Interview

Interview with Dr. Peter Lurie on the ethical controversies of placebo-controlled trials
— As a part of the program of webinar on the 2024 Declaration of Helsinki: Taking forward Bioethics and Human Rights —*

Peter Lurie
Center for Science in the Public Interest, United States

Interviewed by
Chieko Kurihara, Clinical Evaluation

(August 14, 2024, Washington DC, United States)

Abstract

This article is a record of an interview with Dr. Peter Lurie by Chieko Kurihara in Washington DC on 14 August, 2024, as a part of a programme of webinars held on 5 and 26 August to discuss the 2024 revision of the Declaration of Helsinki from the perspectives of external stakeholders. Lurie participated in the 26 August webinar as an invited commentator. Kurihara participated as an invited panelist at the regional meeting organized by the World Medical Association/American Medical Association on the revision of the Declaration of Helsinki in Washington DC on 15 and 16 August. We took this opportunity to discuss the ethical issues of the placebo clause in the Declaration of Helsinki (2013 version and available draft versions for the 2024 revision).

Key words
Declaration of Helsinki, placebo-controlled trial, double standard, justice, developing countries

Rinsho Hyoka (*Clinical Evaluation*). 2025；52(3)：453-62.

抄録

本稿は，2024年8月5日と26日に開催された，ヘルシンキ宣言2024年改訂を外部ステークホルダーの視点から議論するウェビナーの一環として，8月14日にワシントンDCで行われた栗原千絵子によるDr. Peter Lurieへのインタビュー記録である．Lurieは8月26日のウェビナーにコメンテイターとして招かれた．栗原は，8月15・16日にワシントンDCで開催されたヘルシンキ宣言改訂に関する世界医師会／米国医師会主催の地域会議に，パネリストとして招待された．この機会に，ヘルシンキ宣言（2013年版および2024年改訂のための草案）におけるプラセボ条項の倫理的問題について議論した．

キーワード
ヘルシンキ宣言，プラセボ対照試験，ダブルスタンダード，正義，開発途上国

＊ This article is updated from the Preprint published on October 10, 2024, of which related information is available at: http://cont.o.oo7.jp/52pop/52pop_contents_e.html
本稿は2024年10月10日のプレプリント公開から一部形式修正してあり，関連情報と録画は上記URLより閲覧できる．

1. Introduction: Controversy on placebo trials in 1990s and current topics

Chieko Kurihara　Thank you so much for accepting this interview at Washington DC, following our previous collaborations for the ethics of placebo-controlled trials [1, 2]. I am happy to be able to meet you here, just before participating in the regional meeting on the 2024 revision of the Declaration of Helsinki (DoH), held by the World Medical Association (WMA) [3]. As one of the organizers of our webinar held on August 5 and 26 [4], by a group of stakeholders, external from the WMA, to discuss about the 2024 revision of the Declaration of Helsinki (DoH), I wish to have this interview in order to publish together with the proceedings of the webinar. This is because you took a historically important role to open the international debate on ethics of placebo-controlled trial, by the paper published from New England Journal of Medicine in 1997 [5], as well a paper with Prof. Dirceu Greco which appears on the cover page of the Lancet [6]. We published extensive analysis on the issues of placebo [7] and post-trial access [8] in Springer book published last November. Prof. Greco is also an organizer of our webinar and strongly wishes to involve you. First, I would like to ask you to speak about your activity in which you are now most interested in and most involved in.

Peter Lurie　After being deeply involved in research ethics discussions first as an academic and then at the consumer advocacy group Public Citizen, I worked for the FDA (Food and Drug Administration) for about eight years on various issues. When the Trump administration came in, I didn't feel it was the right place for me, so I left and joined the Center for Science in the Public Interest (CSPI), an advocacy group in Washington.

CSPI's primary focus is on food, especially labeling, and claims around nutrients like added sugars, saturated fat, and sodium. As head of the organization, I've expanded our work to include drugs, medical devices, diagnostics, COVID, dietary supplements, and misinformation. These are our current focuses.

Kurihara　Could you introduce how is the starting of the debate on placebo-controlled trials in developing countries?

