Rather, we emphasize that the new version of the *Ethical Guidelines* should be interpreted to consider and favour the interests of research participants. In the three proposed approaches, the revised *Ethical Guidelines* should enable researchers to make their own research design decisions on a case-by-case basis by considering both the purpose of the research and the interests of research participants. We consider that the revised *Ethical Guidelines* will be successful provided they are clearly understood and translated into participant-focused disclosure policies and practices in Japan.

In our research, the Japanese experience provides two messages, which have implications for the international debate. First the duty of genomics researchers to carefully interpret the *Guidelines* for the benefit of research participants, and secondly the need for thoughtful consideration of the *Guidelines* in the context of established ethical principles. The Japanese experience may be useful in considerations of

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[31] M Watanabe et al, "For what am I participating? The need for communication after receiving consent from biobanking project participants: experience in Japan" (2011) 56 *Journal of Human Genetics* 358-363.

[32] Available at http://www.my46.org

[33] J Kaye et al, "Dynamic consent: a patient interface for twenty-first century research networks" (2014) *European Journal of Human Genetics* (doi: 10.1038/ejhg.2014.71); JH Yu et al, "Self-guided management of exome and whole-genome sequencing results: changing the results return model" (2013) 15 *Genetics in Medicine* 684-690.

disclosure policies in other countries with personal information privacy protection laws and without specific laws on human genome research. In the absence of clear international standards on disclosure of genetic research results to participants, it is noted that research is moving towards disclosure of beneficial results to research participants. The revised *Ethical Guidelines* move Japan in this direction, if the *Guidelines* are interpreted as we argue. There is a pressing need to move towards an international harmonization on disclosure policy, particularly in light of global collaborative projects, and the Japanese experience may go some modest way to contributing towards establishing global standardised ethical policies on disclosure.

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Abbreviations
ACMG: American College of Medical Genetics and Genomics; APPI: Act on the Protection of Personal Information.

Competing interests
The authors declare that they have no competing interests.