CHAPTER 4

The Coexistent Temporalities: Multilayered Ethics in Birth Cohort Studies

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Introduction

> This society and life itself have changed. […] Researchers used to try new chemical compounds on themselves because there was no other way. […] Everything is tied to time, the era. The things we do today, if we look at them in thirty or forty years from now, may horrify us: How could we do that, that is as unethical as can be! […] We look at the past in today's context, we are awfully judgmental, and we do not pay attention to the circumstances, the time and opportunities that once existed.[1]

[1] Arja Rautio (AR), interviewed on 7 January 2021. Sirkka Keinänen-Kiukaanniemi (SK-K) also mentions her past experiences as a "guinea pig." Interviewed on 28 January 2021.

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This excerpt from an interview with the epidemiologist Arja Rautio sums up the topic of this chapter, namely the multi-layered way in which the ethics of birth cohort studies is interpreted by cohort scientists. The chapter analyzes how ethical guidelines and prescriptions guiding cohort studies have changed from the mid-1960s to the present and asks how a cohort research community has adjusted to these changes. Birth cohort studies, due to their extensive use of human subjects and their usually extended length, are particularly well suited for investigating the issue.

A birth cohort is formed of a group of people born in a particular period. Birth cohort studies follow such groups to find correlations and causal relationships between early exposures and later outcomes. Birth cohorts can be used to provide answers to specific, often health-related, questions. The data typically consist of health surveys, and many birth cohort studies also collect clinical measurements and biological samples.[2] Time is a defining element in birth cohort studies. They can be retrospective, which means that the cohort is formed long after birth and that the data pertaining to the time between birth and the formation of the cohort are collected retrospectively, usually from different registers, or they can be prospective, which means that data collection has been going on since birth. Successful birth cohort studies are longitudinal, that is, they follow their subjects over an extended period of time. Historian Warwick Anderson sees a family resemblance between history and epidemiology, based on their understanding of temporality and change over time. He regards "modes of epidemiological time-keeping" as "ways in which epidemiology has occupied, or been stretched across, different temporal scales." Anderson wants to draw attention to the aspect of time, because assumptions about temporality influence the assessment of epidemiological problems.[3] While the temporal dimension is one of the greatest assets in birth cohort studies, it also brings continuous challenges with it.

[2] Cristina Canova and Anna Cantarutti, "Population-Based Birth Cohort Studies in Epidemiology," *International Journal of Environmental Research and Public Health* 17:15 (2020), 5276.

[3] Warwick Anderson, "The History in Epidemiology," *International Journal of Epidemiology* 48:3 (2019), 672–4.

This chapter aims to contribute to discussions on the history of birth cohorts and on their use in historical research.[4] The case through which the issue is tackled is the Northern Finland Birth Cohorts 1966 and 1986 (NFBC). Launched in 1965, the NFBC initially comprised 12,231 children and their mothers. At first, the study focused on perinatology and risk factors, because one of the main interests was the high mortality and morbidity rates of newborns in Northern Finland. The second birth cohort was started in 1985. It consisted of 9479 children and their mothers. Over the decades, the range of research topics and fields has expanded, and data have grown more voluminous and more varied, comprising questionnaire data, clinical measurement, and biological samples. Today, the NFBCs are administered by the NFBC project center, located at the University of Oulu, Finland. The NFBC website lists more than thirty research areas where the data has been used, including cardiology, economic research, physical activity research, and gynecology. The NFBC data have also been employed by various international consortia and programs. Around 1700 scientific publications have thus far been based on the data.[5]

The main finding of this study is that the NFBC scientists share a similar understanding of research ethics, an understanding that acknowledges past circumstances in epidemiological knowledge-production but also constantly seeks to adjust to ongoing changes in research ethics.

[4] Penny Tinkler, Resto Cruz and Laura Fenton, "Recomposing Persons: Scavenging and Storytelling in a Birth Cohort Archive," *History of the Human Sciences* 34:3–4 (2021), 266–89; Maiju Mikkonen, Minna Salonen, Antti Häkkinen, Maarit Olkkola, Anu-Katriina Pesonen, Katri Räikkönen, Clive Osmond, Johan Eriksson and Eero Kajantie, "The Lifelong Socioeconomic Disadvantage of Single-Mother Background: The Helsinki Birth Cohort Study 1934–1944," *BMC Public Health* 16:1 (2016), 817; Richard Doll, "Cohort Studies. History of the Method I. Prospective Cohort Studies," *Sozial- und Präventivmedizin* 46 (2001), 75–86; Debbie Lawlor, Anne-Marie Nybo Andersen and G. David Batty, "Birth Cohort Studies: Past, Present and Future," *International Journal of Epidemiology* 38 (2009), 897–902; *A Companion to Life Course Studies: The Social and Historical Context of the British Birth Cohort Studies,* ed. by Michael Wadsworth and John Bynner (London: Routledge, 2011); John Welshman, "Time, Money, and Social Science: The British Birth Cohort Surveys of 1946 and 1958," *Social History of Medicine* 25 (2012), 175–92; Helen Pearson, *The Life Project* (London: Penguin Books, 2016); Hannah J. Elizabeth and Daisy Payling, "From Cohort to Community: The Emotional Work of Birthday Cards in the Medical Research Council National Survey of Health and Development, 1946–2018," *History of the Human Sciences* 35 (2022), 158–88.