Lurie　In early 1997, I was invited to a meeting with journalists in Abidjan, Cote d'Ivoire, West Africa about HIV, focusing on African research and journalism. The CDC Group in Abidjan presented a study on short-course AZT for preventing HIV transmission from pregnant women to infants. The journalists became extremely upset, shouting at the CDC representative, who was African, questioning why they were given only "half a dose" of AZT. The CDC explained that a half dose might be safer and cheaper than the full dose that had been proved effective in a randomized, controlled trial vs. placebo. I went to the microphone and questioned what the comparison group was. The CDC replied it was a placebo. Shocked, I agreed with the African colleagues that the study was troubled.

We then compiled a list of studies by the American government, other governments, and WHO UNAIDS, discovering that all but one study in developing countries used a placebo group. Interestingly, American studies had no placebo group, highlighting a double standard. This led to our New England Journal of Medicine paper, which spurred thinking and inquiry into international research ethics. Many have since advanced the debate, and it was significant to be at the start of it.

Peter Lurie, M.D., M.P.H. is President of the Center for Science in the Public Interest. CSPI envisions a healthy population with reduced impact and burden of preventable diseases and an equitable food system that makes healthy, sustainable food accessible to all. CSPI publishes a newsletter, *Nutrition Action*, and conducts advocacy on Capitol Hill, in the regulatory agencies, in the courts, at the state and local level, and through corporate campaigns. Previously, Lurie was the Associate Commissioner for Public Health Strategy and Analysis at the Food and Drug Administration, where he worked on antimicrobial resistance, agency transparency, caffeinated beverages, arsenic in rice, expanded access to investigational drugs, and prescription drug abuse. Prior to that, he was Deputy Director of Public Citizen's Health Research Group, where he addressed drug and device issues, coauthored the organization's *Worst Pills, Best Pills* consumer guide to medications, and led efforts to reduce worker exposure to hexavalent chromium and beryllium. Earlier, as a faculty member at the University of California, San Francisco and the University of Michigan, he studied needle exchange programs, ethical aspects of mother-to-infant HIV transmission studies, and other HIV policy issues domestically and abroad.

2. Public understanding of placebo-controlled trial

Kurihara How was the public debate involving Congress members or the general public in the US?

Lurie I think many people in the Congress found it a difficult issue and didn't fully understand it. Understanding it required knowledge of technical issues, such as randomized trials, control groups, sample size calculations, and even some economics.

On some level, it was true that the issue was complicated, so people often deferred to those they trusted. I felt people weren't exercising enough independent judgment. However, the debate was simple and elemental enough for most lay people to understand. When explained fairly and objectively, most lay people I knew were horrified by what was happening.

Kurihara In Japan, ethics committee or informal consent process, for any randomized controlled trial, we can accept the trial when we don't know which arms are better. If we stand this argument, "clinical exposure" or "uncertainty" is paramount rather than the level of risk stated in the DoH "no increase of risk of serious or irreversible harm". This is very difficult for the general public to understand, and our group of patient and public expressed their opinion how it was difficult for them [9].

Lurie In the early days of the AIDS epidemic, AIDS activists criticized the lack of drug treatments for HIV. I remember waiting for a movie in San Francisco with an ACT UP activist behind me, who argued that placebos were always unethical. At that time, many AIDS activists shared this view.

Over time, as AIDS activists interacted more with mainstream medicine, they saw that drugs they were confident in often didn't work. Many AIDS activists became very rigorous in their approach, and some of the most rigorous individuals today are former AIDS activists who value good data. Initially, there was hostility

towards placebos and randomization, but AIDS history shows a development of greater trust, which has been highlighted by the COVID situation.

The value of randomized trials became clear with hydroxychloroquine, vaccines, and ivermectin. The COVID experience has demonstrated the importance of randomization in clinical trials.

In my current work, this appreciation for randomized trials continues to grow. Many nutritional recommendations were based on observational studies, which often showed results that conflicted with those from randomized trials.

3. Other examples of ethical controversies of controlled trials

3.1 Surfaxin trial

Kurihara　I'd like to ask for your opinion or experience of the other unethical, not only the unethical but some kind of important examples of the randomized trial or placebo-controlled trial.

Lurie　After completing our work on perinatal trials, we kept an eye out for similar examples. It didn't take long to find one: Surfaxin, a surfactant for use in ventilated neonates to restore normal ventilation [10]. Several placebo-controlled trials showed dramatic benefits in both aeration and mortality. The FDA had approved at least four similar drugs by then.

