

Impact case study (REF3)

Institution: The University of Manchester		
Unit of Assessment: 18 (Law)		
Title of case study: Shaping COVID-19 Vaccination Policy and Practice		
Period when the underpinning research was undertaken: 2000 – 2004; 2009 – 2020		
Details of staff conducting the underpinning research from the submitting unit:		
Name(s):	Role(s) (e.g. job title):	Period(s) employed by submitting HEI:
Søren Holm	Professor of Clinical Bioethics Professor of Bioethics	1999 – 2004; 2009 – present
Period when the claimed impact occurred: 2020		
Is this case study continued from a case study submitted in 2014? No		
<p>1. Summary of the impact</p> <p>Professor Søren Holm's research on infectious disease control, the ethics of human challenge studies and his critiques of ageing in bioethics have directly shaped COVID-19 vaccination policy and practice in Norway, Denmark and England. Informed by his foundational research on the need to develop evidence-based bioethics, his work has produced substantial health benefits to populations at increased risk of death from COVID-19. His input to the COVID-19 vaccination prioritisation policies of Norway and Denmark resulted in the recognition of older people as deserving highest priority for vaccination. Through his expert appointment by the English Health Research Authority his research was used to (i) develop training which enabled members of a newly constituted Research Ethics Committee to review human challenge studies and (ii) to devise an assessment tool that was applied by the human challenge REC members in appraising and then approving the first, and only, COVID-19 human challenge study.</p>		
<p>2. Underpinning research</p> <p>Holm's research underpinning this impact case study draws together three strands of work: (a) public health ethics and infectious diseases; (b) reframing the way that older people are accounted for in mainstream bioethical research; and (c) translating bioethical inquiry into health policy.</p> <p>(a) Public Health Ethics and Infectious Disease</p> <p>Holm's research has addressed the obligations that states have to citizens when implementing public health measures during infectious disease outbreaks. Specifically, he has examined the question of if and when a State has an obligation to compensate those citizens who are burdened or harmed by public health interventions [1] and has concluded that wide-ranging obligations to compensate for burden and harm can be justified, based on ethical theory and more pragmatic considerations in respect of ensuring adherence to the public health measures. The most recent output from this line of research [1] was developed at an invited workshop at the Brocher Foundation organised by Monash University.</p> <p>Challenge studies raise particular ethical issues because they involve infecting healthy volunteers with the disease-causing agent with the sole purpose of generating knowledge. Holm's work on the research ethics of COVID-19 challenge studies [2,3] was undertaken specifically to contribute to a fast-moving academic and public discussion questioning the ethicality of undertaking such studies and whether or not they should be approved by research regulators, and subsequently conducted. Holm's research showed that challenge studies are difficult to reconcile with medical research ethics as developed since the Second World War [2] and that even if there might be a context in which such studies are conceivably justifiable, the conditions under which this could happen will not be met in practice [3].</p> <p>(b) Reframing Ageing in Contemporary Bioethics</p> <p>Holm's research challenges the way in which ageing and the old are represented in contemporary bioethics. His analysis of mainstream bioethical literature [4] showed that 1) the paradigmatic example of 'the person' or the individual in bioethical analysis is the young (male) adult, 2) when the old are considered it is within a framing of a narrative of inevitable decay, and 3) that 1&2 combined leads to a devaluation of the old and their interests in bioethical argument. This framing of ageing is also prevalent in health economics and health policy. Holm's research challenges this dominant framing and its consequences and advances an alternative set of claims as to how older</p>		

people's interests and their contributions can be properly recognised, including the claim that the elderly and their lives count in themselves and not just as (sub-optimal) producers of life years or QALYs. [5]. This work has contributed foundational conceptual bioethics analysis to projects analysing the many different practical ethical issues and policy choices actualised in health care for the old. This research was advanced through an international collaboration (with Professor Inéz de Beaufort and Professor Martje Schermer, Erasmus University, Rotterdam; and Dr Mark Schweda, Göttingen University).

(c) Translating Bioethical Inquiry into Health Policy

Drawing on his experience as a member of two national ethics bodies (the Danish Council of Ethics and the Nuffield Council on Bioethics), Holm undertook an analysis of the issues arising when translating bioethical inquiry and bioethical 'research results' into health policy and the importance of different kinds of evidence pertaining to such translation. The work began with output [6], produced in the course of the EU funded project *Empirical Methods in Bioethics* (i), which Holm co-ordinated as the principal investigator (PI). This project was the first large-scale project globally to investigate the importance of empirical data in bioethical argument and it prefigured what became labelled in the literature as 'the empirical turn' in bioethics.

