1. **Introduction**

Tsachi Keren-Paz introduces the seminar series which aims to fill the gaps of knowledge for the following questions:

- **Empirical questions**: what is the extent of defensive medicine, specifically, its effect on innovation? Is this a real problem and, if so, in what areas of medicine?
- **Methodological questions**: how can innovation be defined and measured? How can the effects of changes in legal rules be measured as well as the effects of disciplinary proceedings and tort liability?
- **Normative questions**: how to balance the interests of patients, clinicians and society? How best to encourage responsible innovation?

The main themes of the series were: the extent to which the combined effect of tort liability and disciplinary proceedings create defensive medicine and, in particular, negatively affect innovation; the relative contribution of changes in the tests that govern the determination of negligence on levels of defensive medicine and innovation, including the likely effect of the Access to Medical Treatments (Innovation) Act 2016; whether law reform is warranted in order to encourage responsible innovation while at the same time protecting patients' safety; and the relationship between research and innovative treatments, the justification for the different regulatory frameworks applicable to both contexts, and whether the regulation of research unduly stifles innovation.

Tsachi Keren-Paz then detailed the topics of the previous seminars and the conclusions drawn from them:

- Seminar 1 addressed the broad question of whether tort liability caused defensive medicine and the relationship between defensive medicine and innovation. A theme that arose was that tort liability did not drive defensive medicine.
- Seminar 2 aimed to examine conflicting findings of whether liability stifled innovation and discussed methodological limitations of such findings. One conclusion was that while anti-innovation bias may have existed in the US, there was no evidence, in the UK, that negligence law stifled innovation.
- Seminar 3 examined the Access to Medical Treatments (Innovation) Bill. The stakeholders’ consensus was that there was no evidence that the current system stifled innovation.
- Seminar 4 dealt with the effect of disciplinary proceedings on innovation. Generally, clinicians were warier of disciplinary proceedings than malpractice claims yet most of the research focused on the latter.
- Seminar 5 explored strict liability and the deviation from using the patients’ best interests as the sole guidance for determining standard of care and damages in the context of innovative treatments. Seminar 5 questioned the perceived wisdoms that the Medical Innovation Bill solution was based on: fault-based liability, full compensation and giving the most importance to the patients’ best interests. The case for strict liability for injuring those receiving innovative treatments was presented and examined. Then, the idea that physicians’ liability should be reduced where there are benefits to third parties was discussed. There was a strong consensus against reducing damages due to benefits to other parties but there was fair amount of support for the proposition of strict liability, or a no fault scheme to patients injured from innovative treatments.
- Seminar 6 will examine the relationship between the regulation of research and innovative treatments and its effect on innovation. The distinction between innovative treatments and research will be discussed as well as the relative threat of tort law on innovation and research. Lastly, whether the level of compensation to research subjects stifles innovation will be addressed.

2. Panel: Regulating Research and Innovative Treatments

Chair: Dr Michael Fay (Lecturer in Law at Keele University)
Speaker: Dr Nayha Sethi (Mason Institute, University of Edinburgh)
Title: Regulating for Uncertainty: Embracing the Fuzziness of Blurred Boundaries in Research and Innovation

Nayha Sethi introduced liminality, an anthropological term, used to describe transformation from one status to another e.g. transition from childhood to adulthood. Graeme Laurie, the Principal Investigator on the Liminal Spaces Project, was concerned by the failure within regulatory approaches to account for human experiences. Some overarching questions for the project include:
- What insights are revealed when compartmentalisation is dissolved and regulatory space is re-conceived as a unitary entity?
- What policy and practice implications flow across areas of health research when we better understand the liminal spaces of regulation?
- What benefits for health research of re-framing regulation and risk as ethical and co-produced practice, rather than instrumental, techno-rational compliance?

Victor Turner identified three phases of the liminal process:
- Pre-liminal phase: an individual is removed from their current status in society and experiences a separation from previous practices and routines
- Liminal phase: individual is subject to certain rites or rituals e.g. conducted under the authority of the Master of Ceremonies
- Post-liminal phase: the individual emerges with a different status having undergone a transformation and is reincorporated into society

With respect to health care research, Nayha mentioned that transformations can apply to objects and processes too.

Then, details of her Fellowship entitled ‘Regulating for Uncertainty’ are presented. The two main research questions being addressed are:
- What values, attitudes and behaviours inform research in spaces where the law is silent and professional discretion is considerable?
- How can empty regulatory spaces be populated in ways that strike an optimal balance between protection and promotion of interests, private and public?

Sethi then went on to argue that treatment should also be considered when discussing research and innovation because a procedure in one context could be seen as a treatment but, in a different context, it could be seen as innovation. The importance of consistency is emphasised when using the terms ‘research’, ‘innovation’ and ‘treatment’; this would aid efficient regulation.

From her preliminary research, Sethi believed that liminality can help capture the processes involved when thinking about transformations in health care regulation as well as human experiences. Additionally, moving away from compartmentalisation to a more fluid approach where thresholds and margins are given less importance would be beneficial.

Fuzziness (or uncertainty) in the interpretation of the law exists whether a rigid or flexible approach is adopted. Sethi’s doctoral work looked at the way in which rules and principles are used in order to support decision makers. There is an intermediary space which can be termed ‘best practice’ which accounts for real world human experiences but they are not completely rigid. How ‘best practice’ can be identified is something that is driving Sethi’s contribution. Within the context of data capture, the concept that not all experiences can be reduced to data is emphasised. It is likely that the anecdotal evidence is limited, however, reducing it to a number could omit something worth investigating.

