Institution: Cardiff University

Unit of Assessment: 32

Title of case study: Transforming practices and influencing debate in genetics research

1. Summary of the impact [Key: **Bold**: text from REF guidelines; ***Bold italic***/*italic*: emphasis; Superscript: references in sections 3 and 5]

Research by Chadwick has influenced research protocols and policies regarding the ethical consequences of collecting DNA for research. Her impact is most visible in the Personal Genome Project, and the work of the Nuffield Council on Bioethics, UN Food and Agriculture Organisation, Human Genome Project and H3Africa. Her contributions to discussions and documents resulted in changes to how consent is gained from DNA donors. In particular, the changes address important issues that she raised regarding the practicality and acceptability of the undertakings made in current consent protocols about confidentiality and the future use of data. Chadwick's underpinning research claims relate to the fact that genetic information, and the attendant genetic technology, are derived from, and significant to, populations as a whole. She maintains that biotechnological advances are changing our ethical values, particularly regarding conflicts between personal interests and large-group needs. For her, practical ethics cannot apply normative ethical concepts and theories arising from abstract philosophical reasoning. Rather, the conceptual and theoretical structures themselves must be developed through philosophical engagement with the scientific details of the project. Her collaboration with bodies responsible for the protocols of consent reflects a 'bottom-up' moral philosophy rather than the traditional 'top-down' theory-driven approach.

2. Underpinning research (pgx = pharmacogenomics; ngx = nutrigenomics)

Ruth Chadwick, Distinguished Research Professor in the Unit's Centre for Applied Ethics, and Director of Cardiff's ESRC Centre for Economic and Social Aspects of Genomics (CESAGen) 06-13, contributed original research insights to philosophical debates regarding the ethics of how biobanks (major repositories of DNA) are created and used. Her research responded to the ethical concerns raised by fast technological and aspirational change in biotechnology, triggered by the first human genome sequences in 2003 and 2007, and took up the challenge raised in *Nature Genetics* 28: 297f in 2001, to "provide pragmatic, moral guidance to all that are affected by genomics" by "defining a new bioethics that promises real world solutions to real world problems."

a. *Value impact*. How changes in our lives impact on our values ('value impact') is nowhere more evident than in biotechnology. Chadwick argues: "we may find that principles that have worked very well in specific contexts in the past are not simply transferable."[3-5] In 2006-13, Chadwick tracked value impact (her own term, Chadwick 1999, *Health, Risk & Society* 1,3: 294), in the wake of new possibilities and expectations. She articulated contradictions that cannot be easily resolved: the individual vs the community;[3-5] autonomy vs responsibility;[3-4] inclusion/equity vs pragmatism and profit; [3-1] confidentiality vs personalised feedback;[3-1,3-4] caution vs veracity;[3-2] intercultural harmonisation vs standardisation.[3-3] By recognising the relevance of the 'communitarian turn' in bioethics to these issues, Chadwick articulated a distinctive and compelling approach to the value impact of biotechnology,[3-1,3-5] whereby the needs of a wider group (family, ethnic group, world-wide population) take precedence over personal interests. Participating in medical research has often entailed altruism, in that the findings will come too late to help the donor, but donations to DNA bio-banks raise the stakes on personal costs because of the many potential long term risks of donation (see ***d*** below). With reference to her research in three domains: pharmacogenomics,[3-1] medical research[3-2,3-3,3-5] and nutrigenomics,[3-4] she demonstrated "how the applicability of traditional ethical frameworks … is coming under challenge … Justice, privacy, informed consent, and autonomy: all these are subject to reconstrual in the light of developments in genetics"[3-1] (p.787-8).

b. The effect of personalisation on autonomy. Genome sequencing enables the personalisation of drug therapies (pharmacogenomics, 'pgx') and dietary advice (nutrigenomics, 'ngx'). Chadwick has contributed three arguments in the ethical debate. (1) Pgx risks creating two-tier medicine. 'Orphan' populations will emerge: those unable to afford personalised medicine, and the minorities whose genetic profile is not suitable for drugs developed, for reasons of profit, only to suit the majority.[3-1] (2) The promise of 'tailored' medicine or nutritional advice understates the continued role of population statistics to determine the most likely profile of the individual.[3-4] In practice, an individual still might not receive the optimum treatment because the statistics conceal finer points of difference or generalise inappropriately.[3-1] (3) Personalised feedback may extend beyond what the individual wishes to know. Ethical practices should include a "right not to know" about, say, "a

late onset disorder for which there was no effective treatment."[3-1]