[5] For further information about the Northern Finland Birth Cohort Studies, see https://www.oulu.fi/nfbc/.

Their understanding of ethical research is thus multi-layered. Although scientists' view of the temporality of birth cohort data differs from that of historians, they have their own way of conceptualizing the passage of time. It resembles what the historian of science Lorraine Daston calls "the science of the archives," the historical practice of storing materials for the future.[6] The history of research ethics in birth cohort studies offers a way to examine how epidemiological knowledge-production has been governed and affected by temporality.

The chapter is primarily based on semi-structured interviews ($n = 18$) with scientists and nurses who have been involved in the design and execution of NFBCs or made use of the data. They come from different disciplinary backgrounds, for instance from perinatology, psychiatry, geography, toxicology, and educational sciences. Some interviewees also work in the NFBC administration, and one has participated in the design and implementation of the follow-up studies. The discussions of ethics are parts of longer interviews, designed to gather information on the history of the NFBCs. In addition to the interview data, the chapter relies on published research, materials produced as part of the cohort research, such as informed consent templates, and archive material from the host institution, the Faculty of Medicine at the University of Oulu.

The remainder of this chapter is structured as follows: The first section introduces the development of research ethics in Finland after the Second World War and discusses the emergence and role of medical research ethics committees. The second delves into the history of the concept of informed consent in the context of the NFBCs. The third focuses on the implications of the General Data Protection Regulation (GDPR), which are also connected with the consent-related challenges. Finally, the fourth section discusses the access of the participants to information generated by the study, and the related problem of intervention versus observation.

[6] Lorraine Daston, "The Sciences of the Archive," *Osiris* 27:1 (2012), 156–87.

The Role of Research Ethics Committees

Prior to the Second World War, Finnish discussions of ethics in medicine focused on collegiality and doctor-patient relationships.[7] Research ethics was not discussed as a separate issue. Finnish physician A.J. Palmén (1885–1974), who published various works on medical ethics in the post-war years, characterized the Second World War as an era that shattered the long tradition of ethics and the post-war years as "waking up from a bad dream."[8] The Nuremberg trials fueled ethical discussions, leading to the first international declarations on medical research ethics. The Nuremberg Code emphasized the human subject's voluntary informed consent, the avoidance of harm to the subject, and the necessity and the quality of research.[9] Due to concerns over medical ethics, the World Medical Association modernized the Hippocratic Oath in the 1948 Declaration of Geneve. In 1949, a more detailed International Code of Medical Ethics was adopted.[10] In 1956, the Finnish Medical Association published the first Finnish regulations, which were heavily influenced by international declarations as well as by the guidelines of the Swedish Medical Association.[11] An updated version, published in 1963, took a stand on consent. The doctor should always aim for the best treatment. "The doctor should not, however, subject the patient without his/her or his/her guardian's consent to the kind of treatment that threatens the life of the patient or causes a danger of invalidity, unless it is necessary for medical reasons."[12] In 1964, the World Medical Assembly gathered in the capital of Finland and adopted new international recommendations for clinical research. The Declaration of Helsinki emphasized the importance of moral and scientific

[7] Sari Aalto, *Medisiinarit, ammattiin kasvaminen ja hiljainen tieto: Suomalaisen lääkärikoulutuksen murroksen vuodet 1933–1969* (Helsinki: Helsingin yliopisto, 2016).

[8] A.J. Palmén, *Lääkärin etiikka muuttuvassa maailmassa* (Tapiola: Weilin + Göös, 1968).

[9] Paul Weindling, "From the Nuremberg 'Doctors Trial' to the 'Nuremberg Code'," *Wiener klinische Wochenschrift* 130 (2018): S162–5; *The Nuremberg Code: International Principles for Human Experimentation* 1949.

[10] World Medical Association, "History," at https://www.wma.net/who-we-are/history/.

[11] Samu Nyström, "Suomen Lääkäriliitto 100 vuotta," in *Vapaus, terveys, toveruus: Lääkärit Suomessa 1910–2010*, ed. by Samu Nyström (Hämeenlinna: Suomen Lääkäriliitto, 2010), 16–51.

[12] *Täydennys Suomen Lääkäriliiton eetillisiin ohjeisiin,* 1963.

principles in medical research and the patient's "freely given consent."[13] According to the guidelines of the Declaration, good research was also ethical research. As the NFBC scientist and psychiatrist Juha Veijola puts it in an interview, "good research is more ethical than bad research."[14]

General guidelines were found insufficient for guiding research in practice, and the 1960s and 1970s saw the emergence of ethics committees. They were established early on, for example, in the Netherlands, Sweden, and the United Kingdom.[15] Committees proliferated in the latter half of the 1970s, because the revised Declaration of Helsinki (1975) stated that the "design and performance of each experimental procedure involving human subjects should be clearly formulated in an experimental protocol which should be transmitted to a specially appointed independent committee for consideration, comment and guidance."[16] The Finnish National Board of Health also strongly recommended the establishment of local ethics committees. Most ethics committees began operating after 1978, as a result of the Board's two circulars to universities and research centers.[17] By 1982, there were a total of 91 medical ethics committees in Finland, the first having been founded at the University of Oulu in 1969.[18] It also became customary for research funders to require

[13] *Declaration of Helsinki,* 1964, https://www.wma.net/wp-content/uploads/2018/07/DoH-Jun1964.pdf.

[14] Juha Veijola (JV), interviewed on 20 November 2020.