Discussion

Alicia El Haj asked for examples where liminality has been applied and there has been change as result. Nayha Sethi explained that the conceptual mapping of the project has been completed and, currently, the findings are being consolidated. Then, case studies and certain areas will be identified to implement the change. The value of the concept can already be considered through the team’s research on liminality, social value and regulatory stewardship. Jonathan Montgomery said that there is good evidence of the project being useful in some areas e.g. the changing status of tissue during the donation process. Roger Brownsword felt that liminality is a disruptive idea that forces us to rethink things that would otherwise be taken for granted in the field e.g. the distinction between treatment and research. He went on to say that the problematic liminal spaces of healthcare arise from disruptive innovation and technology and we should consider how these are to be dealt with.

Jonathan Montgomery then picked up on the labels that are used and the discrepancies between the legal and healthcare system. An American example is where the terms
‘compassionate use’ and ‘right to try’ appear to be about the interests of people who are ill but in actuality are driven by commercial interests. He also believed it is important to discuss the precision of the terminology used. Nayha Sethi agrees and said that students tend to feel that ‘innovation’ is more positive than ‘experimentation’. On the point of inconsistent terminology, Michael Fay asked whether the discrepancies would lead to pushing people away from innovative treatments or whether it undermines a patient’s consent. Nayha Sethi responded by saying that the ‘fuzziness’ in terminology can affect coherence. With respect to consent, it may be more honest to explain to a patient that there are varying degrees of certainty with different treatments.

Jonathan Montgomery brought up the comparison to the rite of passage for a boy entering manhood conducted by a Master of Ceremonies. He said that this may be important in considering what roles supervising authorities and courts have. The liminal transition could apply to patients becoming research participants or the other way around. Nayha Sethi said that it was the role of the Master of Ceremonies to usher the individual or object through a process e.g. this could involve communicating knowns or unknowns to the individual. Alternatively, tricksters may be present in the process; these are individuals or objects who appear to be facilitative but actually inhibit the transition. This may be a false threshold, a false experience, a discrepancy in terminology or the difference between expectations and reality.

Marie-Andrée Jacob raised the hierarchal nature of the Master of Ceremonies metaphor as well as the issues of deception (e.g. by tricksters) when it comes to the translation part of the project. Nayha Sethi and her colleagues acknowledged that there were limitations to the methodology but when borrowing terminology, one can never fully evade the risks of deception within translation. She also felt that the benefits outweigh the risks and limitations of over translating. Dominic Wilkinson observed that an overlap between the anthropological transition and the health care transition could be likened to the transition in the legal status of children i.e. this status will change as they get older as well as their treatment choices.

Speaker: Dr Sarah Devaney (University of Manchester)
Title: Regulating the Innovators: Reputation, Reputation, Reputation

Sarah Devaney introduced her presentation as an insight into why regulators might use reputation as a mechanism to influence their regulatees. Then, the case study of the first three parent baby was presented; a patient approached a medical team seeking help with giving birth to a healthy child as her first two children had passed away from a mitochondrial disease. The implantation took place in Mexico where there were ‘no rules’. So, the following question was posed: ‘what does this scenario mean for regulators and would it help if we used reputation as a regulatory tool?’

Possible concerns about the above case study involved its categorisation as an experiment or treatment, unknown long-term effects (e.g. genetic drift) and the failure to adhere to scientific and research norms. For this case, the patient did not wish to have continued intervention and follow-ups. As a result, the long-term success of the procedure could not be determined.
Devaney said that the priorities of the regulatees need to be taken into account otherwise, it will be challenging for regulators to deploy mechanisms that are targeted and effective. Bioscientists say they want to develop high quality research that benefits society and they want recognition. If recognition is important to scientists, then this could be used in a mechanism to encourage compliance e.g. funding may be vital when considering reputation as an influencing mechanism. However, this may not work in all areas of healthcare e.g. it is unlikely to work for doctors in the NHS. Due to the competitive, collaborative and complicated nature of the field, effective regulation is challenging.

Trying to be compliant with strict regulation may result in the stifling of innovation. Some scientists are aware of a pressure to compromise on research integrity in order to publish. Their response to challenges in regulation may be to innovate e.g. doing a procedure and then asking the regulator whether it is allowed or, where there is no regulation, coming up with their own codes of practice.

In summary, the sector is highly pressurised and incentivised. There are also significant temptations to breach regulatory provisions and breach sector norms (i.e. innovate) to achieve their aims. So, regulators need to consider whether they can use threats (to damage reputation) or promises (to enhance it) as a way of encouraging scientists to comply with provisions. Constituent elements of reputation could include three parts: cognitive, affective and behavioural. The cognitive element looks at the measurable aspects e.g. technical competency. The affective element looks at the ‘softer’ aspects e.g. honesty and integrity. The last element is about how people respond to the cognitive and affective aspects. The behavioural part is particularly interesting because it is not dependant on the regulatee (of which the regulator has oversight) but of the wider population; this makes it difficult for regulators because they do not necessarily know how the public will respond to a certain individual.

Discussion

Tsachi Keren-Paz said it was counterintuitive that the reputational incentives will not work for those in the NHS because they care more about their own reputation than about damages which are not paid from their own pockets. Sarah Devaney agreed. She believed the reason for this was financial; reputation is important to get paid work where privately funded relationships are involved e.g. lawyer or private doctor. NHS employees, do not have to maintain their reputation in the same way to get work and funding. Even though they are aware of reputation, the focus is on the institution’s rather than the individual's.

