## **Progress report 2024**

### **Department of Biostatistics & Bioinformatics**

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#### Introduction and Organization

Biostatistics is an applied statistics in the fields of medical and health sciences and contributes to these fields through developments of statistical methodologies for clinical trials and epidemiological research. Biostatisticians who work at an organization for conducting and coordinating clinical research (e.g., academic research organizations (AROs) in hospitals and institutions are few in Japan. Due to this reason, the Japan funding agency, Agency for Medical Research and Development (AMED), started the Support Program for nurturing Biostatiscians from 2016.

This program, with the objective of cultivating talent of excellent biostatisticians, supports the efforts of training them through collaboration between graduate schools that conduct school education, and hospitals that conduct practical training.

In FY2016, the AMED selected the Graduate School of the University of Tokyo and the Graduate school of the Kyoto University, as 2 centers for training biostatisticians, which function as core facilities, respectively. Each graduate school developed a new biostatistics course, forms a training center upon collaboration with a hospital, and performs on-the-job training (OJT).

This program improves the environment that leads to higher quality in clinical research and trials, with the collaboration of industry, academia, and the government, based upon the donations from drug companies and national research funding. Collaborative projects of industry, academia, and the government through the flow of funds in this program, are the first of their kind in Japan.

On March 1, 2017, the Department of Biostatistics and Bioinformatics was established in the Graduate School of Medicine. In the Graduate School of Interdisciplinary Information Studies in the University of Tokyo, the Biostatistics and Bioinformatics course was established on April 1, 2018. This course provides specialized education to acquire not only statistical methodologies, but also practical skills (e.g., design and analysis of clinical research, programming, reporting) for conducting clinical research. We train biostatisticians with high communication skills and ethics that can promote high quality research in collaboration with health care professionals by teaching and OJT.

The number of graduates each year (and the number of employments at ARO) are as follows: the 1st-period 10(8) in 2019, the 2nd-period 8(8) in 2020, the 3rd-period 9(8) in 2021, the 4th-period 7(5) in 2022, the 5th-period 11(11) in 2023, the 5th-period 5(5) in 2024. AMED has renewed this project for more 5 years since FY2021

## Research Activities

# 1) Education in the Biostatistics and Bioinformatics course

In the Biostatistics and Bioinformatics course, through the following teachings, we educate a wide range of knowledge and skills required to biostatisticians. Its curriculum is made up of 28 subjects including 43 credits. For students who have taken over 40 credits, we issue a certificate along with the Master degree. Ten 6th-period master's students who completed the program in at the end of FY 2024 were awarded this certificate, and total of 45 master's students since the 1st-period were awarded the certificate. Six master's students as the 7th-period have enrolled in April 2024.

# 2) Statistical methodology and design of clinical trials and epidemiology

We study on the statistical methodologies and design for streamlining clinical trial and estimating treatment effect precisely. The research area includes Bayesian design in oncology, clinical trial design using biomarkers, adaptive design, and study on the use of Bayesian statistics in clinical trials, causal inference, and multiple comparison method.

# 3) Epidemiological methodology

Epidemiology deals with health or disease related incidence quantitatively in large populations, evaluates cause and effective factors, and ultimately finds the measures of prevention. It starts from epidemics (such as infectious diseases) and now its focus is on lifestyle related diseases, such as cardiovascular disorders. Also, several kinds of medical databases are developed rapidly in Japan. It is important to conduct epidemiological, pharmacoepidemiological and clinical epidemiological studies using such databases.

### 4) Pharmacoepidemiology

Pharmacoepidemiology is a study to investigate drug use and its effects in a population. We are engaged in research on effectiveness, risk, and cost using data obtained from hospital information system and electronic medical record.

### 5) Clinical Epidemiology

Clinical epidemiology is the application of the principles and methods of epidemiology to conduct clinical research studies focusing on prevention, diagnosis, prognosis, and treatment of disease. As the basic science of Evidence-based Medicine (EBM), the importance of clinical epidemiology has been increasing.

### 6) Medical informatics

Medical informatics is a science of studying how to use data, information and knowledge in the all medical fields, such as clinical, medical studies, education and government. Recently, the area of medical informatics is much expanding because of the progress of genomic studies or bioinformatics, and introduction of new technologies, such as virtual reality and artificial intelligence (AI).

### 7) Algebraic statistics

The focus of research is on developing and applying methods of algebraic statistics to specific statistical problems. In statistical inference, the computation of complicated integrals or summation sometimes makes the problem intractable. When a statistical model has algebraic structure, techniques from algebraic statistics are useful. We currently work on the topics related to Markov basis theory and the holonomic gradient method.

#### Future Directions

It has decided to continue the project for another five years as AMED project to promote the development of biostatisticians since FY2021. Moreover, we will continuously provide one more year of post-graduate education for graduates who are employed as biostatisticians at medical institutions in academia. Also, entrance examinations should be conducted in the summer to select master's students who will enroll in the Biostatistics and Informatics Course of the Interfaculty Initiative in Information Studies and the Graduate School of Interdisciplinary Information Studies, and provide them with the education they need to become biostatisticians, as well as post-graduate education. On the other hand, public lectures on biostatistics for the general public will be provided to contribute to the enlightenment of biostatistics. In addition to the development of new clinical research designs and analysis methods, we will develop human resources capable of conducting analyses using big data such as large-scale medical databases and AI, which are expected to increase in the field of clinical research in the future.

#### Publications

Articles (In English)

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Ikeda M, Ueno M. Early tumor shrinkage as a prognostic predictor in chemotherapy-na?ve patients with locally advanced pancreatic cancer treated with modified FOLFIRINOX or gemcitabine plus nab-paclitaxel combination therapy: An exploratory analysis of JCOG1407. Pancreatology. 2024 Sep;24(6):909-916. doi: 10.1016/j.pan.2024.07.006. Epub 2024 Jul 16. PMID: 39060124.

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- International Conference Presentation
- Miki Ohta, Satoru Miyawaki, Shinichiroh Yokota, Makoto Yoshimoto, Tatsuya Maruyama, Daisuke Koide, Takashi Moritoyo, Nobuhito Saito. The utility of event-specific methods in causality assessment of drug adverse reaction. ACPE 2024, Tokyo. (13 October 2024) (oral)
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