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TOWARDS A BIOETHICS OF INNOVATION

Wendy Lipworth & Renata Axler (2016)

ABSTRACT

In recent years, it has become almost axiomatic that biomedical research and clinical practice should be 'innovative'—that is, that they should be always evolving and directed towards the production, translation and implementation of new technologies and practices. While this drive towards innovation in biomedicine might be beneficial, it also raises serious moral, legal, economic and socio-political questions that require further scrutiny. In this article, we argue that biomedical innovation needs to be accompanied by a dedicated 'bioethics of innovation' that attends systematically to the goals, process and outcomes of biomedical innovation as objects of critical inquiry. Using the example of personalized or precision medicine, we then suggest a preliminary framework for a bioethics of innovation, based on the research policy initiative of 'Responsible Innovation'. We invite and encourage critiques of this framework, and hope that this will provoke a challenging and enriching new bioethical discourse.

The drive to innovate in medicine and the need for a supporting 'bioethics of innovation'

Anyone working in medicine will be aware of the rapidly changing nature of biomedical research and clinical practice, and the drive to 'innovate',[1-4]—that is to produce new knowledge and technologies—and 'translate'[5-8] or 'implement'[9-11] these into policy and practice as quickly as possible. Governments worldwide have called for greater investments in biomedical innovation and translation,[12-18] and attempts have been made to change legislation so that innovation can be take place more freely in science and medicine.[19] Researchers, policymakers and practitioners have made similar pleas, as typified by statements such as this one in *Academic Medicine*:

> Health care environments must foster innovation, not just allowing it but actively encouraging it to happen anywhere and at every level in health care and medicine—from the laboratory, to the operating room, bedside, and clinics.[3 p1424]

Not surprisingly, given the current drive to innovate in medicine, many popular definitions of biomedical innovation assume that such innovation is always desirable. The World Health Organisation, for example, states that: '[i]nnovative technologies refer to novel medical (device) solutions that address health problems and improve quality of life.'[14] We argue,

in contrast, that biomedical innovation *per se* is neither good nor bad and that the concept itself deserves critical attention. To facilitate this attention, we believe that there is a need for a *bioethics of innovation* that provides a moral and socio-political framework for thinking about the values, goals, processes and outcomes of biomedical innovation (as distinct from those of specific emerging technologies) as an object of scrutiny.

Current bioethical approaches to innovation

When it comes to examining novel or 'innovative' technologies, bioethicists have long been interested in evaluating the moral implications of *specific* 'emerging technologies'. As a result, sophisticated frameworks have been developed for thinking about the potential (and often unpredictable) positive and negative implications of specific technologies, such as nanotechnology, stem cell therapies, or bio-enhancement [20]

Insofar as bioethicists have focused on the *process* of innovation*,* the emphasis has tended to be on how to respect and safeguard the human research participants who take risks in order to facilitate innovation, and whether and how to encourage the use of particular 'tools' of innovation, such as animal models, embryonic stem cells or biobanks. Bioethicists have also developed sophisticated frameworks for thinking about how to ensure that patients have equitable access to the products of innovation, without placing too great a burden on health system resources.[21]

These preoccupations of bioethicists who are interested in emerging technologies can be demonstrated by examining the bioethical discourse surrounding 'personalised' or 'precision' medicine'—a key component of the ever-more popular 'translational medicine' paradigm.[12, 13, 22-25] In keeping with the typical bioethical concerns described above, bioethicists with an interest in new 'personalised' therapies have generally focused their attention on the morality of specific laboratory technologies—such as cloning—used in the pursuit of personalised medicine; research ethics questions, such as how to protect those participating in increasingly complex clinical trials and those who donate tissue to the biobanks that are used to identify biomarkers; and resource allocation questions, such as how to ensure equity and efficiency in the funding and distribution of personalised medicines and companion diagnostics.[26-29]

These are important moral and socio-political issues, but to focus solely on these types of issues potentially obscures a broader set of questions focused on health-related *innovation itself*—i.e. on the practices, politics and ethics of the development of novel health technologies, and of making changes to existing, more or less evidence-based health-related practices. Here, bioethics appears to have less to say.

