Trust in Precision Medicine - A Risk Governance Perspective

This background paper is a working document. It sets the scene and serves as basis for discussion for the expert workshop on Trust and Precision Medicine – A Risk Governance Perspective, 23 – 24 November 2017, Campus Biotech, Geneva.

Introduction

This background document seeks to underline the salience of trust for precision medicine. In the previous workshop on ‘Governance of impacts of precision medicine’, organised by the International Risk Governance Center (IRGC), trust was identified as pertinent to the success of precision medicine; hence, the premise for this follow-up workshop.

Precision medicine refers to an emerging field for disease diagnostics, prevention and treatment that considers individual variability in genes, environment and lifestyle, with the aim of improving patients’ health and augmenting disease prevention (Florin & Escher, 2017). Moreover, it caters to both patients and healthcare professionals with respect to patient-centred care, customised patient-provider relationships and effective treatments (Adams & Petersen, 2016).

To a large extent, precision medicine is driven by three main concurrent trends: (i) the increasing availability of heterogeneous large-scale databases from which novel patient aggregates evolve, (ii) advances in the characterisation of medically relevant information, and (iii) novel computational tools for data analytics (Adams & Petersen, 2016; Collins & Varmus, 2015). Exponential growth in data volume is a key feature of precision medicine. Collectively, the accumulation of these data – from genomics, proteomics, metabolomics and mobile health (m-health) among others – work hand in hand with improvements in basic research to promote the concept of precision medicine (Collins & Varmus, 2015).

The promises of precision medicine stem from its ability to transform healthcare approaches to research and delivery for the benefit of human health. National programmes in Estonia (1999) and Finland (2006) for instance, have demonstrated the potential benefits of precision medicine (Estonian Genome Center, 2011; FIMM, 2017). In 2015, US President Obama launched the Precision Medicine Initiative (PMI). A predominant component of the PMI is the All of Us Research Program, which aims to advance precision medicine by combining molecular information with clinical and lifestyle data from a national research cohort of one million individuals (NIH, 2017). The change in the name of the program – from PMI Cohort Program to All of Us Research Program – is indicative of the need for inclusivity in precision medicine (NIH, 2017).

There is an increasing consensus that the notion of trust is paramount to derive maximum capabilities from precision medicine (Hurst, 2012). A 2016 expert workshop held by IRGC identified trust as crucial to participant engagement since it thrives on biomedical data collection and sharing (Florin & Escher, 2017). Similarly, Mirnezami et al. (2012) have highlighted that precision medicine “will deeply affect

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1 This background paper was written by Afua Adjekum, with contributions from Marcello Ienca, Marcel Bürkler, Marie-Valentine Florin and Effy Vayena. It reflects the view of its author and not of IRGC or any other organisations affiliated with this workshop. It was improved thanks to comments and suggestions from Isabella Beretta, Jacques Fellay, Samia Hurst and Adrien Lawrence. For any questions or comments, please contact Afua Adjekum (ETHZ, afua.adjekum@hest.ethz.ch) and Marcel Bürkler (EPFL IRGC, marcel.burkler@epfl.ch).

2 This workshop is organised by the EPFL International Risk Governance Center (IRGC), ETH Zurich, the Swiss Personalized Health Network (SPHN) and the Swiss State Secretariat for Education and Research (SERI). Support from SPHN and SERI is gratefully acknowledged. More information about IRGC is available on irgc.epfl.ch.
public trust and the nature of the patient–clinician relationship”, hence “it will require unprecedented collaboration among healthcare stakeholders.”

Although the salience of trust in precision medicine is a recurring subject, few studies have divulged the subject from a conceptual standpoint. Thus, this paper seeks to underscore the salience of trust in precision medicine and to provide conceptual clarity by developing at least a working definition and characterisation of the trust dynamics. This is followed by identifying three main types of facilitators (technical, ethical and institutional) necessary to building and maintaining trust about precision medicine. Afterwards, we deliberate on the dimensions of precision medicine that have carved out trust as a pertinent tool to its success. We conclude by making some preliminary (albeit non-exhaustive) recommendations on how best to enhance trust in precision medicine.