Jonathan Montgomery, who had chaired the Human Genetics Commission from 2009 to 2012, said that Alison Murdoch invited the Commission to consider whether there were any fundamental ethical issues with Mitochondrial Replacement Therapy. She said that she would not apply for a grant to do the laboratory work if it was not ethically accepted. This is an example of a good faith relationship between the scientist and the regulator. Additionally, regulatory capture is an issue. Montgomery went on to say that the UK legal structure (under the Human Fertilisation and Embryology (Mitochondrial Donation) Regulations 2015) provides for case-by-case decisions to be made and any licence for treatment is limited to a ‘named’ woman (reg 8). This limitation is not possible in the USA due to the limited regulatory remit, so that the judgment had to be made about the technique more generally.
Sarah Devaney felt that creating a dialogue is important because it builds hope to find solutions.

Marie-Andrée Jacob mentioned Sarah Franklin’s paper which uses archives of the Medical Research Council to examine the exchange during the 1970s between scientist Patrick Steptoe and his team and the Medical Research Council (MRC) for their research project on human reproduction and IVF that led to the birth of Louise Brown in 1978. The paper, entitled ‘Why the Medical Research Council refused Robert Edwards and Patrick Steptoe support for research on human conception in 1971’, shows that experiments do not emerge out of a vacuum after which regulators are informed. Rather, the MRC was informed all the way with respect to the research plans, their alternative forms of funding, and policy implications. She argued more generally that the applications for funding can also be a site of reflection because it debunks the idea that law and regulation and policy reflections are always emerging post facto and ‘lagging behind’ scientific developments. Sarah Devaney responded by saying that the Dolly the Sheep experiment was unknown to the legal system until after it had been completed. She went on to say that there might be opportunities for regulators to enhance their relationship with funders e.g. informing them of expected behaviours and norms.

Then, Marie-Andrée Jacob asked how disciplinary proceedings come into the equation of reputation and whether Devaney’s work could be applied to other sectors such as financial. Jonathan Montgomery said that reputation crosses over to commercial sectors. He gave the example of a Kitemark system which would give complying organisations a competitive advantage. Sarah Devaney said that the conceptualisation involved looking across a variety of sectors to draw out ‘meta-lessons’ about reputation before they are applied to a specific area. Reputation applies across most fields e.g. in the finance sector, one may have a reputation to be a risk-taker which is contradictory to what regulators want. However, these lessons will have to be sector specific later on.

Emma Cave questioned whether the same lessons regarding reputation can apply to both an individual and an institution. She went on to say that the reputation of an individual may be more newsworthy than that of an institution. So, there may be a risk of unfairness if the emphasis is put too much on a single person when there is shared blame. Sarah Devaney felt that this is an important point, especially when blame is attached to a single person working in a team.

Leonid Schneider said that in the case of the three-parent baby, an ethical question of whether it was fair to the baby to conduct this experiment arises. Though the parents did not allow a follow-up, the baby could have fallen ill and died suddenly. It may be the case that a couple in a similar situation ask for the same solution. Sarah Devaney replied that advertising and marketing of this procedure has been taken down after written requests by the FDA.
Alicia El Haj introduced the case study of Paolo Macchiarini, a surgeon who was originally considered an extreme pioneer in regenerative medicine because he took the bold decision of using tissue engineering approaches to replace tracheas. However, the innovative step he took was to use stem cells deriving from bone marrow, which have been transplanted before, in the new context of replacing tracheas. Macchiarini used ‘compassionate measures’ cases as a vehicle to test out new approaches. Compassionate measures are used when a patient is very near death e.g. due to breathing difficulties and a doctor may use an innovative technique to try and save them. Macchiarini carried out the treatments in the UK, US, Sweden, Russia and Italy. He is currently under investigation on suspicion of manslaughter.

The first question to panellists was ‘what is the division of responsibility between the scientist and the clinician in the event that something goes wrong?’ Roger Brownsword believed that the regulatory challenges boil down to three desiderata: support and encouragement for beneficial innovation; compensatory or precautionary measure in place to minimise risk; and fundamental values are protected e.g. human rights, equality and autonomy. He then went on to detail the case of Oliver Brüstle who was a pioneering stem cell researcher in Bonn. His work was lawful in his jurisdiction, despite Germany having one of the most restrictive laws relating to human embryos in research. The issue that presented itself to the German courts was whether the research carried out by Brüstle was patentable or if it fell foul of the moral exclusion in the 1998 ‘Biotech Directive’. The European Courts of Justice controversially decided that although Brüstle had not, himself, been involved in the destruction of human embryos, his base materials were embryo derivatives which were subsequently destroyed. Additionally, his work was not patentable. One might argue that this is shocking because beneficial innovation is being stifled i.e. Brüstle’s funding may now be difficult to obtain. Brownsword believed that there are trade-offs to be made by the regulators between the three desiderata. We need to ask ourselves how far we are prepared to compromise values and safety for potentially beneficial innovation to prosper. We also need to consider the whole picture in terms of how well beneficial innovation is being supported, how well we are doing in setting acceptable risk levels and how well fundamental values are being protected. However, there are internal tensions within the three elements which are problematic.

Sarah Devaney said that the answer to the question depends on the type of responsibility e.g. moral, legal or professional. Leonid Schneider said that in the case of Macchiarini it is difficult to decide how the responsibility is divided when considering his role as the researcher and doctor. Schneider went on to mention further examples such as Charles Vacanti who made a trachea to be transplanted but the surgeon involved decided against it. Additionally, Suchitra Sumitran-Holgersson and Michael Olausson, who were found guilty of misconduct after using similar techniques to Macchiarini, caused injury or death in some patients. Currently, Sumitran-Holgersson’s data manipulation is investigated. Schneider said
that the responsibility falls on clinicians; the biologist can come up with anything but it is the clinician who is responsible for applying it to the patient. The last case discussed was of Heike Walles who made trachea patches with pig intestines. These cases show the separation between a scientist and the clinician but in some instances, they are so intricately linked that they cannot be distinguished.