[15] Adam Hedgecoe, "A Form of Practical Machinery: The Origins of Research Ethics Committees in the UK, 1967–1972," *Medical History* 53:3 (2009), 331–50; Adam Hedgecoe et al., "Research Ethics Committees in Europe: Implementing the Directive, Respecting Diversity," *Journal of Medical Ethics* 32:8 (2006), 483–6; Noortje Jacobs, "A Moral Obligation to Proper Experimentation: Research Ethics as Epistemic Filter in the Aftermath of World War II," *Isis* 111: 4 (2020), 759–80. See also the special issue How Ethics Travels: The International Development of Research Ethics Committees in the Late Twentieth Century, ed. by Noortje Jacobs and Helena Tinnerholm Ljungberg, *European Journal for the History of Medicine and Health* 78:2 (2021).

[16] *The Declaration of Helsinki,* 1975, 2. At https://www.wma.net/what-we-do/medical-ethics/declaration-of-helsinki/doh-oct1975/.

[17] *Eettiset toimikunnat: Toimintatietoja* (Helsinki: Lääkintöhallituksen julkaisuja nro 29, 1983).

[18] According to a survey, the committee in Oulu was discontinued and founded again some years later in 1976. There is no available evidence of an ethics committee at the University of Oulu besides the Board's survey. The Faculty of Medicine Archive of the University of Oulu (FOM), Research Ethics Committees, Folder 2. Kysely eettisten toimikuntien toiminnasta. A copy of a completed survey, signed by Juha Kukkonen.

a statement from a research ethics committee. In 1980, the Academy of Finland, the major research funding body in the country, started to require an ethics review in grant applications for research conducted on humans.[19]

In reviewing the research proposals, the Ethics Committee of the Medical Faculty of the University of Oulu relied on the Declaration of Geneva, the first revision of the Declaration of Helsinki, the Declaration of Hawaii, a code of ethics adapted by the World Psychiatric Association,[20] and the 1976 declaration of the European Council on the rights of the sick and dying. In practice, the medical research ethics committee of the University of Oulu in the 1980s based their ethical evaluation on a short research plan that included the name and aim of the study, material and methods, the implementation plan, the current state of research, and a list of publications. Some, although not all, ethics documents on birth cohorts have been preserved in the archive of the Medical Faculty, offering traces of ethical issues connected to birth cohorts in the 1980s.[21] The participants' anonymity was the main topic under ethical discussion. Some applications express the idea that good research guarantees ethical research. For instance, a plan from 1981 described the aim of studying the influence of social and emotional problems in the family at the time of the participant's birth. The research would include interviews with participants who had reached adolescence. In a letter to the Committee, Paula Rantakallio (1930–2012), a pediatrician and the prime mover behind the NFBC, confirmed that the man who would conduct the interviews had been trained by a child psychiatrist and had also studied the topic abroad and was thus skilled for the task. In addition to emphasizing the scientific credentials of the participants, Rantakallio explained the study hypothesis, according to which being "an unwanted child" impacted the mental health of the participant. She emphasized that the research would be double blind: neither the participants nor the analysts knew

[19] FOM, Folder 2. Apurahoja anoville tutkijoille. Pentti J. Taskinen, 29 May 1980.

[20] *Declaration of Hawaii*. The committee guidelines refer to a British Medical Journal issue from 1977, which is also available online in the *Journal of Medical Ethics* 4 (1978), 71–3. https://jme.bmj.com/content/medethics/4/2/71.full.pdf.

[21] The first NFBC-related research ethics committee document is dated 24 May, 1979. FOM, Folder 4. Signed by Pentti Taskinen.

who had been born "unwanted" and who was a control.[22] The arrangement would guarantee the full anonymity of the "unwanted" children and protect them from learning about their background. Commenting on another plan by Rantakallio, the committee expressed concern because participants were asked to sign the survey.[23] Rantakallio explained that the signature was not strictly necessary.[24] The timing of the committee process seems not to have been ideal: 8000 forms had already been returned. Rantakallio reported to the committee that only two young people had expressed any negative feelings about the research: A 14-year-old participant had declared the study useless, and another had stated that their school report and their father's smoking were private matters. And private they will stay, Rantakallio asserted. "This is a statistical analysis, which will not include case reports." She added that the data gathered by means of the form would be amalgamated into pre-existing anonymous data and identified by a number only. No social security numbers or names would be used.[25]

A few years later, the ethics committee discussed the anonymity issue in a different context, that of maintaining the anonymity of participants in small communities. The discussion concerned the upcoming launch of NFBC1986. The municipal board of health of a community in Northern Finland was concerned, because the mothers' social security numbers were included in the survey forms. In her response, Paula Rantakallio promised that all answers would be coded as soon as they reached the faculty.[26] The ethics committee decided that personal data protection had been taken into account as far as possible. The committee referred to Rantakallio's promise that personal data would be secure and to the fact that the participant could seal the form in an envelope immediately after filling it, thus

[22] FOM, Folder 2. Paula Rantakallio to the Oulu University Hospital ethics committee, 4 November 1981.

[23] FOM, Folder 2. The proceedings of the Oulu University Hospital ethics committee, 2 June 1981, § 4.

[24] *Nuorten terveystutkimus*. The Northern Finland Birth Cohort Studies Archive (NFBCSA).

[25] FOM, Folder 2. Paula Rantakallio to L. Kalevi Korhonen, 17 December 1980.