What is Trust?

Although trust is a familiar concept that cuts across a spectrum of disciplines, there is a lack of consensus on its definition. Besides agreeing that trust is relational (occurs between people and or entities) and context-specific, there is continual discourse among scholars on what constitutes trust (Gilson, 2003). Trust has been described as a three-place relation; whereby, ‘A’ (trustor) trusts ‘B’ (trustee) to fulfil ‘C’ (task) (Baier 1986). Overall, the concept of trust conveys the notion of risk and vulnerability on the part of a trustor.

Trust is often dichotomised into affective-based trust and cognitive-based trust. The former conveys the notion that trust stems from conventional norms of morality which are upheld by the goodwill of others; whereas the latter perceives trust as a calculation or rational behaviour that involves some form of risk analyses (Gilson, 2003). It is important to differentiate between trust and trustworthiness even though these two concepts are often used interchangeably. While trust is understood as an expectation of positive motives (Rousseau et al., 1998), trustworthiness is perceived as a characteristic that is projected onto an individual or group (Holm & Nystedt, 2010). O’Neill has famously brought attention to this important distinction arguing further that for trust to be established, trustworthiness needs to be demonstrated. In that respect, trust is a response to trustworthiness, and we should aim to put “trustworthiness before trust”. (O’Neill, 2015)

Some scholars suggest that trust is neither a choice nor a behaviour, but rather, a psychological state that is crucial to organisational life (Rousseau et al., 1998). Other scholars maintain that encapsulated interests, rational predictions of another’s behaviour as well as personality traits compel people to trust (Lang & Hallman, 2005). Nonetheless, reliance is at the core of trust even as it is assumed that a pure trust relationship exists when emotions such as gratitude, betrayal and resentment – ‘reactive attitudes’ – are expressed if expectations go unmet (Holton, 1994).

Trust is also at the helm of social cohesion even as it projects its existence – or lack thereof, – on all aspects of social interactions. Social norms are said to shape individuals’ beliefs and inherent in such beliefs is trust, which in turn cultivates cooperation and vice versa (Gilson, 2003). Within a trustworthy society, individuals balance into equilibrium both interpersonal trust (trust in individuals) and institutional trust (trust in the social system) (Gidman et al., 2012). However, although many scholars agree that these forms of trust rely on each other, they are yet to fully understand their underlying relationship (Gidman et al., 2012; Rousseau et al., 1998).

Societies with optimum levels of trust witness lower transaction costs, conflict aversion within organisations in addition to optimum cooperative behaviour (Rousseau et al., 1998). Within the health system, trust facilitates patient satisfaction, adherence to treatments, health provider continuity, patient disclosures and encourages access to health facilities (Gidman et al., 2012). It is important to
note that trust cannot just be produced or generated, but must consistently be accumulated and reinforced by performance or experience (IRGC, 2005). Furthermore, the presence of conflicts of interests raises specific challenges regarding the maintenance of both trust in and trustworthiness of physicians, which requires special attention (Hurst, 2017).

In instances where there is low generalised trust (individuals’ expectations of the trustworthiness of others) (OECD, 2017), mistrust and distrust are likely to thrive. Mistrust denotes ‘unhealthy cynicism’ resulting from a prior breach of trust while distrust, comprises of ‘healthy scepticism’ (Abelson et al., 2009). From this description, trust can be envisioned as a spectrum containing positive and negative peripheries: on the positive end sits ‘trust’, with ‘mistrust’ on the negative end. As McAllister argues “the amount of knowledge necessary for trust resides somewhere between total knowledge and total ignorance [...] Given total knowledge, there is no need to trust, and given total ignorance, there is no basis upon which to rationally trust”. McAllister (Mcallister 1995, pp. 26).

As much as precision medicine relies on disease patterns to recognise trends, researchers relish voluntary data contributed from healthy individuals. Integral to this paradigm is the belief or expectation that personal data will not be used against the owner of the data and there will be a derivative public good (Bourzac, 2016). A study conducted by researchers at the US National Institute of Health confirms this as individuals’ willingness to participate in the All of Us program involves some risk and benefit analysis (Kauffman et al., 2016).