Tsachi Keren-Paz said that the starting point was that a clinician is responsible unless they were misled by the scientist and it was reasonable for them to be misled. The responsibility of the scientist, however, is less clear. The American doctrine of learned intermediaries is helpful because the consumer of the medicinal product is the physician and not the patient. Therefore, if the science is flawed they should know about it and not implement it. Investigations about Macchiarini showed that there were problems of concept and materials which may lead to issues relating to causation. Problems of concept will give rise to clinician liability. For problems with materials, presumably the clinician should be aware of this and can take an active role to ensure that the quality of manufacturing is high. Keren-Paz was also doubtful as to whether a duty of care can be owed by a scientist to a patient.

Sarah Devaney said that the institutions that Macchiarini worked for are now engaged in holding a person to account which leads to a lack of opportunity to explore why the situation reached the stage that it did and why co-professionals did not ask the difficult questions. It would be challenging to implement a legal mechanism that addresses the ‘holding to account’ issue. Tsachi Keren-Paz said the summary of the Karolinska Hospital inquiry mentioned that part of the problem was the process of consultation. This issue also came up in Jose Miola’s presentation about the Lord Saatchi Bill whereby a mechanism of a non-rigorous pre-ruling was mentioned. Jonathan Montgomery said that one of the learning points of the Macchiarini case is to look at how many things went wrong e.g. faulty procedures, isolated units carrying out research and the transnational element. Roger Brownsword questioned the effectiveness of current regulatory regimes. He said that effectiveness should be examined within the regulatory domain, regulatees and some third party interference. The Macchiarini case should be looked at in light of these.

Marie-Andrée Jacob asked if there were any publications, by the scientist, that Macchiarini could have relied on. Leonid Schneider said that there were no previous publications or animal experiments. Tsachi Keren-Paz identified that after the first operation, some research was published by Macchiarini’s team. Leonid Schneider went on to say that this case study is not the only one; Heike and Thorsten Walles did not carry out a single mouse experiment between 2003 and 2009 which was when they were operating on patients. Alicia El Haj said that animal experiments are not always reliable and that physicians do not always believe the results. This may be why there is a lack of animal data. She also felt that circumventing by way of using ‘compassionate measures’ is the real issue. One of the overarching debates of the series was whether the progress of innovation was being restricted i.e. if an effective process for step-change development is not in place then it will lead to people trying to find a way around it.

Sarah Devaney said that she has not seen whether the compassionate measures in Macchiarini’s case has been used on a ‘no alternative’ or ‘no time’ basis. Leonid Schneider replied that both types were present in this case; Macchiarini presented his patients as having no time or alternatives when the reality was the opposite. Jonathan Montgomery
said that this was not true of all of the cases. Sarah Devaney mentioned that there should be a responsibility to follow up in compassionate measure cases before it is used on a second similar case. Leonid Schneider said that compassionate use is decided by the hospital that will carry out the procedure. He brought up Macchiarini’s second operated patient in Barcelona. The hospital that he intended to operate at did not sign the ethics form so, he stole the trachea and went to a different hospital to perform the surgery.

Jonathan Montgomery pointed out that ‘compassionate use’ is not a European term and it sits within a proper regulatory framework. In the FDA process, a certain degree of permission is required. He was particularly concerned with the arbitrary distinctions within the regulatory system. There are more hoops to go through if you are using an investigative medicinal product (clinical trials) than if you are to go through a medical devices route. So, is the artificial trachea a device? Devices, in comparison to drugs, will be expected to adapt when new information, about the body and its processes, comes to light. Montgomery believes that the Last Resort Principle is important. He went on to talk about a Private Eye story of a surgeon who was carrying out an innovative process for 15 years. It was only when he was challenged by Private Eye that the results were audited and it was shown that the surgeon had not in fact caused more harm than good. Alicia El Haj mentioned that, in the hospital she works in, a survey was sent out asking staff if they were carrying out innovative treatments and the responses came back negative. Nayha Sethi asked whether a definition was provided e.g. what counted as innovation. A study in Australia showed that there was not a common understanding of what innovation meant amongst surgeons. Alicia El Haj responded by saying that a definition was provided and here, the question is not about comprehension but about surgeons presenting what they want to present.

The next questions to panellists were ‘what should the dividing line be between clinicians in experimental research treatments and clinicians in innovative treatments? And, what does Macchiarini’s case tell us about this dividing line?’ Leonid Schneider mentioned that Macchiarini prepared the trachea for his first patient in a veterinary lab. When it came to the second patient, he decided he did not need a bioreactor. The use of bioreactors is subject to numerous laws which are problematic in themselves but he was able to circumvent this with the thought that the human body is the best bioreactor.

Marie-Andrée Jacob considered what would happen if, to describe the process that took place, we replace the term ‘innovation’ with language such as complementary medicine or alternative medicine. If the procedures were so out of line with good practice, why were they able to stay attached to legitimate science and not be casted as ‘alternative' work? Precisely because it was considered legitimate science and not marginalised in this way, it might have benefitted from indulgence for too long. Leonid Schneider disagreed because he felt that what Macchiarini did was not medicine at all and should not be labelled as such. Alicia El Haj said that the procedures carried out were minimally non-invasive which meant that ethical approval was not required. Roger Brownsword asked whether creating a regulatory framework which targets practitioners such as Macchiarini would be too expensive. Jonathan Montgomery argued that there were elements of the case which should and could have been picked up. He went on to talk about transparency; the more transparent the organisations carrying out the clinical trials are, the more easily they can be held accountable, and the more likely that they will therefore take care over their activities. Moreover, an institution is more likely to carry out checks before employing a doctor to see
whether all of his research has been scrutinised. Montgomery said that people like Macchiarini are more likely to get caught if they are required to be fully transparent.