Chadwick[3-1,3-5] argues that the entire foundation of biomedical ethics, "primarily concerned with protecting the interests of individuals in medical contexts," is undermined by personalisation. Personalisation "is associated not only with the rhetoric of 'choice' (and autonomy), but also with facilitating more individual responsibility for health".[3-1] Dietary advice may seem to enable what she terms 'thin' individual autonomy: factual information is provided, for free choice of action. However, there is a continuum from smoking advice, where others can be caused harm by one's actions, to binge eating, which can cost the health service money. Thus, she argues that the vision of ngx presented in the UK Dept of Health white paper 'Choosing Health' (2005) entails 'thick' autonomy: there is an agenda of responsibility, even though the rhetoric is still one of choice. "[T]here is a barely hidden assumption that people given information will make certain sorts of choices."

c. Harmonisation vs standardisation. Chadwick argues that, as many biobanks are international, harmonised or standardised ethical procedures are needed so that data collected under tight control in one place is not misused under laxer controls in another. Chadwick & Strange[3-3] point out that some existing policies are culture-centric in their assumptions about the relative importance of individual and group interests. Yet cultural differences make it difficult to have a single approach: "the harmonisation of ethics may be better served by establishing broad universal foundations that allow for diverse interpretations rather than many specific guidelines or principles."[3-3] This idea is put into practice in policy documents such as the H3Africa ethics guidelines (see section 4).

d. Veracity and open access. For Chadwick, a major ethical issue is lack of transparency about the possible future uses of data, and the potential risks for the donor. This led her to examine the potential for greater openness, or veracity. In an agenda-setting piece in *Nature Genetics* 2008[3-2] Chadwick and her co-authors observe that, with genetic data, "the guarantee of absolute privacy and confidentiality is not a promise that medical and scientific researchers can deliver any longer." They argue that "the reality of the new genetics and genomics urges us to abandon the traditional concept of medical confidentiality" and "new models are needed to offer robust moral guidance while keeping the reality of a dynamic science in mind." Cyber-attack, data mismanagement, and, particularly, unforeseen new technological capabilities, are a "real threat to privacy."[3-5] The key question raised is whether it is ethical to reiterate and strengthen current promises of privacy and confidentiality, without knowing if they are actually robust. DNA is not like other kinds of data. Even if the donor's name and address are not collected, information from a sample could be tracked back to the individual, e.g. through cross-comparison with medical records, police databases, ngx data, genealogy data. And the risks extend to family members, because of their shared DNA.

DNA samples are increasingly stored for long-term sharing. Ethics protocols typically require an articulation of the future uses of the data, but this is impossible, since many will involve techniques yet to be invented. The default of returning to the donor for additional consent is impractical and would hinder research progress. Various kinds of consent (e.g. default with opt out, blanket, informed, broad) all have their problems. Chadwick is co-author of a paper that introduces 'open consent.' Here, "volunteers consent to unrestricted re-disclosure of data originating from a confidential relationship, namely their health records, and to unrestricted disclosure of information that emerges from any future research on their genotype–phenotype data set, the information content of which cannot be predicted. No promises of anonymity, privacy or confidentiality are made."[3-2] Open consent blows open the hidden contrast between what donors typically expect and are promised, and what is, or in future might, actually happen to their data. In open consent, "The leading moral principle is veracity—telling the truth—which should precede autonomy".[3-2]

Notwithstanding Chadwick's involvement with the development of open consent practices, her role is less one of advocacy than balanced advice. Open consent does not solve the confidentiality problem, only adopts veracity in place of unsustainable promises. Through her practical work with policy-makers (see section 4), Chadwick continues to surface contradictions and ask new questions about what is ethically appropriate for current and future biotechnological data collection.

3. References to the research All publications are available from the HEI.

1. **Chadwick, R** (2007) Pharmacogenomics. In Ashcroft, R, Dawson, A. Draper, H & McMillan, J (eds.) *Principles of Health Care Ethics*. (2nd ed.) Wiley, 783-8. ISBN: 978-0470027134
2. Lunshof, J, **Chadwick, R,** Vorhaus, D & Church, G (2008) From genetic privacy to open consent *Nature Reviews Genetics* 9, 406-411. ISSN 1471-0056 (print) DOI 10.1038/nrg2360
3. **Chadwick, R** & Strange, H (2009) Harmonisation and standardisation in ethics and governance:

conceptual and practical challenges. In Widdows, H & Mullen, C (eds) *The Governance of Genetic Information: Who Decides?* Cambridge UP, 201-213. ISBN: 9780521509916
4. **Chadwick, R**. (2010) Nutrigenomics and statistical power: the ethics of genetically informed nutritional advice. In D. Bagchi et al., *Genomics, Proteomics and Metabolomics in Nutraceuticals and Functional Foods*, Iowa: Wiley-Blackwell, 23-33. ISBN: 9780813814025
5. **Chadwick, R** (2011) The Communitarian Turn: Myth or Reality? *Cambridge Quarterly of Healthcare Ethics* 20 (4), 546-553. DOI 10.1017/S0963180111000284