Based on these evaluations, a working definition of trust in precision medicine could be the willingness of a trustor to accept the potential risks involved in the use of their sensitive health-related data resulting from both optimism about the trustees’ goodwill, interest in the public good, and capacity to limit these risks.

While a trustor can be both an individual and a multi-individual entity (e.g. a corporation, research group or other organisation), we are particularly concerned in this paper with the issue of trust from the perspective of the single individual towards the data initiatives for precision medicine. In fact, we consider the individual citizen to be the fundamental and atomic unit of trust. The reason for that stems from the fact that the individual citizen or natural person is the social actor to which fundamental human rights can be granted. Although beyond the scope of this paper, another reason may be due to trust acting as a psychological state influenced by a plethora of factors.

It is also important to point out that trust dynamics are often multi-layered and might follow chain reaction patterns. In fact, when sharing data with a certain trustee Y, a trustor X should not simply trust Y, but also all actors that Y might further share X’s data with. The longer the chain of trust, the harder it is for the individual to predict the risks and benefits of her voluntary data contribution as well as to assess the trustworthiness of all trustees involved. This problem is exacerbated by the fact that, in many circumstances, the individual citizen might have only partial (if any) knowledge about actors beyond the first trustee.

Figure 1: The complex data sharing relationship between a trustor and relevant trustees (either individuals or institutions). The arrows indicate the various trust relationships are occurring at different phases of the data-sharing process. The fading represents diminishing trustors’ knowledge about data-sharing mechanisms and actors.
Some Facilitators for Sustaining Trust

The drivers for building trust in precision medicine can be categorised into three: 1) technological innovation, 2) ethical and sociocultural values and 3) institutional practices & governance measures. In this section, we discuss these three drivers.

1) Technological innovation is a viable means of facilitating accountability relating to data sharing, quality and integrity. For example, the White House published a “Data Security Policy Principles and Framework (Security Framework)” that healthcare organisations are advised to follow to secure data in the All of Us program, recommending to be “careful not to poison the well-being of patient trust”. A typical example is blockchain technology, which refers to a digital ledger made up of linked peer-to-peer transaction blocks on which unalterable records are shared. The features of the blockchain make it potentially well-suited to address the disjointed nature of health-related records by eliminating the need to rely on third parties for their security (Krawiec et al., 2016). Consequently, the blockchain aims to improve the protection of privacy, security and to enable interoperability in health and medical data transactions (IRGC, 2017).

Differential privacy and homomorphic encryption are technological solutions that have been proposed to minimise the risks associated with the use of sensitive data. These approaches aim to uphold the analysis of databases containing confidential information by, among others, minimising the risks associated with the re-identification of anonymised data (Dwork & Roth, 2014). In ensuring a high standard of data anonymisation – by shrinking the risks associated with being re-identified with publicly available data for instance – individuals are more likely to participate in precision medicine initiatives.

It is crucial to recognise that technology alone cannot ensure that citizens and other stakeholders place their full trust in the advances that precision medicine has to offer. It can help build and sustain trust by reassuring participants of the privacy and security of their sensitive data as well as increasing the capacity to protect against impending risks. However, technology as a tool to help build and sustain trust in precision medicine would only attain optimum results if it accompanies sound medical analysis coupled with meaningful and equitable relationships with citizens.

2) Acknowledging the importance of ethical and socio-cultural values as facilitators to trust in precision medicine stems from experiences with trust in similar conditions. The relevance of transparency and public trust in novel biomedical research has been echoed ever since major strides were accomplished in recombinant DNA and beyond (Baltimore et al., 2015). Concerning precision medicine, it is essential to prioritise transparency – built on public engagement – that ranges from healthcare delivery, research and institutional management practices.

Preferred forms of consent, data sharing in addition to the motivations for participation must constantly be assessed to alleviate participant concerns (Kaufman et al., 2016). In prioritising the participant (truster), the researcher or health personnel (trustee) is better able to relay their proficiency to undertake the tasks assigned them and likely reinforce their goodwill. This matters as, for example, the information sheets and consent forms that are used during research projects have been shown to merely serve as ‘symbolic tokens’. Instead, participants’ ‘faith’ in the objective of the project and an assurance of minimal risks that is what motivates them to participate (Carter et al. 2015).