[26] FOM, Folder 4. Paula Rantakallio to the Inari-Utsjoki municipal federation for public health, 28 November 1984.

ensuring that no outsiders could see the information before it reached the faculty.[27]

At the turn of the millennium, the Medical Research Act (488/1999) changed the functioning of research ethics committees. According to the law, regional ethics committees had to be established in all hospital districts providing medical education, and the Government set up the National Committee on Medical Research Ethics.[28] Researchers who worked on birth cohorts at the time recall no significant changes, except that requirements became stricter and more specific.[29] Psychiatrist Matti Isohanni says that, as someone from his research group was always in the ethics committee, they always knew the "name of the game."[30] The interviewees perceived the role of the ethics committee as guiding and preventive. It helped the applicants to understand how the research plan needed to be improved—how, for instance, participants should be informed. The researchers mention the increasing amount of information that one had to provide for the participants as one of the disadvantages of the stricter ethics review.[31]

The birth cohort scientists traveled back and forth in time when they continued their former studies. The older research ethics committee reports and former ethics statements became entangled with the present ones, thus forming a multi-layered temporal environment. Accepting former ethical criteria was a prerequisite for using the old data. As the historian Tess Lanzarotta reminds us, acceptance carries the risk of reproducing problematic stances and it is therefore important to pay attention to whose ethical standards and whose time are being discussed.[32]

[27] FOM, Folder 4. The Ethics Committee of the Medical Faculty of the University of Oulu. 12 December 1984.

[28] Medical Research Act 488/1999, in English at https://finlex.fi/en/laki/kaannokset/1999/en19990488_20100794.pdf, 9–10.

[29] Irma Moilanen (IM), interviewed on 25 November 2020; Matti Isohanni (MI), interviewed on 10 November 2020.

[30] MI.

[31] SK-K; MI; IM; Eero Kajantie (EK), interviewed on 25 January 2021; Minna Ruddock (MR), interviewed on 14 December 2020 and 17 February 2023.

[32] Tess Lanzarotta, "Ethics in Retrospect: Biomedical Research, Colonial Violence, and Iñupiat Sovereignty in the Alaskan Arctic," *Social Studies of Science* 50:5 (2020), 778–801.

From Implied to Informed Consent

"It [informed consent] is quite a palette, having been collected differently each time."[33] This quotation characterizes not only the dimension of time but also the recent challenges birth cohort scientists have faced. The understanding of informed consent gradually changed and became more detailed. The 1964 Declaration of Helsinki had already recommended consent in written form, but NFBC scientists are under the impression that no written consent was sought when the first cohort was launched in 1965 and 1966. They believe that consent was understood differently then. This is in line with Ruth Faden's and Tom Beauchamp's view that, before the 1970s, the field of medicine was no more than "dimly aware" about informed consent.[34] Anna-Liisa Hartikainen, a gynecologist who has long worked with the NFBCs, recalls that, in the early days, completing questionnaires with the client at the maternity clinic was taken to imply consent.[35] Another researcher similarly characterizes consent as something that was "implicitly built in" when the participant completed a questionnaire or joined a study.[36] Implied consent differs from informed consent, the main difference being that the former is obtained implicitly through action or inaction. The concept of informed consent refers to voluntary consent after receiving relevant information. The subject must have civil competence to validate the consent.[37]

The invitation letter to a NFBC1966 youth health follow-up study in 1980 did not include a written consent form, indicating that consent was still seen as implicit, but the letter did provide information about the upcoming study. The letter described the potential significance of the factors observed in early childhood on later development and health. The letter also described how social and health services could be improved

[33] MR.

[34] Ruth R. Faden and Tom L. Beauchamp, *A History and Theory of Informed Consent* (Oxford University Press, 1986), 90. On the history of informed consent in the United States, see also Lydia Bazzano, Jaquail Durant and Paula Rhode Brantley, "A Modern History of Informed Consent and the Role of Key Information," *Ochsner Journal* 21:1 (2021), 81–5.

[35] Anna-Liisa Hartikainen (A-LH), interviewed on 14 January 2021.

[36] IM.

[37] Sorin Houstiuc, "Introduction," in *The Age of Informed Consent: A European History*, ed. by Sorin Hostiuc and Octavian Buda (Newcastle upon Tyne: Cambridge Scholars Publishing, 2018), 1–14.

with the help of combining the data of all participants. It was emphasized that participation was essential and that confidentiality would be guaranteed.[38] The first questionnaires of NFBC1986 included a brief description of the target group: All northern Finnish mothers with an expected delivery between 1 July 1985 and 30 June 1986. It was also stated that all data would be "kept confidential," and that the participant could seal her answers in an envelope.[39] The data gathered prior to 1997 can still be used in research, because informed consent is interpreted differently compared to newer data: As informed consent did not exist in its present form, it is not required.[40] This is an example of flexibility in the interpretation of research ethics in relation to the use of old data and former ethical criteria: Different criteria coexist.

The NFBC1966 follow-up study in 1997 shifted from implied to explicit consent. It was also the first time that biological samples were collected and clinical tests taken. The invitation letter described some of these tests. It also informed the participants that they would get some of the test results immediately, whereas blood sample results on cholesterol and blood sugar levels would be mailed to them later. The principle of voluntary participation was clearly expressed: "By participating voluntarily, you are making an important contribution to combating public health problems and, in particular, to improving the health of people in Northern Finland. You will also gain valuable information about your health during the study." The letter included a separate section entitled "Data protection is important," which assured that all data would be handled without the name and personal identification number of the participant, and that the data would be used for research purposes only.[41] Interestingly, this follow-up study was the last to mention the health of people in Northern Finland, which may indicate a slight change in the goals of the research program, which was increasingly heading toward

[38] FOM, Folder 2. Paula Rantakallio, an invitation to take part in a study.