This lacuna has long been recognised by social scientists, who have worried about the institutionalisation of bioethics as a set of governance tools that downplays both the politics of innovation and the uncertainties inherent in knowledge and technology production. In response, they have suggested that there is a need to shift attention 'upstream', away from just the risks and impacts of innovation and towards its processes, as well as a need to make innovation more democratically accountable.[30, 31]

This is not to say that bioethicists are completely uninterested in innovation as an object of inquiry. Debates about whether legislation should be passed that makes it easier for clinicians to try new treatment strategies;[32] whether, when and how surgeons should try out new operative techniques;[33] and how to conceptualise and manage the prescribing of

unregistered medicines,[34] all point to concerns within the bioethics community about innovative practice outside the context of formal biomedical research. But each of these issues tends to be dealt with in isolation, rather than by drawing on a framework that attends *systematically* to the goals, process and outcomes of *any kind* of biomedical innovation. In the remainder of this article, we will outline a potential framework for a 'bioethics of innovation' that might be able to fill this gap.

Developing a bioethics of innovation based on Responsible Innovation

Fortunately those with an interest in developing a bioethics of innovation would not need to start from scratch, and could draw upon a set of frameworks that have already been developed for innovation in general: those of 'Responsible Innovation' or 'Responsible Research and Innovation'.[35] In recent years, Responsible Innovation has garnered much attention and traction as a policy and scholarly agenda. For example, it is now used as a multi-institutional policy tool in Europe, and the Journal of Responsible Innovation was launched in 2014.[36]

The Responsible Innovation agenda has emerged as a result of recognition of both the many unquestioned assumptions underpinning innovation, and an apparent loss of public trust in innovation. It has also been stimulated by the concern that those governing science (including bioethicists) have tended to focus too much on protecting individual consumers from the potential harms associated with specific products of innovation. Scholars in this field have therefore argued that there is a need to 'move from the governance of risk to the governance of innovation itself.'[35 p1570]

Responsible Innovation aims to be forward-looking—'taking care of the future through collective stewardship of science and innovation in the present.'[35 p1570] It also aims to embed societal deliberation into the innovation process. As Stahl has noted, Responsible Innovation comprises a number of 'actors', 'activities' and 'norms', and proposes a view of Responsible Innovation as:

> 'a higher-level responsibility or meta-responsibility that aims to shape, maintain, develop, coordinate and align existing and novel research and innovation-related processes, actors and responsibilities with a view to ensuring desirable and acceptable research outcomes.'[37 p708]

One foundational conceptualization of Responsible Innovation, that has been put forward by Stilgoe and colleagues focuses on a set of four principles or dimensions, namely: anticipation, reflexivity, inclusion, and responsiveness. Anticipation calls for a consideration of desirable futures of the technology; reflexivity calls for scientists and institutions to engage in moral reflection about innovation; inclusion calls for new voices to be brought into the governance of science and innovation; and responsiveness refers to the need for attention to the political (e.g. regulatory) and commercial (e.g. intellectual property) forces that may hold power over innovation, as well as the need for courses of innovation to be adjusted according to emerging findings from the three previous domains[35] In addition to considering specific technologies, such as nanomedicine,[38] synthetic biology,[39] and theranostics,[40], discourses of Responsible Innovation have been used widely to examine the socio-political ethical, moral, legal, and economic issues arising in technology innovation more broadly.[41, 42]

Despite this widespread use of Responsible (Research and) Innovation in research policy and scholarship, it is important to note that Responsible Innovation has often not been deliberately and explicitly attentive to the context of health in biomedical research. This is potentially a problem because there are some features of *health* innovations that make them different from other kinds of innovations. Health products and service innovations are different from consumer product innovations, both in the contexts in which there are produced, and the contexts in which they are consumed—and this uniqueness of health is often obscured in discussions of innovation in general.[43-45]. To this end, we suggest that a framework of Responsible Innovation that is attentive to health and biomedicine should form the foundation of a bioethics of innovation.