Public engagement strategies based on communication are another tool that is widely used to assess ethical and sociocultural values. Communication in public engagement strategies is understood as a two-way dialogue between relevant stakeholders and the public. Good practices in risk communication

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3 See for example [www.genomeprivacy.org](http://www.genomeprivacy.org)
help stakeholders make informed choices about matters of concern to them and hence create mutual trust (IRGC, 2005). The absence of dialogue-based communication regarding the roles and expectations of both a trustor and trustee results in misplaced trust.

Stakeholder engagement on a broad scale supports better decision-making (IRGC, 2017b). Involving all the entities to whom precision medicine matters will enable the identification and prioritisation of the motivations behind individuals’ values and interests. In a survey conducted by Kaufman et al. (2016) thirty percent of survey participants changed their willingness to participate after being informed of the potential risks and benefits of the PMI cohort study. This suggests the importance of consistent stakeholder engagement prior and during precision medicine initiatives.

3) Institutional practices and governance are involved in building social cohesion, making them critical trust facilitators. Gilson (2003) maintains that institutions (both public institutions and other social organisations including private ones) bolster the social order by ensuring interpersonal trust, which in turn strengthens generalised trust. Hence, management practices and decisions do not only matter to those said institutions but to society as a whole. Equity, fairness and a general sense of prioritising the public good at the institutional or governance levels all stand to foster trust in precision medicine and society as a whole.

Public institutions that aim to foster trust must communicate about their competence and values as they are perceived by the public. Competence is the capacity to undertake an intended task, while values foretell the intentions and ethics of the said institution (OECD, 2017). However, inasmuch as competence and values matter, it is crucial to bear in mind that individuals’ overall trust judgements regarding an organisation are equally influenced by transparency and openness, public interest (organisational aim to tackle bias) and honesty (truthful about risk) (Lang & Hallman, 2005).

Governance models include a variety of options such as incentives, frameworks, initiatives, guidelines, or public regulation (IRGC, 2012). Institutions that implement effective governance approaches are better equipped to achieve a common ground for measurable, transparent and comparable quality standards. In the case of precision medicine, the standardisation of precision medicine initiatives can contribute to building public trust. An example of governance relevant for precision medicine is the Committee of Ministers of the Council of Europe Recommendation CM/Rec (2016)6. The committee emphasises the importance of building trust. It contains specific guidelines for research on biological materials of human origin. It recommends that EU governments adapt their laws and practices to ensure the implementation of the guidelines and promote the establishment of codes of conduct to ensure compliance with the guidelines. The Committee aims to safeguard the fundamental rights of individuals from whom biological materials are obtained, stored and used (Council of Europe 2016).

Generic guidelines for medical research also prove useful to standardising institutional practices. In Switzerland, swisseehtics, a joint working group of Ethics Committees addresses ethical issues relating to research on humans, educates and trains members, as well as standardises and coordinates their actions (swisseehtics, 2017).

Schlesinger and Gray (2016) argue that trustworthiness is never guaranteed in healthcare due to the challenges involved with measuring trust within this setting, combined with the ubiquity of provider discretion. Yet, studies show that experts and organisations can favourably impact public perception, which in turn helps to advance efforts to build and maintain overall trust within society. As a result, efforts to build and sustain trust in precision medicine must recognise and acknowledge this paradigm moving forward.
How to Achieve Trust in Precision Medicine?

Precision medicine depends on the aggregation of a broad quantity and variety of individuals’ private data. Typical health data sources such as medical records, results of laboratory tests, genomics, immunisation records, are supplemented with, among others, data from self-tracking devices, loyalty cards, store transactions, wellness and social media (Vayena et al., 2017). For these heterogeneous data to be available (hence, for such data aggregation to be possible), researchers and clinicians need to rely on voluntary data contributions from individuals. Since familiarity is vital to building and maintaining trust, it will take some time to ensure public acquaintance with these novel health data sources and stakeholders. In addition, increasing breadth and variety of data sources will increasingly require collaborative efforts between several disciplines as well as novel stakeholders.