[39] NFBCSA, Mother–Child 1985 Project. Questionnaire form. See https://www.oulu.fi/sites/default/files/kysely%20valkoinen%20eng.pdf; https://www.oulu.fi/sites/default/files/kysely%20keltainen%20eng.pdf.

[40] JV.

[41] NFBCSA, Selvitys Pohjois-Suomen kohortti 1966:n hyvinvointi- ja terveystutkimusohjelmasta. A document sent to NFBC1966 research participants in 1997.

international arenas.[42] Originally, the participants agreed to enhance the health of the people in Northern Finland, but, over time, the follow-up studies became more clearly seen as an opportunity to learn about one's personal health.[43]

Psychiatrist Juha Veijola, who has been actively involved in birth cohort studies since the 1990s, remembers how the informed consent form of the 1997 follow-up study changed his way of thinking. The form was more detailed than before; the participants gave their consent and also permission to gather other data. This provided Veijola with the insight that the researcher did not own the data; he refers to a shift from a researcher-driven to a participant-driven approach.[44] The process prioritized the participant in a new way, questioned the researchers' position, and made them reflect upon their position as epidemiologists. Although an improvement from the participant's perspective, the change has presented researchers with new challenges that sometimes frustrate them. As one scientist puts it, "Obviously, I appreciate that personal data must be protected, and people need to know what their data are used for, but these changing policies and cultures complicate the work of researchers." She adds that "Sometimes, it would be better to make interpretations considering what is best for research, because we are not offending anyone's privacy in any way."[45]

In 2012, the NFBC1966 participants were invited to a 46-year follow-up study, which now seems like a turning point in many respects. First, the amount of research subsequently exploded. Second, new obstacles connected to the issue of informed consent emerged because of certain wordings in the invitation. The invitation letter told the participants that, by participating, they would help the researchers gain important information about the health of their generation and improve the health and

[42] Katariina Parhi, "Kohti tasa-arvoisia terveyspalveluja: Pohjoissuomalaisten terveys syntymäkohorttitutkimuksen lähtökohtana," *Historiallinen Aikakauskirja* 119:3 (2021), 318–31.

[43] On NFBC participants' motivations and the significance that they assigned to the study, see Anna Rönkä, "'From Birth to Death, From Beginning to End': Participant Experience and the Meaning of Research Participation in a Longitudinal Birth Cohort Study," *SAGE Open* (April–June 2022, 1–16), https://doi.org/10.1177/21582440221099297

[44] JV.

[45] SK-K.

wellbeing of the population. It ensured that all data would be handled without names and social security numbers. As a new element, the cost of clinical examinations was estimated at between 800 and 2000 euros. Some population and health registers were mentioned as an additional source of information in the study. A new motivational factor was also mentioned: In taking part in the research, the participants might help to create possibilities to develop new medical equipment and research and treatment methods, possibly in cooperation with local companies.[46]

Several new ethical and legal challenges have emerged since 2012. The use of register data has become more complicated, as participants should now be informed about all registers that might be used in the research. The epidemiologist Jouko Miettunen explains how this might hamper the NFBCs in the future: "If you [the participant] don't want to give permission [to use certain registers], you forbid them all […]. This has an impact on research, I think, on the results and on their reliability."[47] Business collaboration is another challenge. The NFBC research director Minna Ruddock recounts that the national data protection ombudsman and the lawyers consulted by the cohort center found that the information in the old consent document failed to meet the requirements of the GDPR, enacted years after the consent document was designed. The participants had consented to their data being used for creating new biomedical business opportunities, but the nature of these ventures had not been specified in the form, as they were not known, or did not exist, at the time. According to the lawyers, the consent form should have been more specific; the participants should have been told the specific commercial uses of the data. This interpretation, Ruddock regrets, "watered down the collaboration with companies."[48] One cohort scientist suspects that the legal challenges might be connected to caution and inexperience in the legal field. Legal advisers failed to see that asking for a new informed consent from 6000 participants was unrealistic. "If you think about it, we would need staff for months to contact people, to send them consent forms, to persuade them. We would then get three or four thousand forms back. We could be in a situation that we would not have a representative

[46] NFBCSA, Selvitys Pohjois-Suomen kohortti 1966:n hyvinvointi- ja terveystutkimusohjelmasta. A document sent to NFBC1966 research participants in 2012.

[47] Jouko Miettunen (JM), interviewed on 16 November 2020 and 16 February 2023.