4. Details of the impact

Type of impact: The impact is **change to society and public policy** in relation to **awareness, policy and practice** on the part of **organisations** with national and international responsibilities. It includes impact on research ethics itself, as a practical procedure in science and commerce. The **beneficiaries** are (a) national and international bodies engaged with the collection, storage and research of genetic biodata, (b) individuals donating their genetic material, and their families, (c) wider national and international communities benefiting from research made possible by biobanks.

Process and substantive nature of impact: Chadwick maintains that ethicists must engage with "real questions about what is possible and appropriate in a variety of circumstances."[3-2] Her core research claims have fed into policy formation, and responded to policy imperatives, addressing the practical challenges of biobank development in the light of the complex and often contradictory ethical concerns with new biotechnologies. The research-to-impact trails outlined here demonstrate that the impact is ***centrally founded on Chadwick's research***. Her membership of the committees drafting policies indicates her as ***a core contributor*** to the outcomes.

Impact on the practice of DNA collection:

a) Chadwick was invited by the ethics consultant of the Personal Genome Project (PGP), Lunshof, to join the team reporting[3-2] the adoption of 'open consent',[5-1] as an instantiation of PGP's core principle of veracity (http://1.usa.gov/GP2D28) (see box). PGP invites donors to provide DNA for sequencing. By 26/10/13, 2884 donor profiles were listed (http://bit.ly/GWgkg0) PGP publishes the entire genome sequence, linked to medical and lifestyle records, for researchers to access without restriction. The project monitors the effect of open consent on recruitment, as outlined in the team's 2008 paper.[3-2] Such monitoring aligns with Chadwick's position that the value impact of bio-technology is far from static. In 2012, PGP Canada adopted open consent, with built-in three-monthly monitorings of the consequences, positive and negative, of donation.[5-2] This step reflects Chadwick's articulation of the need to surface the consequences of biobanking in order to inform future decision-making.[3-5] Open consent is a social experiment, testing the power of the communitarian turn in bioethics[3-5] by relying on the willingness of donors to give DNA in full knowledge of the potential risks.[3-2] Are humans that altruistic, and will they remain so when more is known about the reality of the hypothetical risks? The Personal Genome Projects (PGP) in the US and Canada are gathering data from participants to find out.

Personal Genome Project's rationale for open consent
http://www.personalgenomes.org/non-anonymous
Because we cannot guarantee privacy and we are committed to sharing data for the advancement of science, we feel the most ethical and practical solution is to collaborate with individuals who are comfortable sharing their data without any promises of privacy, confidentiality or anonymity. We call this "open consent".

b) The Wellcome Trust and NIH funded Human Heredity and Health Africa (H3Africa) Consortium facilitates "a contemporary research approach to the study of genomics and environmental determinants of common diseases with the goal of improving the health of African populations" (http://www.h3africa.org/). In 2013, H3Africa developed guidelines for 'informed consent' that bear many hallmarks of open consent, for use in DNA data collection across projects in Africa.[5-3] They include not only wordings for consent forms, but explanations of the underlying issues, and advice on how to ensure the generalised material is appropriate to the local context (e.g.p.8). Chadwick, a member of the Expert Committee,[5-4] presented the case for open consent at the H3Africa inaugural conference[5-5] and is acknowledged (p.4) as a primary advisor on the draft. The text reflects her case[3-3] that while consent practices need to be harmonised, to protect vulnerable populations, they must be sensitive to local conditions and beliefs, without undermining equity or veracity (e.g. p.18).