It should also be noted that the paradigm of Responsible Innovation has itself been criticised for being somewhat limited in its focus on certain elements of 'responsibility' and not others (e.g. on responsibility to certain publics but not others), and on the potentially atheoretical and acritical notion its puts forward of 'responsibility" in innovation.[41] However, we emphasise that Responsible Innovation should only be the broad organising framework for a complete bioethics of innovation. In developing a comprehensive bioethics of innovation—i.e. in 'fleshing out' the Responsible Innovation framework in the context of health and biomedical innovation—it will also be crucial to draw upon insights from other biomedical disciplines focused on the study and critique of biomedicine.

Other sources of guidance for a bioethics of innovation

Insights to inform a bioethics of innovation could, for example, be derived from the social and political sciences, including science and technology studies (STS), social epistemology, sociology and anthropology of science and medicine, and organizational studies, where the organisational and political dimensions of scientific practice and technological development are explored.[46-49] While these disciplines tend to be analytic rather than prescriptive, they do provide a rich understanding of the social norms, values and power relations that underpin biomedical innovation, and that need to be taken into account in any application of a bioethics of innovation. In particular, as mentioned above, the field of STS has long established the need for reflexivity and democratic participation in technological innovation, and for focusing not only on downstream risk, but also on the cultural and political dimensions of technology.[30] Knowledge about norms, values, power relations, and political factors derived from these social science disciplines could be particularly helpful in achieving the principles of *reflexivity* (which requires reflection on embedded norms and values), genuine *inclusiveness* (which requires identification and management of power imbalances), and *responsiveness* by illuminating the effects on innovation of governance and regulatory regimes, and social institutions.

Health economics, with its focus on cost-benefit analyses, the allocation of resources, and economic health technology assessment, could also provide useful insights for a bioethics of innovation.[50] It is noteworthy that a view is emerging that those assessing health technologies should focus not only on clinical safety, effectiveness and cost-effectiveness, but also on aligning technology development with population values, and defining and rewarding genuine (value-adding) innovation.[51] Insights from health economics and technology assessment could be particularly helpful when it comes to the *anticipation* dimension of responsible innovation, which entails identifying unmet needs and determining whether they can, or cannot, be met by a particular emergent technology, as well as *responsiveness* by grounding the field in health-related economic insights.[48, 52, 53]

Those interested in developing a framework for a bioethics of innovation could also draw on insights from applied disciplines such as 'implementation science,'[9, 10, 54] 'translation science,'[6-8, 55-57] and 'research and innovation policy.'[58, 59] It is important to bear in mind, however, that these disciplines tend to focus on questions of how to foster and speed up innovation through, for example, removing organisational barriers, rather than on whether innovation *should* be promoted, and what harms or competing goals need to be balanced against the benefits of innovation. Nonetheless, an understanding of the dynamics of biomedical implementation and translation could assist in ensuring that new technologies are developed with the appropriate degree of responsiveness to barriers to implementation, and to changing clinical, economic and social circumstances.

Finally, while bioethics in its current form is lacking in its approach to the totality of innovation, bioethics is a dynamic field, and some emerging sub-fields within bioethics could shed light on some of the moral complexities of a bioethics of innovation. Public health ethics, global health ethics, and health policy ethics[60-63] all focus on broad systems, populations and processes, and might therefore, provide useful conceptualisations for those with an interest in developing a bioethics of innovation. These domains of bioethics are promising in their macro-level approaches to bioethics, and though the focus on innovation is currently limited within them, insights could be systematically developed on how the conceptualization of public interests, global agendas, and policy processes affect biomedical innovation.

Other branches of applied ethics, such as academic ethics[64], business ethics[65] and publication ethics[66] could also shine light on the moral dilemmas and obligations of particular stakeholders in biomedical innovation processes, particularly by focussing a bioethics of innovation on how the commitments of academic institutions, such as publication and research, affect innovation agendas; or how business arrangements and obligations impact upon innovation cycles . Furthermore, the normative theories upon which bioethics is based, such as virtue ethics, principlism, consequentialism, and examinations of justice, may provide useful frameworks for thinking about the process of innovation.