[48] MR.

set of data, and we would have to give [the research] up. In practice, new informed consent can be a disastrous decision […]."[49]

The use and deposition of the so-called legacy samples—older biological samples transferred to the new biobanks—are another thorny ethical and legal issue related to the reuse of NFBC resources. The University of Oulu has developed a way to tackle the problem of changing requirements pertaining to biological samples. Each cohort participant will be informed that their samples will be transferred to the Arctic Biobank, established in 2020, and handled following the Biobank Act (2013), currently under revision.[50] At the time of the interview, the biobank was expected to reduce bureaucracy, but since then, new issues have emerged.[51]

Although the scientists regard it as important to inform the participants about the study, they also feel that there is a point after which added information no longer benefits the participant. "If they [invitation letters] are too long, they [the participants] do not necessarily read them properly, they sort of skim through them," research nurse Anu Outinen-Tuuponen suspects. All participants in the recent NFBC1986 33–35-year follow-up study had time to go through the information when it was sent to their homes, and everyone was reserved time to ask questions when they came to the follow-up study examinations. Outinen-Tuuponen emphasizes the importance of clarity and understandability. These should be permanent standards and not affected by the legal changes over time. "The experience I have of working as a research nurse is that these issues are changing constantly. Now everything has to be really specific, and everything needs to be described—how you use the data. And decades ago, everything had to be clearly expressed, and the letter couldn't be more than one A4 sheet. Nowadays, they're huge. It's a challenge to know which of

[49] EK.

[50] On the challenges related to the GDPR and biobanks, see e.g. Ciara Staunton, Santa Slokenberga and Deborah Mascalzoni, "The GDPR and the Research Exemption: Considerations on the Necessary Safeguards for Research Biobanks," *European Journal of Human Genetics* 27 (2019), 1159–67. On this issue of legacy samples in the national context, see Marjut Salokannel, Heta Tarkkala and Karoliina Snell, "Legacy Samples in Finnish Biobanks: Social and Legal Issues Related to the Transfer of Old Sample Collections into Biobanks," *Human Genetics* 138 (2019), 1287–99. On Finnish biobanks, see Ministry of Social Affairs and Health, "Biobank Activities Will be Harmonised," at https://stm.fi/en/personalized-medicine/biobank-operations.

[51] MR.

the participants has read that text carefully."[52] The epidemiologist Jouko Miettunen wonders if informed consent will scare away participants in the future. He has discussed the possibility of placing some of the consent-related information at the beginning and some at the end of the invitation letter to avoid exhaustion.[53]

It is not always possible to provide the participants with all the information that is relevant for the research. For example, in a study that examined the significance of the mothers' smoking during pregnancy, the participants only knew they were invited to a study on smoking; they did not know whether they were controls or not. The purpose was to guarantee the confidentiality of the mothers' earlier answers. In another study, on psychosis, the scientists considered if they should inform the participants that they had been invited because they had had psychosis; and the solution was that they were informed.[54]

Data Protection

The European General Data Protection Regulation (GDPR) has highlighted the importance of detailed informed consent forms, with major implications for birth cohort studies.[55] Prior to the introduction of the GDPR in 2018, cohort scientists followed the Finnish Personal Data Act (523/1999). Data protection had been a big issue for two decades before the GDPR. Minna Ruddock explains the difference made by the GDPR: "The GDPR brought a change that required us to be able to tell these things to the participants, not just to other researchers. It has been a big change to understand." She continues that another challenge for researchers is to grasp the new definition of personal data, that even coded health-related data are defined as personal, sensitive data.[56] With

[52] Anu Outinen-Tuuponen (AO-T), interviewed on 10 February 2021.

[53] JM.

[54] JV.

[55] See the rules for the protection of data inside and outside the European Union at https://ec.europa.eu/info/law/law-topic/data-protection_en. Various interviewees mentioned the GDPR even before being asked and emphasized the challenges it poses to research. E.g., Jarmo Rusanen (JR), interviewed on 30 November 2020; Anneli Yliherva (AY), interviewed on 29 October 2020; JM; TL.

[56] MR.

changes in legislation, researchers are thus required to renew their definition of data and data protection. According to the cultural anthropologist Alison Cool, who has studied the anxieties of researchers concerning the GDPR in Sweden, the law has reinforced the researchers' thinking of themselves as ethical subjects who must consider the "real people" and their intentions behind the data, even if the researchers only handle data in an abstract form.[57]

"The GDPR has been a challenge," Ruddock states, referring to the time it has taken to try to interpret it in the context of birth cohorts. However, she continues by admitting that it has also brought something positive to birth cohort studies, including clarity. She notes: "It takes time before new laws fit, especially in the context of old data such as ours. The GDPR […] was designed because big companies use people's data and collect data about us. But how do you apply it to data such as ours, with old consent forms and lots of research material?"[58] The process has been arduous, and lawyers have played a major role in the transition. It is evident that legal experts and epidemiologists have different interpretations concerning the use of longitudinal data. Ruddock also found that the very specific wordings favored by lawyers tended to lead to long and complicated expressions.[59] According to one NFBC scientist, the quality of legal consultation has improved in recent years, "but still, it [the GDPR] causes an incredible amount of work."[60] Transnational data exchange is another challenge exacerbated by the GDPR. NFBC scientists participate in many international collaborations involving data exchange. It has become difficult to know if and on what conditions NFBC data can be used by international partners. "If you ask one lawyer, you will get a different answer from the one you get from another, and different answers at different times. This is awfully uncertain," Ruddock says. She believes that technical innovations such as data shield solutions will become more common and make it easier to analyze personal data without transferring it to different locations.[61] At the time of the

[57] Alison Cool, "Impossible, Unknowable, Accountable: Dramas and Dilemmas of Data Law," *Social Studies of Science* 49:4 (2019), 503–30.

[58] MR.

[59] MR.

[60] EK.