Discovery Laboratories wanted to develop a fifth drug and faced a dilemma: compare it to nothing or to one of the existing drugs. We argued that with four proven effective drugs and the poor prognosis of the patients for whom the drug was indicated, continuing placebo-controlled trials was unacceptable. The study design was already set, but the location was still undecided, a clear indication that it was not locally initiated.

Interestingly, many found the Surfaxin case easier to understand than the perinatal trials. This was likely because Surfaxin involved a drug company, whereas the perinatal trials involved organizations advocating for patients like governments or the UNAIDS program.

From my perspective, it doesn't matter if the entity withholding effective therapy is a government, NGO, or drug company. For patients, the distinction is irrelevant if they're not receiving effective treatment. The National Bioethics Advisory Commission in the US also implicitly made this distinction, focusing on condemning Surfaxin while avoiding the perinatal trials issue.

3.2 Needle Exchange Program

Lurie　Another example, a lesser-known case involved Needle Exchange Programs. I had previously worked on needle exchange programs and had written a report for the CDC in which we concluded that the needle exchange programs reduced new HIV infections without increasing drug use. Major public health organizations globally endorsed needle exchange as part of HIV prevention for drug users. However, I was invited by a researcher in Alaska to join an ethics committee for a randomized trial involving drug users. The study planned to randomly assign participants to either a Needle Exchange Program or to receive advice on obtaining syringes from a pharmacy.

Participants in the Needle Exchange Program could exchange syringes, while those not selected were given tips on how to trick pharmacists into selling them syringes. This approach seemed absurd and unethical, resembling the issues seen in Surfaxin or the perinatal trials.

Furthermore, the study aimed to measure needle exchange effectiveness by comparing hepatitis B rates between the groups, because there wasn't enough HIV up in Anchorage where the study was to take place, despite the availability of an effective FDA-approved hepatitis B vaccine. This approach was similar to the Tuskegee study, where individuals were deliberately left untreated to observe outcomes.

Ultimately, Harold Varmus, head of the NIH, overruled the advisory group on the vaccination (but not the needle exchange) aspect and mandated vaccination for participants. This decision presumably undermined the trial's design as the vaccine was highly effective. The study eventually failed due to low participant numbers and infections, but it highlighted unethical practices in global research, if applied domestically, could have an injurious outcome, especially in a country with significant health disparities.

3.3 COVID-19 vaccine: issues of acceptable risk and double standard

Kurihara Next, COVID-19 vaccine, you talked previously in the webinar [2].

Lurie There were a number of ways I compared COVID to the examples I just mentioned [11]. One was the magnitude of the risk. As soon as the COVID epidemic occurred and people pursued vaccines, we wondered about the practice with placebos. Many infections were in developing countries, so we wondered what would happen [12]. It wasn't long before the WHO Experts said that even if a first vaccine was effective, it was still okay to trial a subsequent vaccine in the developing world with a placebo [13], revisiting the same argument as in perinatal trials.

That was very disappointing. The arguments are similar. One difference is the degree of risk in COVID was much less than in perinatal. The perinatal example was extraordinary because the Number Needed to Treat (NNT) to prevent a baby from getting a fatal infection was about six, as high as anything in medicine. It was remarkably effective. Part of what went wrong in the perinatal debate was not fully appreciating that effectiveness and its implications.

Even I remember when it came out, people said, "Well, maybe it works, but it causes anemia." I said, "Yes, I don't care much if it causes anemia when one time in six it saves a baby's life." I'm willing to tolerate a lot of anemia for that. They said maybe it doesn't work in the developing world or something. They kept coming up with these arguments. Many were saying nothing about the original trial with AZT. I thought it was a remarkable intervention, and it was worse that it was being withheld.

The COVID vaccine was different because while a baby with HIV would likely die within 10 years, most COVID cases were not as severe, and, in epidemiological terms, few died. Thus, the number needed to treat was in the hundreds. This made it different from perinatal.

Was that difference enough to come out the other way on the ethical question? I don't think so. At some point, the risk is very, very small. It's truly minimal. But that was not where we were with COVID.