Impact on the biobanks debate

c) As a member of the UN Panel of Eminent Experts on Ethics in Food and Agriculture, Chadwick contributed research ideas[3-4] to a report on the future of global food security, authoring the section

on nutrigenomics[5-6] (p.40-44). It raises asks whether ngx might: distract from the right to food; contribute to or distract from public health goals; benefit only selected populations; and create challenges for cultural difference, and it asks what an ethically robust ngx policy should look like.

d) Two reports for the Nuffield Council on Bioethics (NCB) drew on Chadwick's research. The NCB promotes discussion of ethical issues arising from biological and medical research, and publishes recommendations on policy. One report was an independent evaluation of solidarity as a concept in bioethics (2011).[5-7] At two workshops, Chadwick explained and debated solidarity and open consent, informing the report's emerging account of the 'communitarian turn' in bioethics. Addressing the ownership of information and the notion of open consent (chap 6), veracity as a driving force is acknowledged as a core claim of the 2008 paper.[3-1] The authors propose an approach "based on the core assumption that when individuals decide to participate in biobank-based research, they are willing to accept the possibility that [a] certain level of costs may need to be carried by them for the sake of communal benefit"[5-7] They cite the PGP (see ***a***), as a model for their recommended practices (p.61). The NCB 2012 report on *Emerging Biotechnologies*[5-8] also reflects and acknowledges Chadwick's research. Of the principles of public solidarity, the report states: "This new orientation is towards a notion of the public good rather than—and distinct from—the concern for negotiation between individual interests engaged by bioethical questions"[5-8] (p.62). Hugh Whittall, Director of NCB since 2007, states: "The Council's work on both publications to which Professor Chadwick has contributed has been influential in promoting the principle of solidarity in bioethics and in developing it as an underpinning framework for policy." He adds, "Especially useful was her research into the way concepts of solidarity have changed in the context of modern genetics, and her interest in openness and honesty with those donating to biobanks."[5-9]

e) Chadwick chaired a working group to draft a White Paper for the Human Genome Organisation (HUGO), 2013.[5-10] It explores issues arising from relinquishing confidentiality. Acknowledging open consent in the PGP's as socially beneficial, it yet notes: "privacy and confidentially still have a role in genetic data processing and storage," echoing Chadwick's position that the ethical entailments of consent remain, at this time of rapid development in biotechnology, conflicting and unresolved.

5. Sources to corroborate the impact (The HEI can supply copies/web captures of all items)

1. The Risks and Benefits page, under the tab 'Non-anonymous' on the PGP website, http://www.personalgenomes.org/risks-benefits. (2007 or later). It demonstrates open consent in practice, reflecting the principles in the 2008 paper to which Chadwick contributed.[3-2]
2. The full participant consent form , PGP Canada. 2012.The safety questionnaire (p.8-9) tracks the impact of open consent, in line with the monitoring recommendations in the 2008 paper.[3-2] http://www.personalgenomes.ca/consent/PGPCanada_Full_Consent_Form_Jan2012.pdf
3. Guidelines for Informed Consent, H3Africa Working Group on Ethics and Regulatory Issues. 2013. Drawing on input from Chadwick these guidelines explain the ethical challenges articulated in her research, and reflect a strong commitment to veracity. http://bit.ly/19yTlhf
4. List of Independent Expert Committee members, H3Africa. 2012. It confirms Chadwick's membership, http://www.h3africa.org/consortium/independent-expert-committee
5. Chadwick's lecture at the H3Africa inaugural conference, 2012, where she presents the case for informed, open and broad consent in the African context (slides 13-21) and invites debate (22)
6. Final report of the Panel of Eminent Experts in Food and Agriculture, UN Food and Agriculture Organisation, published 2011. http://www.fao.org/docrep/014/i2043e/i2043e00.htm Pages 40-4, by Chadwick, reflect issues raised in her research[3-4] regarding the ethics of nutrigenomics.
7. *Solidarity: Reflections on an emerging concept in Bioethics,* Nuffield Council on Bioethics, http://bit.ly/1aJ38DX. 2011. The chapter on biobanks, pp.54-63 drew on Chadwick's direct input. Fn 53, p.47 acknowledges Chadwick's influence in the composition of the report.
8. *Emerging biotechnologies: technology, choice and the public good*. Nuffield Council on Bioethics. 2012. Reflects Chadwick's influence in "argu[ing] for a new 'public ethics' approach to biotechnolo-gy governance" (p.xx) and noting that "the implications of [the communitarian turn in bioethics] are significant." http://bit.ly/X7p1of (p.62)
9. Testimony from Director of the Nuffield Council on Bioethics. 2013. Confirms Chadwick's role in shaping NCB policy with respect to solidarity, openness and honesty, and "her influence in orienting bioethical debate towards concepts of the public good, rather than individual interest."
10. *Imagined Futures: Capturing the Benefits of Genome Sequencing for Society*. Human Genome Organisation, 2013. This White Paper reflects Chadwick's influence in shaping the debate over consent and biobanks, embedding the concept of solidarity at an international level.