Tsachi Keren-Paz, addressing the Macchiarini investigation summary by the hospital, said that there was not enough information to see why they decided that research was being carried out, rather than treatment, and what they meant by a ‘humanitarian element’. This could mean having the patient’s best interest at the forefront of any decision. Keren-Paz got the impression from the report that the procedures were considered to be research with a humanitarian element. Having said that, all therapeutic research is presumed to have such an element.

Alicia El Haj said that there is virtually no monitoring after an event takes place and asked whether this can be done. Jonathan Montgomery responded by saying that there are examples of it being done e.g. in the use of stem cells but it is not easy or a universal solution. Dominic Wilkinson said that he would be cautious about making vast changes to systems in response to extreme examples of wickedness. He went on to say that society would welcome innovative therapies, however, innovation will happen whether it is safe or not. From an ethical viewpoint, it is important to give patients information so that they can make the decisions. Sometimes, patients will be informed by an enthusiastic individual who is mistaken about the therapy or they can be misled by dishonest people. Wilkinson suggested making the information about a proposed treatment easily available. This would provide other viewpoints to the patient e.g. sceptics as well as enthusiasts. Sarah Devaney said that the dynamic between the patient and the person informing them of the treatment is an interesting one. She had been looking at deference in a doctor-patient relationship; specifically, at how patients inform themselves. Currently, patients go to the internet to search for the information and discuss it on forums but ultimately, it comes back to the clinic. It is difficult to make a choice with information presented in this way.

Tsachi Keren-Paz said that cognitive biases suggest that patients will cling to hope. Leonid Schneider said that he cannot recall any compassionate measure cases in the trachea transplant affair where the circumstances were so urgent that the proper procedures needed to be bypassed. Schneider suggested that every hospital exemption needs to pass certain procedures and the ethics reports need to be published. This would allow doctors to check the procedures and give their input. However, some doctors would not be happy with this because everyone would be able to see the treatments being carried out. Tina Cockburn said that this was the only thing that survived in the Saatchi Bill and asked whether the register could be established. Nayha Sethi said that there has been some commentary of who might be involved in it as well as concerns about its effectiveness. Jonathan Montgomery said that due to exposing people to public scrutiny, there was not much enthusiasm for the register. He then said that when he makes a decision about his own health care, he cares more about who is making the treatment decisions rather than the transfer of information. He felt that this may be important when thinking of a better way to go about things in the innovation context.

Roger Brownsword asked why adults are not being left to make their own decisions about clinical procedures. Alicia El Haj said that her innovation is to do with controlling stem cells and that she has seen enthusiasm for her treatment. However, she is unsure that it is right for these people to make a decision after speaking to the person who came up with it.
Leonid Schneider used a train analogy to respond to Brownsword’s question; people who buy train tickets are still entitled to have the trains inspected by safety experts. Likewise, patients who opt in for treatment are entitled to checks being carried out and for regulations to be in place. Marie-Andrée Jacob said that it may not be about consent. As seen with El Haj, patients can be extremely enthusiastic and sometimes, this enthusiasm will override consent. Leonid Schneider disagreed and mentioned that once patients are aware of the risks, their attitudes change.

Thomas Appleyard said that retrospective checks don’t do a lot to prevent surgeons like Macchiarini; if Appleyard wanted to go rogue, he would still be able to jump through the relevant hoops easily. Moreover, the culture in which Macchiarini was working in should be considered; he was working in a number of countries but no one felt comfortable to speak up. Leonid Schneider said that most of Macchiarini’s patients were young so they were persuaded by their parents to undergo the transplant. Additionally, where a young patient has died, the parents may just believe that they are unlucky and so they do not speak out. In terms of colleagues speaking out, Schneider described Macchiarini as an aggressive individual who had been known to intimidate his colleagues. Thomas Appleyard replied by saying that this is a problem with the culture rather than the individual as there are no protections in place for colleagues who do speak out. Leonid Schneider said that the whistle blowers in the Karolinska Institute were threatened with losing their jobs and being subject to a police investigation. In relation to patient enthusiasm, Abigail Pearson mentioned that acquiescence needed to be considered too.

4. Roundtable: Charlie Gard

Chair: Professor Marie-Andrée Jacob
Participants: Professor Jonathan Montgomery (UCL), (Professor Dominic Wilkinson (Oxford Uehiro Centre for Practical Ethics), Professor Roger Brownsword (King’s College London), Dr Michael Fay (Keele University) and Abigail Pearson (Keele University)

Marie-Andrée Jacob started off by introducing the panellists. Jonathan Montgomery said he wanted to introduce what he called ‘The “Tragedy” of Charlie Gard’. This is a way in to the challenges of regulating medical innovation and clinical dilemmas which might also help decide what the regulatory tools should be.

He went on to say that Greek tragedy is all about the character flaws of the protagonist which get exposed by difficult circumstances and then lead to either their destruction, someone else’s destruction or a cathartic resolution. One issue that caused problems in the Charlie Gard case were character flaws; more specifically, medical hubris and obsessive parental love. When thinking about medical hubris, we should consider how are proud doctors who don’t take their responsibilities seriously distinguished from caring doctors who are trying to do the right thing. Additionally, how do we distinguish parents who are doing the right thing for their children from obsessive parents who can’t actually face up to the problem that they are dealing with?