We tried to find if there were any COVID vaccine trials with placebos after the initial ones had shown effectiveness and eventually found a small phase II trial. It was already completed. We didn't follow up due to our focus on other COVID issues.

Kurihara The first point concerns the difference in acceptable risk from losing opportunity of effective treatment. The second point involves a double standard. In Japan, a pharmaceutical company conducted a placebo study, for example, in Vietnam. This situation is similar to the WHO's statement. In Japan there is no additional vaccine needed, because Japanese government bought top vaccines 7 times of volume for entire

population [14]. The need would be only for assuring capacity of Japanese company to produce vaccine. For this reason, the company conducted a placebo trial outside Japan. In Japan, only a pharmacological study was conducted as "bridging study" to find immunological response in Japanese research participants.

Lurie　Yes, you make a good point. The question I was addressing was the magnitude of the risk, which raises the issue of how much risk is acceptable. Reasonable people can disagree about that, but none of it justified the double standard. It also reached a point where the vaccines – Moderna, Pfizer, and so on – were somewhat available in these countries, so even the argument that "nothing" was the standard of care didn't hold up. It wasn't like when we were dealing with perinatal, where there was very little AZT available.

But even then, a wealthy woman in Abidjan, for instance, could likely get AZT if pregnant and HIV-positive, but that was the top 1%. For COVID, WHO's recommendation occurred at a time that hardly any countries had fewer than 10% vaccinated. This undermined that part of the argument and exposed the double standard, especially given the availability already present.

4. Public involvement

Kurihara　Next, please share your experience and opinions on public involvement.

Lurie　This kind of activism is different from street activism, where big rallies occur. It's elite activism based on science, taking place in closed, dark rooms. It's activism nonetheless but in a different form. Influencing decisions can be easier if you have the right training and can express yourself in ways that those in power understand.

Being trained and experienced helps you enter these rooms and make arguments, though sometimes you may be invited just as a token. Some places don't even invite you, despite the potential benefits of saying they did. In the US, there are opportunities to be heard.

When the government proposes a rule, there is a public comment period where you can express your views. The government must address each comment in writing before finalizing the rule. Additionally, you can obtain documents through the Freedom of Information Act, which can provide valuable information. For instance, during the perinatal issue, documents revealing internal CDC discussions were obtained, showing lack of equipoise by those involved in the trials.

You can also file petitions with the government, which must respond, and if they fail to act or respond as desired, you can take legal action. Access to the courts allows for challenging government decisions, providing a chance to win cases through legal means. And sometimes there are public meetings at which you can testify.

Kurihara　For the government, it is better to request for public comment rather than battle in the court.

Lurie　The government generally wants to avoid court because it is time-consuming, distracting, and carries the risk of losing. Having been in government, I can confirm that being pulled into court is something the government tries to avoid at all costs.

Currently, this is even more complexity due to recent Supreme Court decisions that have been unhelpful to the government and likely empower big corporations. These rulings make it harder for the government to pursue actions in the public interest, as they are now more vulnerable to challenges than before, especially from industry. The current direction is not favorable for public-interest governance.

Meeting with Dr. Peter Lurie
August 14, 2024
The Westin Washington DC City Center
(Venue of the WMA meeting)

Discussion at a restaurant in front of the Brazilian Embassy (right) and an open park.

5. Current draft of the 2024 revision of he DoH

Kurihara How is your impression of the DoH current draft?

Lurie I don't follow these issues as closely as I used to, but what's striking is how similar the current debate is to the old one. It's the same issues and arguments repeating. I'm still struck by the lack of a true ethical basis for placebo use in the developing world. It seems driven to a significant extent by a desire for data, with ethical arguments retrofitted to justify that.

The same arguments persist in this kind of work, requiring eternal vigilance. Even when you think you've won, the issue can resurface. I'm grateful for your work because without resistance, companies and governments will win. It's critical to have people pushing back.

In the long term, I believe people will see they were defending the indefensible, driven by expediency to gather data. There never was a good ethical argument for placebo use in developing countries when existing therapies were available. With time, I hope people will recognize the mistakes made in the HIV world in the 1990s and avoid repeating them.