Scope of a bioethics of innovation

In order to be sufficiently comprehensive, it would be important for a bioethics of innovation to attend systematically to *all* dimensions of biomedical innovation, from the conceptualisation of a new health technology through to its development, testing, manufacture, registration, funding, marketing, and implementation in practice.

Returning to our case of personalized medicine, and using Stilgoe et al's framework for Responsible Innovation as an organising framework, a exemplar set of critical questions would include:

- **Anticipation:** What forces (political, economic, or social) have determined that targeted therapies and companion diagnostic *should* be developed and promoted, and what is driving this commitment? Is there a defined (and ideally currently under-served) patient population who would benefit from the development of personalised medicine (e.g. individuals with genetic mutations that render existing treatments ineffective)? How will the unanticipated consequences of targeted therapies be dealt with, beyond simple risk mitigation?
- **Reflexivity:** Have ethical, social and political concerns been taken into account in the development of personalised medicine? For example, given that personalised

medicines and companion diagnostics are often so expensive, has thought been given to whether the technology will be affordable for the target patient population or purchaser? Will genetic testing for relevant biomarkers lead to genetic discrimination for individuals who carry that trait?

- **Inclusiveness:** (How) have stakeholders (patients, citizens, regulators, payers/insurers and lay and professional caregivers) been involved in the development, regulation, funding and translation of personalised medicines? Has this been done in a manner that accounts for differential power structures (e.g. the difference in power between regulators or the pharmaceutical industry and patients with rare forms of cancer)?
  Responsiveness: Has the process of developing personalised medicines been attentive to political, social and economic barriers to implementation (e.g. slow regulatory and clinical uptake of targeted therapies)? How will contemporary biomedical publication practices, and the forces of (both academic and commercial) intellectual property protection affect the development of, and access to targeted therapies and their companion genetic diagnostic tools, and how can knowledge and benefit sharing be encouraged within these systems? When and how should targeted therapies be introduced into practice (including for uses that might run contrary to regulatory, funding or clinical guidelines)? Who should be responsible for monitoring them? How will the development or commercialization and implementation of personalised medicine be reconsidered in the context of new information about targeted therapies, and in the context of other emergent technologies?

A comprehensive bioethics of innovation would also need to acknowledge that biomedical innovation, and the challenges it aims to address, exist on a global scale, and that innovation is shaped by the secularization, individualization, pluralisation and fragmentation of Western societies. As Stahl observes, all of these forces lead simultaneously to 'the increased importance of research and innovation' and the 'decreasing ability to steer it using conventional science and innovation governance measures.'[37 p709]

A bioethics of innovation would therefore need to attend to the moral and socio-political dimensions of 'bigger picture' influences on health and biomedicine, including the effects of globalisation of biomedical research, where biomedical innovation is concurrently expected to cross national borders and also provide national health and economic benefits; changing relationships between academic, political and commercial stakeholders, where, for example, political forces increasingly encourage and foster academic research commercialization; changing global economic regimes, favouring industrialization and economization in health research; changing global and regional regulatory and legal environments, with an increased focus on knowledge ownership and trade-related intellectual property protection; increasing imperatives towards consumer engagement in health-related innovation; changing biomedical scientific paradigms (e.g. towards targeted therapies, genetic manipulations, and more broadly differing understandings of 'evidence' in the production of scientific knowledge)**;** and new information technologies and systems.[35, 60, 67-69]

Conclusion

We have argued that, while the drive towards innovation in biomedicine might be beneficial, it is also a domain that requires scrutiny and moral questioning, and needs to be accompanied by a systematic and sophisticated 'bioethics of innovation.' We have argued that this bioethics of innovation could draw upon frameworks of Responsible Innovation, as

well as a number of other relevant disciplines. While we have focused in this article on biomedical innovation, we see no reason that these ideas could not be applied to health-related innovation more generally, including public health and health services innovation. We hope that this will provide a starting point for a challenging and enriching new bioethical discourse.

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