Montgomery highlighted the example of Jonathan Simms, a person with new variant CJD. The court authorised a therapy when no one knew its success rates but accepted that it was
in his best interest. Butler-Sloss addressed the prior-to-court situation; where there is no application to court and the patient does not have capacity. She identified two fundamental duties: acting professionally and in the best interests of the patient. Best interest is a term that is deeply problematic because of its superlative nature. To act in best interest is to pick the most preferred method but this doesn’t make much sense in the context where there might be more than one.

The evidence from the Charlie Gard case, indicated that apart from Dr Hirano, the body of experienced medical opinion available to the judge was unanimous to the effect that the prospect of this treatment having any benefit was effectively zero and would be futile. There were a number of reasons to be concerned about medical hubris in Dr Hirano’s suggested treatment; the absence of peer review, the failure to examine the patient, and the conflict between his tentative evidence to the court and the optimism he expressed to the parents. In some contexts, a legal licence is required to make the offer. This might guard against medical hubris. The fair offer question is addressed by looking at the nature of the offer, its permissibility within current regulatory framework and the integrity of the innovators.

Montgomery held the view that Great Ormond Street missed a trick when they withdrew their application to the hospital ethics committee to consider the proposed treatment. If they had gone through with it and if the ethics committee had rejected it, the situation would have been easier to handle.

If the fair offer approach is pursued, then we should also look at when acceptance is permitted. Whether there is a legal right for parents to put their child into trials is unknown. The 1970s idea that children can be involved in clinical trials where there is only a minimal risk has never been tested out. It wouldn’t be a big jump in medical innovation to say that relying on parental consent is not appropriate and that court authorisation is required.

Montgomery went on to say that if parents have the power to consent, then one must go on to look at their understanding and their competency when they do so. Adults can decide to accept treatment for good reasons, bad reasons or no reasons. It is not clear whether that would extend to a proxy consent.

‘Best interests’ for reasons given above is deeply problematic because it never actually is the best interest but ‘persuasive enough’ interests. However, should we stick with the decisions of parents so long as they are reasonable? One test case involved a liver transplant in which the court went for the parental view which clearly opposed the professional view. It was influenced by the fact that the parents would be involved post-treatment by supporting the child.

Moreover, there could be a treatment where more than one is appropriate so it is not necessarily the best. One might say this is a conflict about state and family decision making in which case that would lead us to the child protection standard of whether or not there was a risk of significant harm. The Court of Appeal closed all those off by deciding that the child was at risk of significant harm based on the quality of the evidence. They thought they had set it up so the legal tests would still find in their favour. The House of Lords and European Court of Human rights looked at changing the ground rules in this area.
Discussion

**Tina Cockburn** read out the family barrister’s speech which mentioned that ECHR article 8 rights were at the heart of the case and that it was ‘neither necessary nor proportionate for the state to override the parent’s legitimate choice of treatment’. **Dominic Wilkinson** said that from an ethical viewpoint, one should ask when should the state intervene in parental decision making. Generally, society does not think that the state should intervene whenever parents fail to live up to the best interests of the child; many parents fail to live up to this for various reasons. Arguably, the state should intervene when there is significant harm.

Wilkinson went on to say that medical professionals should respect decisions made by parents so long as they do not cross the threshold of harm. Arturo Estopiñan, who has the myopathic form of mitochondrial DNA depletion syndrome, was expected to die at the age of one. His parents did not accept this and sought out a researcher who had done animal experiments. His results suggested that the supplementation of nucleotides might diminish the biochemical defects. The parents had convinced him to treat their child. Their son is now six years old and he is still on a ventilator but his muscle strength has improved. This was the story that Charlie Gard’s parents had found.

**Jonathan Montgomery** wanted to test why this is highly relevant. Medical uncertainty cases such as Jaymie Bowen and Charlotte Wyatt have been before the courts in the UK. In these cases, the medical prognosis was far more pessimistic than actually turned out. Gard’s parents believed their case was the same whilst GOSH disagreed. **Dominic Wilkinson** said that the Gard parents saw their child with the same genetic condition as Estopiñan, just a different variant. They wanted the success of a treatment for their own child. One striking feature of the Charlie Gard case is that it tests the epistemic limits of such cases where there is no available evidence as to the benefit of a treatment.

**Abigail Pearson** pointed out that Arturo and Charlie are both children and said that one should consider at what point do they have the right to a life independent to their families. If left as a family decision, it may result in a person with a disability without any consideration for what the disabled person would want further down the line. Arturo is currently disabled and will continue to be so for his adult life. Pearson went on to say that there is a lot of literature written by the disability studies movement about how parents have ameliorated their children’s condition with corrective therapy but they have not been asked about whether we should have the right to decide if someone else should live with a disability. If Charlie Gard lived in an impaired state and subsequently his parents had gone, what right would Charlie have had to his own private life as an individual when his care would probably be taken over by the state? What about his right to live in a family of his own? **Tsachi Keren-Paz** asked how Pearson would answer the question. **Abigail Pearson** said that she doesn't think she could answer it but the discussion needs to be had. The experience of a child with this condition will be totally different to when they become an adult. As a child, they will have the family around them to ameliorate their disability but that cannot be guaranteed to the same extent as that child matures. The child also takes on the stresses, strains and worries that the parents have for their disabled child. It would be wrong to say that the child won’t take on those worries.
Jonathan Montgomery said that the ECHR discussions had one element of this which was whether family integrity is in issue or there is a set of individual entitlements of family members. The ECHR jurisprudence is now clear that the child’s right to private family life is independent of the family’s right to a private life. So, there is scope to take into account the will of the individual with respect to their private life. This was difficult to envisage in the Charlie Gard case. However, with later onset genetic disorders and the right to an open future in adoption proceedings, Montgomery felt that things should not be closed off earlier than they have to. Thus, the criticism of parental views is enabled which were based on not keeping the future open. There are ways in which some of the options can be constrained. Based on the discussion of ‘best’ in the ‘best interest’ test indicates that there is a right answer but, in fact, there are plausible answers which are hard to choose between.