[61] MR.

interview, the NFBC Project Center had improved data protection by using double pseudonyms. However, as Jouko Miettunen explains, they slowed down the research process. Previously, each participant had an ID number which was kept in the Center, but now every project was given its own participant ID number. Today, when cohort data is combined with nationwide health registers, it is done in secured environments, such as the Findata-provided Kapseli environment, and double pseudonyms are not needed.[62]

The geographer Tiina Lankila describes the change that has taken place over ten years: "It was completely different when I started. One person could get me the data I needed […], and I didn't have to plan what I wanted beforehand. I could go data mining. Today, I have to clearly define the data I need, and then the NFBC Project Center collects the data after a research permit process. The data can no longer be stored on the researcher's own computer."[63] On a general level, the NFBC researchers confirm that the use of data has been less careful in the past and that GDPR has improved the general attitude and awareness.[64]

Scientists are also concerned that public discussion of problems of data protection may cause attrition. As one interviewee puts it, "you no longer want to give data because you doubt what it will be used for."[65] Younger cohort participants ask more questions about data protection. During the personal meetings in the follow-up studies, the nurses are trained to provide answers to the questions the participants may have. Anu Outinen-Tuuponen perceives answering such questions as an essential part of the study: "It's extremely important that the participants know where the data are going, and what the data are used for."[66]

Keeping the Participants Informed

The relationship between the birth cohort study scientists and the participants is central to the success of a long-term birth cohort study.

[62] JM.

[63] Tiina Lankila (TL), interviewed on 30 October 2020.

[64] Esa Läärä (EL), interviewed on 29 January 2021; Raija Korpelainen (RK), interviewed on 7 December 2020; JR.

[65] Anja Taanila (AT), interviewed on 26 November 2020.

[66] AO-T.

Participants should remain committed to the study, which, in the case of NFBC1966, has been going on for almost sixty years. Some birth cohort research teams are in the habit of sending birthday cards to participants, thus reminding the latter about the continued significance of participation and checking their whereabouts. Hannah J. Elizabeth and Daisy Payling have studied the changing significance of birthday cards that were originally sent to British cohort participants. To begin with, the cards were above all a means of updating contact information. Over time, they started to express emotions and stress the collaboration between the researchers and the participants.[67]

NFBC team does not keep in contact with participants in this manner. Neither do NFBC researchers evoke emotional or collaborative aspects between researchers and participants in their interviews. Rather, they discuss participant experience in terms of the objectives of the study. On the one hand, participants should feel committed to the study and motivated to remain in the cohort. On the other hand, the birth cohort study, not being interventionist, should meddle with the participant's life as little as possible. The research focuses on populations, not individuals, who benefit indirectly from the knowledge generated about the population. However, a cohort member who takes part in the study and is examined during the follow-ups is inevitably also interacting with the experts associated with the study. Interaction takes place when the participants are contacted and invited to take part in the study, when they are examined and tested, and when they are informed about the test results. Apart from that, interaction is kept to a minimum.

Ute Kalender and Christine Holmberg have discussed the concept of "courtesy work" in the context of cohort studies. The term underlines the need to treat participants with courtesy and respect during all stages of a cohort study, both in written and spoken communication and during the physical examinations. Care practices include mitigating the discomfort caused by bodily measurements, minimizing participant shame, providing reinforcement, and withholding information about results. In the words of Kalender and Holmberg, courtesy work has succeeded if the participant is not left feeling "bad, ugly, addicted, or old."[68]

[67] Elizabeth and Payling (2022).

[68] Ute Kalender and Christine Holmberg, "Courtesy Work: Care Practices for Quality Assurance in a Cohort Study," *Social Studies of Science* 49:4 (2019), 583–604.

Although NFBC interviewees do not use the term "courtesy work," they are aware of the concept. Research nurse Anu Outinen-Tuuponen, for instance, stresses the need to train the NFBC nurses to listen to the participants' concerns and to answer their questions. "They [the participants] are the most important thing—and their motivation. Without their active participation, we wouldn't be doing this research,"[69] says Outinen-Tuuponen. The follow-up studies follow the Good Clinical Practice guidelines, an international ethical and scientific quality standard for research that involves human subjects.[70] A sub-group that calls for especially intensive courtesy work are cohort members who have undergone psychosis. Matti Isohanni emphasizes that they are important for psychiatric research, but recognizes that examinations can burden them. Participants' recollections of earlier encounters with the NFBC staff influence their willingness to take part in the future: "We had some patients with psychosis whose mother said that when the patient went to the follow-ups eight years earlier, he or she was messed up for weeks afterwards. Then they were forbidden to come this time. Often, we asked if the nurses could visit their home, and many of them said yes; some of them said no."[71] Home examinations are carried out by experienced nurses.[72] An article evaluating such home examinations concludes that they were worth the effort, as they increased the participation rate and helped attain non-biased data.[73]

NFBC participants are informed about the results of their follow-up examinations, but the cohort does not offer them any treatment. The NFBCs have a clear policy: patients are notified if abnormalities defined in the study protocol are found.[74] Serious illnesses such as leukemia are reported to the participant immediately. Participants whose test results do not fall within predefined reference values are contacted and advised

[69] AO-T.

[70] See European Medicines Agency, ICH E6 (R2) Good Clinical Practice, https://www.ema.europa.eu/en/ich-e6-r2-good-clinical-practice.

[71] MI.

[72] MI.