Furthermore, precision medicine relies heavily on sensitive personal data that may be made available to new and previously unfamiliar actors in healthcare. Reports indicate that health data is currently more valuable than credit card information, and cyber incidents at health organisations have increased from 20% in 2009 to 40% in 2013 (Reuters, 2014). This calls for an increased need to ensure optimum health data privacy and security. Strengthening regulation concerning negligence with health data might be a necessary to combat health data breaches. However, increasing regulations often tends to adversely affect institutional trust (Calnan & Rowe, 2007).

It is vital to consider these elements in the future to avoid repeating past and even novel mistakes. In 2012, under the Health and Social Care Act, the NHS proposed the care.data initiative. Despite meeting all of the legal prerequisites required to exploit medical records for research, care.data floundered (Sterckx & Cockbain, 2014; Carter et al., 2015). Its failure has been attributed to three main factors: (1) ambiguity of derivative public good, (2) faulty warrants of trust, and (3) uncertainties surrounding the duties of general practitioners. Indeed, it was not inadequate publicity that derailed care.data, but rather, an absence of faith and a lack of transparency compounded by ambivalence about the risks involved (Carter et al. 2015, pp. 3)\(^4\).

More recently the NHS England had another controversial collaboration with Google’s DeepMind. In this case, DeepMind received access to millions of identifiable patient data to develop applications that would support patients with kidney disease. An investigation of the data sharing agreement between DeepMind and the NHS by the UK’s National Data Guardian concluded that this arrangement took place on inappropriate legal basis (Revell, 2017; Powles & Hudson, 2017). (See Box 1 below)

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\(^4\) care.data has been relaunched in the form of NHS Digital: [https://digital.nhs.uk/](https://digital.nhs.uk/)
Box 1: The crucial role of engaging with stakeholders through transparency and communication – The NHS care.data initiative and DeepMind in the UK

NHS
In 2013, National Health Service (NHS) England launched care.data, a programme aimed to combine health and social care data, including patient records stored on machines of general practitioners or from hospitals. Its main goal was for researchers to use the anonymised patient data to assess the performance of NHS services and to develop new treatments. However, the initiative faced constant criticism over the sharing of medical information with commercial third parties without explicit patient consent as well as over data security and confidentiality concerns. When it was disbanded, over one million people had already opted out of the programme. This lack of trust and ultimately the failure of the programme were mainly blamed on unclear mechanisms of consent and criteria for accessing the collected health data, and the fact that communication with the public was not prioritised (Presser, 2015; Temperton, 2016).

DeepMind
In an effort to develop ‘Patient Safety Alerts for Acute Kidney Injury (AKI)’ clinicians from the Royal Free London NHS Foundation Trust solicited the help of Google DeepMind Technologies Limited (an artificial intelligence and machine learning company) in July 2015. By November 2015, sensitive and identifiable patient data had been transferred from the Royal Free to third-party data processing entities contracted by Google. DeepMind publicised this relationship in February 2016 claiming to act merely as a channel through which real time analysis and alert systems for AKI is provided through the app ‘Streams’. After an independent investigation by the New Scientist, both parties were compelled to elaborate on the uses of the data. However, to date, little is known about the overall uses of the data, the reasons why more data than required was transferred, the reasons for bypassing relevant data governing entities nor the failure to obtain patients’ consent. Consequently, tremendous doubts have been raised about the underlying motive for the programme (Powles & Hodson, 2017).

The two controversial cases above highlight problems that can easily emerge in the sensitive space of patient data. They also illustrate some specific aspects that can facilitate our consideration of how best to promote trust in the data-rich environment of precision medicine. Below is a preliminary list of suggestion:

First, we identify a need for the widespread implementation of technical facilitators of trust in precision medicine initiatives. These include, but are not restricted to, blockchain, differential privacy or homomorphic encryption technology. On the long term, the successful implementation of security & privacy-enhancing techniques might enhance existing security protocols and models regarding both format and structure and “add additional layers of security and trust” (Versel, 2017). In fact, these technologies potentially allow to disintermediate data from hosts, increase transparency and process integrity, increase the ability to withstand data leakage and malicious attacks, and ultimately empower trustors. Therefore, this is likely to have a positive effect not only on the management of healthcare data but also on their large-scale collection as well as on the social dissemination of scientific findings.

