THE UNIVERSITY of EDINBURGH
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The challenges of uncertainty in health research

How can regulatory systems remain fit for purpose?

Policy brief

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Overview

This policy brief discusses challenges raised by the uncertainty that threads throughout health research regulatory systems. It offers a series of recommendations that aim to strengthen systems' ability to respond to, and learn from, such uncertainty.

This brief draws on research by the Liminal Spaces Project at Edinburgh Law School, a five-year Wellcome-funded project which examined health research regulatory systems and how their operation could be improved.

What we mean by 'uncertainty'

We suggest uncertainty applies to health research regulatory systems in two respects.

Uncertainty across the health research environment

Health research is carried out to address situations where health practitioners do not know what the best course of action is for a particular healthcare scenario. That is, they are uncertain about what treatment or intervention is the best or whether a new treatment or intervention is safe and effective. Uncertainty therefore both threads throughout the health research environment, and also gives purpose to research.

Uncertainty about what regulations require

In addition to characterising the entire health research environment, there may also be uncertainties about how to interpret health research regulations. In particular, there could be uncertainties about:

- What regulations apply to a particular piece of research – particularly when research involves a question that could be governed by different regulatory regimes.
- How to balance regulatory requirements that might jar against each other – for example, sharing information openly, and keeping participants' information confidential.
- Applying existing regulations to new areas of biomedical research.

Why it is important to think about the role of uncertainty in health research

Because uncertainty cuts across the health research environment and the regulations that govern that environment, **uncertainty is therefore a challenge that regulatory systems must tackle head-on** as its place in health research will not waver.

But instead of looking on such uncertainty as a problem, we suggest that **uncertainty should be seen as vital to the practice of research**. This is because uncertainty **encourages health research regulatory systems to constantly learn and evolve**.

As we note below, however, casting a positive light on uncertainty can only be achieved if health research regulatory systems embrace opportunities to learn from uncertainties through increasing their flexibility.

How can health research regulatory systems respond to uncertainty?

Supporting a learning regulatory system

We have argued elsewhere that to turn uncertainty into a learning opportunity for regulatory systems, the conditions in which those systems operate need to:

- Have **values at their heart**, specifically ethical values that matter to everyone working across, and affected by, health research.
- Be **trustworthy** to those who rely on them, including researchers and the public.[i]
- **Promote openness** between people and organisations working across health research, so that uncertainties and lessons for dealing with these can be shared and **a whole system approach** supported.[ii]
- **Push back against a culture of caution and promote a culture of confidence** so that researchers do not fear punishment and can be more confident when dealing with uncertainties.
- Be able to **respond to unexpected events**, particularly those that are high-risk and could affect many people (for example, the COVID-19 pandemic), while remaining true to the values at its heart.

For learning regulatory systems to be achieved, these conditions need to be supported by **actions or mechanisms** including:

- **High quality evidence-gathering** to assess the impact and performance of regulation and learn what goes well or less well for the systems that support this regulation.
- **Programmes to gather and include researchers' and public views** on how regulation is designed, and whether it should be reformed.
- **Appropriate incentives** such as recognition or reward for researchers who contribute to a whole system approach to learning.
- **Structures that allow for 'feedback loops'** – that is, a continuous cycle of learning from uncertainties that affect research. This could include researchers and institutions **looking back** to assess if previous regulatory practices were practical and ethical, and share those assessments with regulators to inform future guidelines.
- **An interconnected system** to support lessons to be learnt across areas of research regulated separately.

Recommendation: We recommend that each of these actions should be considered by all research regulatory systems that aspire to learning lessons from the uncertainties that occur throughout research. While there are doubtless examples of some of these elements in many regulatory systems internationally, the identification, publishing, and sharing of good and bad lessons learned does not yet occur on a level that optimises learning for all.

Increasing flexibility

Regulatory systems can also respond positively to the uncertainty that cuts through health research through **practising greater flexibility in their approach to research governance**. In addition to more accurately reflecting the uncertainties of research, a more flexible approach could also help researchers who sometimes find regulation difficult to navigate. **Achieving increased regulatory flexibility would therefore require regulators to work with researchers to discuss their experiences**. Although there have been actions taken to make regulation more adaptive to some new types of research – the MHRA Innovation Office, for example, which offers a 'one stop shop' for regulatory advice for researchers or developers working on innovative medicines or medical devices – **regulatory systems are less good at capturing researchers' experiences** to show how complexity can be better navigated and uncertainty better managed.

Recommendation: Health research regulators should work together, and with researchers, to explore and make explicit how more flexible research governance systems can be developed. Where this is already happening, examples of good practice should be routinely published and offered as learning experiences for researchers and regulators alike.

Increased flexibility for health research regulation was an aspiration for UK regulators and researchers who participated in a study we carried out to capture experiences of health research regulation. Participants suggested that **research regulation should be the subject of greater collaboration** so that the breadth of challenges that can affect research could be better captured and the realities of uncertainties that affect research embraced. Simply, if people who work across research share experiences of challenges and work through how to respond to them together, **research systems can aspire to improved coherence and flexibility**.

To enable a more flexible approach to regulation, we suggest that two forms of support are needed: (1) a focus on principles as action-guiding measures; and (2) the increased use of regulatory stewardship.[iii]

Principles as support for flexibility and responsiveness

One option for increasing flexibility in health research regulation is to **consider moving more towards principle-based systems**. For a system that regulates the uncertain activity that is health research, looking to principles as a way of negotiating and navigating what ethical conduct 'looks like' for a particular study might be a better fit than a predominantly rules-based system. This might be especially helpful during crises that test the established structures of health research systems, such as the COVID-19 pandemic.