[73] Marianne Haapea, Matti Isohanni, Erika Jääskeläinen, Juha Veijola and Jouko Miettunen, "Using Home Recruitment to Increase Participation and Representativeness in Research Among Individuals with Psychosis," *Psychiatria Fennica* 51 (2020), 108–21.

[74] NFBCSA, e.g. 46-year follow-up study protocol https://www.oulu.fi/sites/default/files/86/Koh66%2046-v%20protokolla%20040412_muokattu_25022021.pdf, 68–9.

to visit their health center.[75] In addition, they receive a summary of the results of the clinical tests, for example blood pressure and breathing capacity. The interviewees perceive test results as something that motivates the participants to remain in the study. However, the research ethics committee told the investigators to remove a table that detailed the normal cost of the tests and measurements from the invitation letter, because "luring participants is unethical," as one of the interviewees paraphrased the resolution.[76]

Some studies have argued that interaction with birth cohort participants is beneficial. For example, Patricia Lucas and others have studied how European cohort studies engage with young cohort members. They recommend engagement, exchange of information, consultation and coproduction with participants.[77] The interviewed NFBC scientists mainly disagree, believing that interventions should be kept to a minimum and the cohort thus as "natural" as possible.[78] In practice, this means that the participants should not be contacted between follow-up studies or given any guidance during them. For example, the nurses who conduct the clinical examinations during follow-up studies should not comment on the participants' weight or other health-related issues. As the research nurse Anu Outinen-Tuuponen puts it, "It is not our task to offer guidance in making certain choices."[79] Matti Isohanni agrees that interventions should be avoided, but he also notes that this is one of the things that disadvantages epidemiological studies in the eyes of funders, who prefer interventionist studies with practical results, for example studies that test the efficacy of a treatment. "We just watch how badly it [the participant's life] is going—what's the benefit in that?"[80] Isohanni's discontent about the second place that non-interventionist studies hold is partly borne out by the history of science. As Lorraine Daston and Elizabeth Lunbeck have noted, there has, since the first half of the nineteenth century, been a

[75] Marjo-Riitta Järvelin (M-RJ), interviewed on 16 December 2020.

[76] JM.

[77] Patricia J. Lucas, Debra Allnock and Tricia Jessiman, "How Are European Birth-Cohort Studies Engaging and Consulting with Young Cohort Members?" *BMC Medical Research Methodology* 13:56 (2013), http://www.biomedcentral.com/1471-2288/13/56.

[78] AT.

[79] AO-T.

[80] MI.

tendency to value "active" experimentation more than "passive" observation: "Whereas experiment demanded ideas and ingenuity on the part of a creative researcher, observation was reconceived as the mere registration of data […]."[81]

Neither does NFBC actively communicate the research results based on the cohort data to the participants. Although NFBC experts mainly agree that it would be a good thing to inform the participants about research results (currently, the best way to find research is the NFBC website, which is not specifically designed to serve the participants), they also see some problems in active science communication. When population-level risk predictions are applied on an individual level, the conclusions can be both misleading and disconcerting.[82] The statistician Esa Läärä discusses the dilemma: "There is a certain problem in epidemiology: What if something new is found out about a certain risk factor and its impact, something that has a more or less weak association with an illness—what do the participants think if they have this risk factor?"[83] He continues that "epidemiological knowledge is also problematic on an individual level, because we cannot predict what is going to happen."[84] Sociologists of science have discussed the problem identified by Läärä on a more general level. David Armstrong has noted that while a population is a "sum of individual identities," a "fluid denominator, comparator, context and analytic space," it is increasingly used to define individuals. The two constructs are bound together through prediction.[85]

[81] Lorraine Daston and Elizabeth Lunbeck, "Introduction," in *Histories of Scientific Observation*, ed. by Lorraine Daston and Elizabeth Lunbeck (Chicago: University of Chicago Press, 2011), 1–9.

[82] See also Susanne Bauer, "Modeling Population Health: Reflections on the Performativity of Epidemiological Techniques in the Age of Genomics," *Medical Anthropology Quarterly* 27:4 (2013), 510–30.

[83] EL.

[84] EL.

[85] David Armstrong, "Clinical Prediction and the Idea of a Population," *Social Studies of Science* 47:2 (2017), 288–99.

Conclusion

Longitudinal epidemiological research is slow to respond to changes. Old data cannot be discarded just because they become outdated. The long history of birth cohort studies seems to have a time-dependent downside. When trends in science change, birth cohort studies need to find ways to respond to novel requirements. Scientists shift between the meanings and interpretations of research ethics in different temporalities. Epidemiological knowledge-production is tied to various temporal aspects, including changing interpretations of central concepts such as informed consent, legal changes, technical novelties, and the changing role of the scientist and the participants. Past, present, and future coexist in a specific way in epidemiological knowledge-production by means of longitudinal cohort studies.

This chapter has illustrated how the foci in medical research ethics have shifted. High-quality research, as opposed to poor research, used to be perceived as ethical. In the 1960s, increasing the wellbeing of the population in Northern Finland was considered an ethical goal. The importance of research was emphasized in the invitation letters to the participants—they were offered an opportunity to contribute to the greater good of the local society. Over decades, this emphasis has diminished, and research has become increasingly international. The criteria for ethical research are assessed as a separate aspect and from various perspectives, including informed consent and data protection above all. The NFBC scientists go back and forth between different ethical criteria, making sense of coexistent temporalities, which may be the only way to continue using longitudinal data successfully.

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