3. References to the research

1. Solbakk JH, Bentzen HB, **Holm S**, Heggstad AK, Hofmann B, Robertsen A, Alnæs AH, Cox S, Pedersen R, Bernabe R. 2020. Back to WHAT? The role of research ethics in pandemic times. *Medicine, Health Care and Philosophy*. 24, 3-20. doi: [10.1007/s11019-020-09984-x](https://doi.org/10.1007/s11019-020-09984-x)
2. **Holm S**. 2020. A general approach to compensation for losses incurred due to public health interventions in the infectious disease context. *Monash Bioethics Review*. 38: 32-46. doi: [10.1007/s40592-020-00104-2](https://doi.org/10.1007/s40592-020-00104-2)
3. **Holm S**. 2020. Controlled human infection with SARS-CoV-2 to study COVID-19 vaccines and treatments: bioethics in Utopia. *Journal of Medical Ethics*. doi: [10.1136/medethics-2020-106476](https://doi.org/10.1136/medethics-2020-106476)
4. **Holm S**. 2013. The Implicit Anthropology of Bioethics and the Problem of the Aging Person. In: Schermer M, Pinxten W (eds.) *Ethics, Health Policy and (Anti-) Aging: Mixed Blessings*. Springer: Dordrecht, 59-71.
5. **Holm S**. 2020. Wise Old Men (and Women). Recovering a Positive Anthropology of Aging. In: Schweda, M, Coors M and Bozzaro C (eds) *Aging and Human Nature* Springer, Cham, 233-240.
6. **Holm S**, Jonas MF (eds.) 2004. *Engaging the World: The Use of Empirical Research in Bioethics and the Regulation of Biotechnology*. Amsterdam: IOS Press

Related Grants

- i. *Empirical Methods in Bioethics (EMPIRE)*. Holm, S. (PI). EUR510,000. 2000 – 2003. European Commission Quality of Life and Living resources Research Programme.

4. Details of the impact

Holm's research on empirical bioethics [6] has enabled him to articulate policy-relevant evidence and arguments and make these available in a way that is understandable and persuasive to policy-makers. The success of this work on empirical ethics and policy making underpins two key strands of impact relating to COVID-19 vaccination policy and practice. First, Holm's research has had a direct bearing on two national vaccination prioritisation policies in Scandinavia and the communication of their credibility to the general public and key stakeholders. This contribution is highly significant, since Norway and Denmark are acknowledged as two of only 10 European States which have adopted an overtly ethical basis for national vaccination prioritisation policy [A]. Second, it has contributed to the training of members of a dedicated Research Ethics Committee (REC) in England, and the development of key analytical tools used by that Committee to appraise the world's first COVID-19 human challenge trial.

1. Shaping COVID-19 Vaccination Policy in Scandinavia

Norway

In 2020 The Norwegian Ministry of Health and Care Services commissioned the Norwegian Institute of Public Health to prepare a national immunisation plan which included preparing, implementing and following up vaccination against COVID-19. As part of the assignment, the Norwegian Institute of Public Health was charged with developing recommendations to prioritise groups for vaccination. The Institute appointed an expert group for ethics and prioritisation, comprising six members with expertise in health resource prioritisation. Holm was the only non-Norwegian expert member of the group and was appointed because of his research and expertise in public health ethics [B], not least his previous research on the obligations that states have to citizens when implementing public health measures [B].

The group published its report on 17 November 2020 [C]. It recommended that the values of equal respect, welfare, equity, trust and legitimacy ought to underpin the policy on prioritisation. The group then agreed a descending ranking of key goals pertaining to a future policy: 1) reduction of the risk of death; 2) reduction of the risk of severe illness; 3) maintenance of essential services and critical infrastructure; 4) protection of employment and the economy; 5) re-opening society. Finally, the group advocated that any strategy and prioritisation order be adjusted in light of shifts in the course of the pandemic; the properties of vaccines; and the infection rates within Norway. The report recommended that people over the age of 65 and people with underlying health conditions be deemed the highest priority groups for vaccination. It also recommended that second priority status should be given to healthcare workers, subject to review in the event of a significant rise in infection rates.