Kurihara The DoH may not change, but there is a change with CIOMS [15]. Another change involves the International Federation of Associations of Pharmaceutical Physicians and Pharmaceutical Medicine (IFAPP). I will participate in the regional meeting held by the WMA, representing the IFAPP, although my argument is not representing them, just authorization of my presentation slide [16]. IFAPP includes company staff and experts in drug development in academia, working with companies. Previously, IFAPP's stance is

not supporting the 2000 version of the DoH, but now the President and some members support the idea of 2000 version, which may be derived from Hippocratic principles [17]. Some of IFAPP members and Dirceu Greco and Ames Dhai are writing a paper just before publication (published after this interview) [18], supporting our ideas on placebo-controlled trials, post-trial access. We are advocating for CIOMS's risk minimization approach over the current DoH. This is one significant shift.

Additionally, I am working with a patient and public group to share their opinions on the DoH [9]. They offer excellent ideas, especially about the risk threshold described in the DoH is difficult for them to understand. They argue that comparative studies should be justified based on uncertainty about which treatment arm is better. This group is developing a Patient and Public Declaration of Research Ethics [19]. These external voices are vital for changing practices, even if the DoH itself does not change.

6. Some examples of unethical placebo trials acceptable by the current DoH

Lurie　Do you want to know if there's a recent example, similar to Surfaxin, of a placebo study in a developing country that might be considered unethical? Has there been a case since Surfaxin where the use of a placebo was questionable?

Kurihara　Yes, there were some cases in Japan. I wrote a paper criticizing the withdrawal trial of a psychiatric drug, an antidepressant already approved in many countries but not in Japan. They conducted a trial to compare its effectiveness, which we argued was unnecessary and unethical [20, 21].

Lurie　We had a paper, though unpublished, that addressed questions about acceptable risk levels. We reviewed all randomized trials of studies on drugs for recurrent genital herpes. There were two or three drugs involved, such as acyclovir and valacyclovir. We examined these trials over time, and it was remarkable.

From the outset, acyclovir was highly effective in reducing the incidence of recurrences. There were around two dozen placebo-controlled trials, all demonstrating significant effectiveness, yet they continued doing the same trials repeatedly. The results were consistent, with clear differences between placebo and treatment groups, but the trials were still repeated unnecessarily. Though genital herpes is not typically fatal, it's unpleasant and disruptive. The study highlighted the question of acceptable risk and discomfort.

Kurihara　It seems that perhaps your case exemplifies the differences between DOH and CIOMS. During the COVID-19 pandemic, after the development of the BioNTech-Pfizer and Moderna vaccines, a number of placebo-controlled trials were conducted for new vaccine candidates [22]. Differently from the period when the top runner vaccines were successfully developed at the end of 2020, COVID-19 vaccines may no longer fit the definition of reducing the risk of serious or irreversible harm. Even in such settings, double standard would not be ethically acceptable.

Lurie　As I mentioned, we investigated and found that many COVID vaccine trials were complicated by timing. Some participants received the vaccine or placebo before the Moderna or Pfizer results were released. For instance, vaccinations occurred in September, but results weren't available until November or December. In other cases, vaccinations in November, when the initial trial results were being released, wouldn't show effectiveness until follow-up in May. Most trials we found followed this pattern, except for one small trial that differed.

Kurihara　I recall many papers statistically showing the discrepancy between conduct of clinical trials

and post-trial access [23~25]. In developing countries, numerous trials are conducted, but approval in these same countries is often significantly delayed. Such situations should be discussed more in depth continuously before and after the 2024 revision of the DoH.