Dominic Wilkinson mentioned a paper by Loretta Kopelman about the different meaning of best interest. She talked about best interest as an ideal, standard or a threshold for treatment. These all imply different futures for the patient. This only adds to the indeterminacy of best interest. Roger Brownsword highlighted Lord Mustill’s view in the Tony Bland case that discussing best interest is nonsense unless the patient is alive. In the case of Jaymee Bowen, the Article 2 right to life argument didn’t work because it was seen as public money being spent on futile procedures. The parallel here is if Charlie Gard were to be taken to Harley Street and the worst that could be said was that it would be futile and it was crowdfunded so no public money was involved. Jonathan Montgomery responded that the court finding was that there was current distress (although he thought this conclusion was problematic). He understood that the Hospital’s evidence suggested that Charlie was not feeling anything but that if he were to feel anything the intrusion of being intubated would be distressing. The Court of Appeal viewed this as significant harm.

Abigail Pearson asked ‘what is meant by right to life?’ Is it just breathing in and out or does it refer to being able to experience the world? Michael Fay talked about the difference between the right to life and the right to exist. In the Bland case, there is the right to sufficient medical treatment; however, there is no right to keep a person breathing indefinitely. He felt that Charlie Gard was more analogous to a persistent vegetative state rather than a disability. The fact that there was no clarity about whether Charlie was feeling anything lent weight to him being in a persistent vegetative state. GOSH stated that he was deriving no pleasurable benefit from life which also pointed towards this state.

Fay also raised the issue of communication. Parents are likely to listen to the person who says they can save their child. So, the question is not about whether the parents have the ability to choose the best interests because they did not have the ability to do so. The parents were emotional, they did not have the relevant information and Dr Hirano was not giving them an opinion based on evidence. Ultimately, it is how information is communicated that influences people’s decision the most. Raymond Tallis said that Harold Shipman was loved by his patients because he was an attentive and excellent communicator even though he was murdering them all.

Alicia El Haj asked how the compassionate measures case fits in; where the only option is an innovative one. Michael Fay answered that it is context dependent. There is the case of a little girl, Leila, who had leukaemia and was going to die in months. She was treated by using edited stem cells which could offer a cure. The difference between this and Charlie
Gard’s case is that Leila had a clear and sought after end point where she may achieve a normal life. With Charlie, however, a successful treatment would not take him off the ventilator. Alicia El Haj stated that there are a lot of unknowns with gene editing techniques. You may get a random insertion so there could be a 0.001 chance that it could have been successful.

Dominic Wilkinson said the condition is rare. Without treatment, he was certainly going to die. However, the question was whether it was going to harm him to continue intensive care for three months. Jonathan Montgomery said that the court was not considering the harm in administering the treatment, rather the harm to Charlie by continuing living because that, in itself, was harmful to him. The argument about the direct harm from the treatment would have been much more powerful in January rather than July.

Abigail Pearson said that we should be careful not to return back to a point in time when people with disabilities were used as medical experiments and were institutionalised. The human rights framework has been built up on the inclusion of people with disabilities and by deciding to allow a child to die rather than live a life of disability. Jonathan Montgomery said that in the Charlie Gard case, the financial interests needed to be teased out. Michael Fay said that there is a great difference where the hospital finds a recommended expert and this situation where the family found one. Dominic Wilkinson then clarified that the family first contacted the family of Arturo Estopiñan who introduced them to Dr Hirano. Dr Hirano had a conversation with the mitochondrial experts at GOSH and reluctantly agreed to perform a tracheostomy and attempt a trial after doing some initial neurological examinations. He said it would be a contra-indication if Charlie had severe brain damage. When hospital found severe brain damage, the trial was off and the family did not accept this.

Leonid Schneider agreed with Michael Fay that this is not a question about disability but rather of a person in a vegetative state. Bioquark in India had an idea to revive dead people using lasers and stem cells. They registered for a trial in the US and people said that there is nothing to lose where the patient is already dead. Dominic Wilkinson said that you either think he is profoundly disabled and has some limited awareness or you think he is completely unaware of everything and in this case there is no harm in providing three months of intensive care. Abigail Pearson said that it is not dignified. Dominic Wilkinson responded that whilst it is a legitimate view, there are contested conceptions of dignity. One of which is his family’s love for him and prolonging treatment. Abigail Pearson said that images of him on a ventilator beamed around the world did not further his dignity or right to privacy so having three more months would have degraded his dignity further. Michael Fay said that as well as the right to life, Charlie has the right to bodily integrity. The justification for the interference with bodily integrity would have had to be questioned if medical treatment is showing no benefit. So, to unpick that knot of allowing treatment after severe brain damage would make it easier for the next time someone wants to proceed with innovative treatment.

Alicia El Haj mentioned that the perceptions of a nanny state imply that parents do not have an opinion. Jonathan Montgomery said that the parents have the right to express an opinion. Michael Fay said that with an emotive issue like this, it is difficult for parents to interpret the information provided. Jonathan Montgomery brought up the case of Ashya
King where the parents abducted their child to Spain, seeking therapy that was not readily available in the UK. So, if you thought that the child was going to be taken to New York and it was going to be harmful, then there is an obligation on the paediatrician to resort to the courts.