Holm played a central role in the development of these recommendations. In particular, his claims about how older people's interests should be properly recognised [4,5] influenced the decision of the panel to confer highest priority on older and more vulnerable people, rather than younger groups of critical workers. The underlying basis of this decision is affirmed by Dr Japser Litmann, Deputy Director of the Coronavirus Immunisation Programme in Norway. He observes that Holm's arguments on the moral worth of older people "*persuaded panel members to depart from the Norwegian Government's standard approach of focussing exclusively on the number of life years saved as the key driver for prioritisation, rather than lives saved*" [B]. As a result of this intervention, the panel ultimately noted:

The ethics advisory group believes that the distribution of limited health resources, should aim to reduce the number of years of life lost, with particular priority to the most disadvantaged. However, in a pandemic like this, the vaccine distribution will affect behaviour and welfare beyond health. The indirect value of avoided deaths is so great for society that an adjustment to years of life lost will likely have little significance. The more lives saved by the vaccine, the faster the other four goals will be reached. [C, p. 14].

The report created significant discussion, in leading Norwegian press outputs and in professional journals, on whether health care professionals or younger people should be prioritised over older people, on the basis of arguments discussed by, but eventually rejected by the expert group, as a result of Holm's research [D].

The panel's recommendations are described by Littmann as "*an important component of the immunisation strategy that was adopted by the Ministry of Health and Care Services on 5 December 2020, and implemented on 27 December 2020*" [B]. Holm's "*crucial*" involvement in the priority-setting process is acknowledged as having "*greatly improved the consistency and clarity of the recommendations that form the basic principles for the distribution of vaccines against COVID-19 in Norway*" [B]. Implementation of the policy has proceeded according to the priority list recommended by the group, commencing with the vaccination of the 1,300,000 people in the highest priority category and subsequently adopted the dynamic shift recommended by the group, to give higher priority to health care workers in the event of changes to the epidemic [E].

Denmark

On 1 December 2020, Holm was appointed to a philosophers' group which was convened to provide advice on the ethical issues of COVID-19 vaccine prioritisation in Denmark. His

appointment was based on his research expertise on ethics and infectious disease and his recent participation in the Norwegian ethics group advising on vaccine prioritisation and his contributions to the group's final report. The Danish group reported directly to the Danish Health Authority, which has responsibility for the Danish vaccine priority plan and its implementation. The Danish Health Authority published a prioritisation strategy which in large part replicated the strategy recommended by the Norwegian ethics group, but with a stronger emphasis on priority to vulnerable groups in the community [F]. Preparation and publication of that strategy resulted in widespread public and professional debate on the tension of focussing on the old as a priority group in the first phase of the vaccine roll out as against health care workers [D].

The Philosophers' group helped to clarify a robust ethical basis for the Danish Health Authority's vaccine priority plan. According to Dr Stine Ulendorf Jacobsen, the Danish Health Authority's Special Adviser on Emergency Preparedness for Infectious Disease, Holm advanced the interests of older people in his advice:

"In the discussion Professor Holm emphasised how a policy giving priority to the old can be justified by considerations of the equal value of the lives of older people, and can also be defended by taking account of the evidence of the very large age differentials in mortality among those infected... He also articulated how more abstract philosophical arguments can be made accessible to key stakeholders and the general public." [G]

The group had its first meeting with the Director General on 3 December 2020. Its advice had a beneficial impact on the development and roll out of the vaccination strategy in that it supported and enabled the Danish Health Authority to prioritise older and more vulnerable people over younger health care workers during the first phase of vaccinations. Ulendorf Jacobsen notes that *"Professor Holm's research and expertise were invaluable in shaping the advice of the group to the Danish Health Authority, and the communication of the credibility of the vaccination policy to key stakeholders and the public."* [G]. The roll-out of the vaccination strategy as at 31 December 2020 demonstrates adherence to the prioritisation policy [H].

2. Shaping Good Governance in COVID-19 Challenge Studies

The UK's Vaccine Task Force, established in May 2020 to progress the development of a COVID-19 vaccine, identified that human challenge studies for COVID-19 vaccines were likely to be of critical importance given the short timeframes needed to meet public health demands. The UK government accepted the Task Force's recommendation and invested GBP33,000,000 in a partnership involving pharmaceutical company Open Orphan, Imperial College London and the Royal Free Hospital to develop the world's first human challenge trial for COVID-19 vaccines. Although virus challenge studies per se are not novel, it is highly unusual to conduct them so soon after the emergence of a potentially lethal pathogen. The need to confirm a robust ethical basis for these studies was accepted from the outset and noted in Parliament [I].