References

1) Robert J. Levine, Peter Lurie, Stephan W. Lagakos. Kurihara C, Interview. Interview with Robert J. Levine, Peter Lurie and Stephan W. Lagakos: Discussion on the Declaration of Helsinki and its background. *Clin Eval.* 2001; 28(3): 409-22.Japanese. http://cont.o.oo7.jp/28_3/p409-22/report.html [Levine RJ, Lurie P, Lagakos SW. 栗原千絵子, インタビュー・構成・補足解説. ヘルシンキ宣言をめぐる議論ーLevine, Lurie, Lagakosによるコメントとその背景ー. 臨床評価. 2001; 28(3): 409-22. http://cont.o.oo7.jp/28_3/p409-22/report.html]
2) COVID-19 and bioethics - Part 3. Co-organized by the COVID-19 Task Force, Japanese Association for Bioethics and Brazilian Society of Bioethics. June 4, 2021. *Clin Eval*. 2023; 49 (Suppl 38). http://cont.o.oo7.jp/49sup38/49sup38contents_e.html
3) WMA Declaration of Helsinki Revision: Advocacy and Communication: North American Regional Meeting on the Declaration of Helsinki. August 15, 16, 2024[cited 2025 Jan 10]. Washington DC. https://www.wma.net/events-post/wma-declaration-of-helsinki-revision-advocacy-and-communication/
4) The 2024 Declaration of Helsinki: Taking Forward Bioethics and Human Rights. Co-organized by: The Brazilian Society of Bioethics (SBB); International Federation of Associations of Pharmaceutical Physicians and Pharmaceutical Medicine (IFAPP); Clinical Evaluation Inc.; The 129th Pharmaceutical Study Group; and supported by The Japan Association for Bioethics (JAB). August 5 and 26, 2024. *Clin Eval*. 52(3).http://cont.o.oo7.jp/52pop/52pop_contents_e.html
5) Lurie P, Wolfe SM. Unethical trials of interventions to reduce perinatal transmission of the human immunodeficiency virus in developing countries. *N Engl J Med.* 1997 Sep 18;337(12):853-6. doi: 10.1056/NEJM199709183371212.
6) Lurie P, Greco DB. US exceptionalism comes to research ethics. *Lancet.* 2005 Mar 26-Apr 1;365(9465):1117-9.
7) Kurihara C, Greco D, Dhai A, Saio T, Tsubaki H. Ethics of placebo-controlled trials: historical analysis including experiences during the COVID-19 pandemic. In: Kurihara C, Greco D, Dhai A, editors. *Ethical innovation for global health: pandemic, democracy and ethics in research*. Springer; 2023. p. 195-224.
8) Kurihara C, Greco D, Dhai A. Post-trial access: historical analysis considering the experience of COVID-19 pandemic. In: Kurihara C, Greco D, Dhai A, editors. *Ethical innovation for global health: pandemic, democracy and ethics in research*. Springer; 2023. p.225-41.
9) Kurihara C, Inoue K, Kai H, Suzuki K, Saeki H, Funabashi Y, Kishi N, Kuge A, Murakami T, Saito Y, Uchida E, Tsutsumi N, Imamura K. Our “WMA Declaration of Helsinki”: opinions and proposals from patient and public for research ethics. In: Kurihara C, Greco D, Dhai A, editors. *Ethical innovation for global health: pandemic, democracy and ethics in research.* Springer; 2023. p.243-69.
10) Lurie P, Wolfe SM. Commentary 9.2: The developing world as the “Answer” to the dreams of pharmaceutical companies: the Surfaxin story. In: Lavery JV, Grady C, Wahl ER, Emanuel EJ, eds. Ethical issues in international biomedical research: a casebook. Oxford University Press; February 15, 2007. p. 159-70.
11) Lurie P. Revisiting the debate over placebo use in developing countries in the age of COVID-19. In: COVID-19 and bioethics - Part 3. Co-organized by the COVID-19 Task Force, Japanese Association for Bioethics and Brazilian Society of Bioethics. June 4, 2021. *Clin Eval*. 2023; 49 (Suppl 38): 30-41. http://cont.o.oo7.jp/49sup38/49sup38contents_e.html
12) Lurie P. Trials for second generation Covid-19 vaccines: Revisiting the debate over placebo use in developing coun-

try clinical trials. *Indian J Med Ethics.* 2021 Apr-Jun;VI(2):1-10. doi: 10.20529/IJME.2021.023.