**Dominic Wilkinson** said that one of the claims in the European Court was whether Charlie was effectively being imprisoned unlawfully under article 5 of the ECHR. So, this turns to the question as to whether parents have a right to take their children overseas for treatment when that treatment does not meet local laws or norms.

**A question from the floor** was that at the time of the publicity around Charlie Gard, a lady appeared on television who had a twelve-year-old daughter with severe disability and she was on a ventilator daily. In this case, the mother actually wanted her to have the right to die. What is the difference between these two cases? **Michael Fay** said that there is a perception when dealing with young children that there is nothing there - they are a blank slate so why put them through this suffering. **Abigail Pearson** brought up the bigger division between disability and impairment. With the older disabled children, societal pressures contribute to why these children want to die. With Charlie Gard, he was brought up like a normal child for a while so it can be said that his disability was an accident of nature.

**Emma Cave** considered the difference between the application of the best interest test in the court and the best interest test applied prior to that. Prior to coming to court, it may be appropriate to consider options that are 'not against' best interests. In court, the best interest assessment is normally between two options whereas before it goes to court there is a myriad of dynamic choices. There should be professional guidance to doctors of what is expected of best interest prior to going to court and what the expectations should be in court.

**Jonathan Montgomery** said that doctors have to act in accordance with the responsible body of professional opinion which is orientated to the interest of the patient. The implication of the 'best' superlative at this point is that if they had given Charlie the treatment, it would have been unlawful. A comment from the floor was that it would be a misjudgement of the word 'best' based on incorrect factual information. **Jonathan Montgomery** asked to consider the scenario where the parents managed to give Charlie the powder brought across by the pro-life activists. On the basis of drafting an order on the best interests, the above scenario would mean that the parents are in contempt of court and have kidnapped their child i.e. the legal ruling has made it this way. Montgomery felt that in cases like this, there is a coordination problem. Where there are negotiations, there needs to be somebody who has the last say in whether treatment is suitable or not. In the present case, the courts play this role. A question from the floor was how the reasonableness test would fit in. **Jonathan Montgomery** replied by saying that the reasonableness test was rejected and so is not used. However, if it was used then it would be similar to Wednesbury and Bolam. His analysis of the human rights dimension would be that the child should be favoured over the parent’s private family life when a choice of this nature is required. Having said that, the parent’s rights are still engaged so they have the right to be involved, express their opinion and challenge the other side.

**Tsachi Keren-Paz** followed up on Emma Cave’s point about the distinction of best interests in a court and before. When applied to Charlie Gard, there seems to be no difference.
Emma Cave agreed but said that she was thinking more about which future cases should proceed to court. In the Court of Appeal, there was a mention of mediation and she was thinking about the form it may take and how some of these cases can be avoided in this way. Dominic Wilkinson said that the two different groups are the professionals and the parents which make for an uncomfortable situation. Mediation can help the parties come to an agreement, a compromise or to identify that an agreement can’t be reached. In the event that an agreement cannot be reached, the reasonableness of the parent’s request must be looked at. If the request is not reasonable, then the professionals can decide to take the parents to court. There are situations where professionals are not doing what they think is best for the child but they do not think it is so wrong that they will put their team and the patient’s family through the courts. Wilkinson felt that the parents’ views should be taken into account when the courts decide what is best for the child whereas, currently, it is not.

Jonathan Montgomery said that the courts do consider it but it is not given weight simply because the parent’s think it. The only cases where it has made a difference is when the preferred medical solution requires long-term care and the parents are unwilling to cooperate.

Michael Fay said that one interesting thing is when the parties go from negotiating to being adversarial in court. The floor agreed that this may be a liminal space. Fay went on to say that the courts are always suspicious of relatives. One example is the nearest relative in mental health law; in legislation there is some power to object to being sectioned but the courts overrule every time. This is thought to be because the relatives may not have the best interests of the person at heart. Then, Fay mentioned a BBC article dated 25th August 2017 which talked about the Eveline programme which deals with early intervention and discussion with parents. The article discussed the parents of a young patient who had to move wards. The parents had built relationships with the previous ward and feared that the child would not be safe in the new one, giving rise to a potential breakdown. In this case, the matter was discussed and the scenario was cleared. However, the outcome favoured the doctor. There is still the belief that the medical professional is right which means that the parents’ wishes are overridden.

Jonathan Montgomery said that with mediation, you have to decide what it is meant to achieve. If mediation is supposed to be a less intrusive way of getting to the same outcome than the courts, then it would work in the way that Fay explained. Although, in the Charlie Gard case, this would not have made a difference. Michael Fay made a comparison to an employment relationship where certain procedures must be followed before the dispute goes to a tribunal and then to a court. Dominic Wilkinson said that Justice Francis’ comments in the Gard case reflect this; hospitals feel obliged to go through mediation before they can reach the courts. Wilkinson described this as not being a good faith motivation for mediation.

Marie-Andrée Jacob said that it would not be harmful to get people in a room with the ‘Master of Ceremonies’ to discuss the situation. Tsachi Keren-Paz said that in the US, patients can win cases, not because of substandard clinical treatment by the treating physicians, but due to inferior communication skills which both make the patient more likely to sue and the physician more likely to settle or lose.

Jonathan Montgomery mentioned that the guardians of children usually agree with the medical model e.g. Gard’s guardian was in the same camp as GOSH. This is a reinforcement of the systemic view that the medical model is the correct one.
5. **Concluding Comments**

Tsachi Keren-Paz concluded the seminar by thanking the speakers and participants for their valued contributions as well as the collaborators for their work on the series. Finally, he thanked Bushra Jalil and the Faculty Research Office for supporting the seminar.