In recognition of these unique demands, the Health Research Authority (HRA) established a special Research Ethics Committee (REC) in November 2020 to consider future applications for COVID-19 challenge studies. As a result of his research expertise, recent relevant publications (especially outputs [1] and [3]) and his experience as a member of the HRA advisory panel, Holm was invited by the HRA to train the members of the newly constituted HRA REC. Holm's input was requested specifically because he has cautioned of the ethical and operational challenges of running such real-world studies.

Around 20 Committee Members attended the training over two days, with training devised and delivered by Holm and four other experts. As part of a debate on the ethical considerations, Holm presented the ethical case against COVID-19 challenge studies, based on his work on the role of research ethics in pandemics and his recent paper on controlled human infection with COVID-19 to study vaccines and treatments [3]. He highlighted the fact that the idealised assumption that might make challenge studies ethically acceptable in principle are unlikely to be met in practice. Members had the opportunity to discuss the issues with the aim of learning how to think about the ethical issues that might be raised by specific studies presented to the Committee.

The training was highly beneficial to members of the REC, with 80% recording their training experience as 'excellent' [J]. Crucially, it was instrumental in the development of guidance by the HRA for the REC members, as it was used by the HRA to develop and refine a framework of ethical considerations that was subsequently applied in the review of a COVID-19 challenge study [K]. By 31 December 2020, the framework had been used to evaluate applications for the first two phases of the COVID-19 challenge trial and resulted in the demand by the REC for further information about the research protocol for the identification and screening of volunteers, and the protocol for the viral dosing [J]. The HRA confirm that "*Professor Holm's training for the members of the Committee has provided a vitally important means by which [REC] members may hold researchers accountable for their proposed trials, maintain public confidence in regulatory processes, and ensure public safety*" [J].

5. Sources to corroborate the impact

- A. European Centre for Disease Prevention and Control, 2020. *Technical Report: Overview of COVID-19 Vaccination Strategies and Vaccine Deployment Plans in the EU/EEA and the UK*. <https://bit.ly/3sMbCby>
- B. Testimonial from Deputy Director of the Coronavirus Immunisation Programme, Norwegian Institute of Public Health. Received February 2021.
- C. Feiring et al., 2020. *Advice on Priority Groups for Coronavirus Vaccination in Norway: Expert Group in Ethics and Priority Setting*. Norwegian Institute of Public Health. <https://bit.ly/30sZ6lv>
- D. Media coverage of vaccine prioritisation in Denmark and Norway (sources in Danish and Norwegian): (a) *The debate in Denmark is Underway: Who should be Vaccinated Against Corona First?* Kristeligt Dagblad, 9 August 2020, <http://bit.ly/3bhnwnT>; (b) *Ethics experts on the wrong track*, Tidsskriftet (Journal of the Norwegian Medical Association), 24 November 2020, <http://bit.ly/38cBWUK>; (c) *Who should get corona vaccine first?* Tidsskriftet, 26 November 2020, <http://bit.ly/30h9BYY>; (d) *Who Should Get Corona Vaccine First? Who can Wait?* Dagens Næringsliv, 26 November 2020, <http://bit.ly/3c7FgBB>; (e) *Doctors on COVID vaccination plan: Good with vaccines for vulnerable first, but need a quick plan for the spread of the vaccine*, Danish Medical Association, 27 November 2020, <http://bit.ly/2MTnjy6>
- E. Article on the start of the rollout from Norwegian state broadcaster showing that the recommended priority list is being followed. 18 December 2020. <http://bit.ly/30hwZW1> (source in Norwegian)
- F. Danish Health Authority, *Who should be vaccinated?* <http://bit.ly/30gTEly>
- G. Testimonial from Danish Health Authority's Special Adviser on Emergency Preparedness for Infectious Disease. Received February 2021.
- H. Danish Vaccination Dashboard. <http://bit.ly/389bhYz> (source in Danish)
- I. Westminster Hall debate on COVID-19 vaccine, (vol 683 col 364WH-378WH). 10 November 2020. <https://bit.ly/3bfdLXw>
- J. Testimonial and email from Director of Approvals Service, Health Research Authority. Received February 2021.