13) WHO Ad Hoc Expert Group on the Next Steps for Covid-19 Vaccine Evaluation, Krause PR, Fleming TR, Longini IM, Peto R, Beral V, Bhargava B, Cravioto A, Cramer JP, Ellenberg SS, Figueroa JP, Halloran E, Henao-Restrepo AM, Ryan MJ, Levine MM, Nason M, Nohynek HM, Plotkin S, Rees H, Singh JA, Swaminathan S. Placebo-Controlled Trials of Covid-19 Vaccines - Why We Still Need Them. *N Engl J Med.* 2021 Jan 14; 384(2): e2. doi: 10.1056/NEJMp2033538. Epub 2020 Dec 2. PMID: 33264543.
14) Kurihara C, Saio T. Therapeutic misconception as the basis for vaccine nationalism of Japan: a historical reflection and perspectives for global public health. In: Kurihara C, Greco D, Dhai A, editors. *Ethical innovation for global health: pandemic, democracy and ethics in research*. Springer; 2023. p.105-30.
15) Council for International Organizations of Medical Sciences. International ethical guidelines for health-related research involving humans. 2016. https://cioms.ch/publications/product/international-ethical-guidelines-for-health-related-research-involving-humans/
16) Kurihara C. Next Steps for implementation of the revised Declaration of Helsinki (DoH): Networking pharmaceutical experts, patients, bioethicists, and other stakeholders. WMA Declaration of Helsinki Revision: Advocacy and Communication: North American Regional Meeting on the Declaration of Helsinki. August 15, 16, 2024. Washington DC.
17) Kurihara C, Kerpel-Fronius S, Becker S, Chan A, Nagaty Y, Naseem S, Schenk J, Matsuyama K, Baroutsou V. Declaration of Helsinki: ethical norm in pursuit of common global goals. *Front Med (Lausanne).* 2024 Apr 2;11:1360653. doi: 10.3389/fmed.2024.1360653.
18) Kurihara C, Greco D, Dhai A, Matsuyama K, Baroutsou V. Vulnerability, social value and the equitable sharing of benefits from research: beyond the placebo and access debates. *Front. Med.* 2024; 11:1432267. doi: 10.3389/fmed.2024.1432267
19) Kurihara C, Saito Y, Kai H, Funabashi Y, Inoue K, Kishi N, Kuge A, Murakami T, Suzuki K, Takahashi Y, Uchida E, Imamura I. Patient Public Declaration of Research Ethics (1st edition)：Research ethics of the people, by the people, for the people－Expanding the impact of 2024 revision of the Declaration of Helsinki. *Clin Eval.* 52(3). http://cont.o.oo7.jp/52pop/52pop_contents_e.html
20) Saio T, Kurihara C. The randomized withdrawal study of sertraline in Japan ― Was the study truly indispensable?. *Clin Eval.* 2007; 35(2): 321-44. http://cont.o.oo7.jp/35_2/p321-44.pdf
21) Kurihara C, Saio T. Provisions 29 and 30 of the Declaration of Helsinki and the ICH-E10 Guideline ― A case study of randomized placebo-controlled withdrawal trials of antidepressants and the real status of outsourcing clinical trials―. *Clin Eval*. 2007; 35(2): 345-62. Japanese. http://cont.o.oo7.jp/35_2/p345-62.pdf
22) Dal-Ré R. Placebo control group in COVID-19 vaccine trials: context and timing matters. *Eur J Clin Pharmacol.* 2022 Mar;78(3):523-526. doi: 10.1007/s00228-021-03259-x.
23) Miller JE, Mello MM, Wallach JD, Gudbranson EM, Bohlig B, Ross JS, Gross CP, Bach PB. Evaluation of drug trials in High-, Middle-, and Low-Income Countries and local commercial availability of newly approved drugs. *JAMA Netw Open*. (2021) May 3;4(5):e217075. doi: 10.1001/jamanetworkopen.2021.7075.
24) Gyawali B, Carson LM, Berry S, Moraes FY. Challenges of globalization of cancer drug trials- recruitment in LMICs, approval in HICs. *Lancet Reg Health Am*. (2021) Dec 27;7:100157. doi: 10.1016/j.lana.2021.100157.
25) Rubagumya F, Hopman WM, Gyawali B, Mukherji D, Hammad N, Pramesh CS, Zubaryev M, Eniu A, Tsunoda AT, Kutluk T, Aggarwal A, Sullivan R, Booth CM. Participation of Lower and Upper Middle-Income Countries in clinical trials led by High-Income Countries. *JAMA Netw Open*. (2022) Aug 1;5(8):e2227252. doi: 10.1001/jamanetworkopen.2022.27252. Erratum in: *JAMA Netw Open*. (2022) Sep 1;5(9):e2235554. doi: 10.1001/jamanetworkopen.2022.35554.