A note on principles and rules

Principles are often related to, but different from, rules. Principles inform and guide practice without telling people exactly what to do and can therefore offer more flexibility than rules. This flexibility is a quality which we think health research regulation should adopt more strongly than

at present. Principles invite reflection, discussion and sometimes negotiation on how best to proceed.

While rules have unquestionable value in many situations, they can sometimes encourage a 'tick box' mentality that limits regulatory systems' consideration of core ethical values. This can support a cautious interpretation of regulation which could lead to research being stifled.

There are already many examples of principles-based frameworks in health research, such as the UK's Policy Framework for Health and Social Care Research. However, there is a risk that such frameworks come to be treated more as a rules-based system rather than a principles-based approach. Principles do not hold up if they are interpreted in a rule-like manner. This can often happen in practice. To avoid this, principles-based approaches require regular review and engagement.

Recommendation: Regulators, researchers, and other stakeholders should be given opportunities to engage on a regular basis to keep guiding principles of health research regulation under review. Reviews should aim:

- To help ensure that the right principles are in operation for new and emerging research;
- To reassess the relative weight of certain principles at certain times, especially during crisis and change; and
- To reflect on situations where principles support desirable flexibility, while also being aware that a rules-based approach might sometimes be required.

The **objective** should be the genuine co-production of regulatory arrangements between those who regulate and those who are regulated. This is supported by participants in our research who suggested that this is an optimal way to improve responsiveness and trustworthiness in health research regulation.

Some may suggest, however, that principles require too much interpretation and can therefore be at risk of being interpreted with bias to promote people's self-interest in a particular aspect of health research. However, involving different groups in the process of interpreting principles, and being open about these interpretive activities, can help to insure against this concern and support the further use of principles as a tool through which uncertainties can be addressed.

Regulatory stewardship as support for flexibility

In addition to considering how principles might support more flexible and responsive regulatory systems, a further concept – regulatory stewardship[iv] – may also offer an opportunity to support decision-makers in dealing with uncertainty.

Regulatory stewardship describes a research system where assistance and support are exchanged between researchers and others who might be more familiar with regulatory requirements. Instead of calling on rules to uphold research integrity, regulators could instead rely more on a network of regulatory stewards. The stewards' role is twofold: first, they can guide researchers through the

regulatory maze to support researchers seeking to demonstrate that their research is ethical and compliant with multiple requirements; and second, they can help researchers cope with the burden of regulation, including reducing that burden by knowing how the system works.

Recommendation: Further support should be offered to researchers who face uncertainties in navigating regulatory requirements through the role of regulatory stewards. To support regulatory stewards, due recognition should be given to this role and its value in navigating uncertainty and complexity in regulation. Where regulatory stewardship is already happening, more work should be done to publish the benefits of this role and demonstrate how it operates in practice.

Increasing regulatory stewardship would, we suggest, support the emergence of more efficient, collegiate research systems in the future, where regulatory requirements will weigh less heavily on those who must fulfil them. It would also **represent systems which see regulation as a partnership between those who regulate and those who seek to conduct research**. Our research has shown considerable appetite for this approach. This, in turn, can help to promote trust in the systems as a whole, both for researchers and citizens.[v]

Regulatory stewardship may be especially helpful where there are **blurred boundaries across activities such as innovation, treatment, and research**. This is because while there can often be overlap between activities in practice, these fields are often regulated in distinct and disconnected ways. For example, 'treatment' is often seen as a clinical matter affecting individual patients. In contrast, research can be seen as affecting large groups of participants. In practice, the reality is that these divisions often collapse. We have argued that fresh thought needs to be given to how each of these concepts is understood and how they relate to each other to promote a more joined-up research system. This might be achieved through greater collaboration across these systems, especially in the identification and exchange of (good and bad) lessons learned.

Recommendation: Regulators and funders should take the lead in promoting active collaboration between researchers and practitioners working across innovation, treatment, and research. In particular, this should involve the identification and exchange of good and bad lessons learned.

Opening a more defined role for regulatory stewards also humanises the research endeavour and could put people, rather than rules, at the heart of regulatory systems.[vi]

Conclusion

Uncertainties are a key characteristic of all health research. They are therefore here to stay and are a challenge that health research regulatory systems must meet head on. But this challenge also offers opportunities for systems. These opportunities are twofold: to support systems that learn from uncertainties; and to usher in regulatory systems that embrace those uncertainties through a more flexible approach to regulation that helps to ensure that it remains fit for purpose now and in the future.

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Read more about Liminal Spaces' work on responsiveness:

- Co-production and managing uncertainty in health research regulation: a Delphi study
- Delivering proportionate governance in the era of eHealth
- Regulating for uncertainty: bridging blurred boundaries in medical innovation, research and treatment
- Research during global health emergencies: on the essential role of best Practice
- Reimagining regulatory approaches: on the essential role of principles in health research regulation
- Towards principles-based approaches to governance of health-related research using personal data
- The Cambridge handbook of health research regulation (chapter on rules, principles and best practice; and afterword)

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[i] Liminal Spaces (2021) How can health research regulatory systems strengthen their trustworthiness?
[ii] Liminal Spaces (2021) End of project vision statement: driving a whole system approach to health research regulation.
[iii] Liminal Spaces (2021) Regulatory stewardship: concept note.
[iv] See note iii.
[v] See note i.
[vi] See note ii.