Concurrently, this technical transition should be coordinated with the responsible promotion of ethical and socio-cultural facilitators. Ethical values such as privacy, transparency and fairness are likely to be co-determinants of trust at both the individual and collective levels. They should be prioritised to maximise the benefits of precision medicine in an ethically and sustainable manner. Therefore, public engagement and awareness-raising activities should be incentivised to enable competent decision making within the precision medicine ecosystem, especially from the perspective of the trustor-trustee relationship. As the failure of the care.data initiative indicates, stakeholder
engagement should be sustained through an unambiguous anticipation of derivative public good, reliable warrants of trust, and a clear specification of the duties of health professionals.

Finally, calibrated institutional interventions and governance solutions should be advanced to enhance trust in precision medicine and orient research for the public good. A good example in this direction is represented by Switzerland, where, in recent years, several institutional initiatives have been proposed. The Swiss Personalized Health Network (SPHN) prioritises respect for persons, privacy, data fairness and accountability. It has put forward the ‘Ethical Framework for Responsible Data Processing in the Swiss Personalized Health Network’ (SPHN ELSI Advisory Group, 2017). Ideally, these networks of researchers should be established not only at the national level but also internationally. An initiative taking this international approach (albeit focusing on genomics) is the Global Alliance for Genomics and Health. Platforms may also facilitate dialogue and information sharing not only between researchers but also between the PM research and other societal actors. Finally, to promote and sustain trust in PM research, institutional review board (IRBs) and other deliberative assemblies should clearly define effective and reliable ethical review processes for PM research. Table 1 below summarises our analysis of trust facilitators and the subsequent points of consideration.

Table 1: Overview of Trust Facilitators in Precision Medicine

<table>
<thead>
<tr>
<th>Type of Trust Facilitator</th>
<th>Points of Consideration</th>
<th>Normative Suggestions</th>
<th>Examples</th>
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<tbody>
<tr>
<td>Technical</td>
<td>Value of sensitive data, Susceptibility to data breaches</td>
<td>Disintermediating data from hosts, Increasing transparency &amp; process integrity, Reducing vulnerability to data leakage and malicious attacks</td>
<td>Differential privacy, Blockchain, Encryption</td>
</tr>
<tr>
<td>Ethical/Socio-cultural</td>
<td>Unfamiliarity of the public with novel healthcare actors</td>
<td>Prioritising privacy, transparency and fairness, Promoting public engagement &amp; awareness, Unambiguously anticipating public good, Identifying reliable warrants of trust</td>
<td>Privacy protection, Accountability mechanisms, Transparency of process, Fair benefit sharing plans, Public engagement</td>
</tr>
<tr>
<td>Institutional</td>
<td>Data misuse, Benefit sharing</td>
<td>Establishing international networks of researchers, Creating trustworthy platforms for exchange between, Defining a clearer ethical process for precision medicine research</td>
<td>Standardised guidelines, Ethical review recommendations</td>
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</table>
Conclusion

Trust is essential in precision medicine. However, the characterisation of trust dynamics in this rapidly evolving field of medicine is often affected by uncertainty and conceptual variability. In this paper, we provide a definition of trust and a detailed characterisation of trustor-trustee dynamics in precision medicine. We highlight that trust is necessary for facilitating participants’ involvement in precision medicine initiatives. It is a catalyst for socially responsible scientific advancement and practical implementation in this field. Technical solutions, ethical and sociocultural values, as well as effective governance measures, are all identified as facilitators of trust in precision medicine. Based on this analysis and learning from previous precision medicine initiatives, we see a need to formulate a minimal set of recommendations aimed at mitigating the risks associated with the sharing of sensitive data, increasing transparency, empowering trustors and augmenting public trust in precision medicine.

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