



**TOHOKU**  
UNIVERSITY

# Introduction of Tohoku Medical Megabank Cohort Study. How to achieve personalized health care using big data.

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Feb 12, 2020

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# The Great Eastern Japan Earthquake

March 11, 2011

- The total number of dead and missing persons is 18,550
- Many key hospitals suffered from the Tsunami
- As an emergency support, Tohoku University Hospital and Medical School sent more than 1,500 doctors (total) to the damaged coastal area

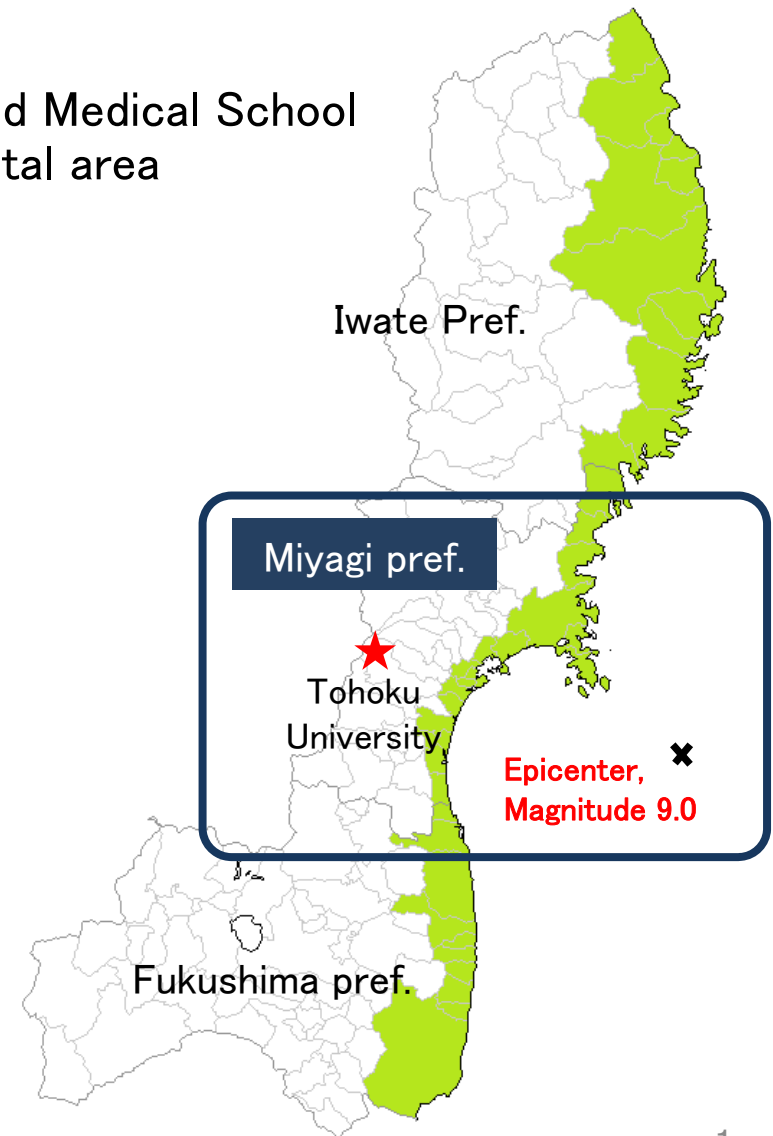
What shall we do as medical scientists ?

## Creative Reconstruction

- A **core project** is required to revitalize the Tohoku region
- Create an **attractive and thriving center of innovation** leading to fast-track recovery of the Tohoku region



March 25, 2011



## Residents Cohort and Birth & Three Generation Cohort

### ■ Community / Residents Cohort

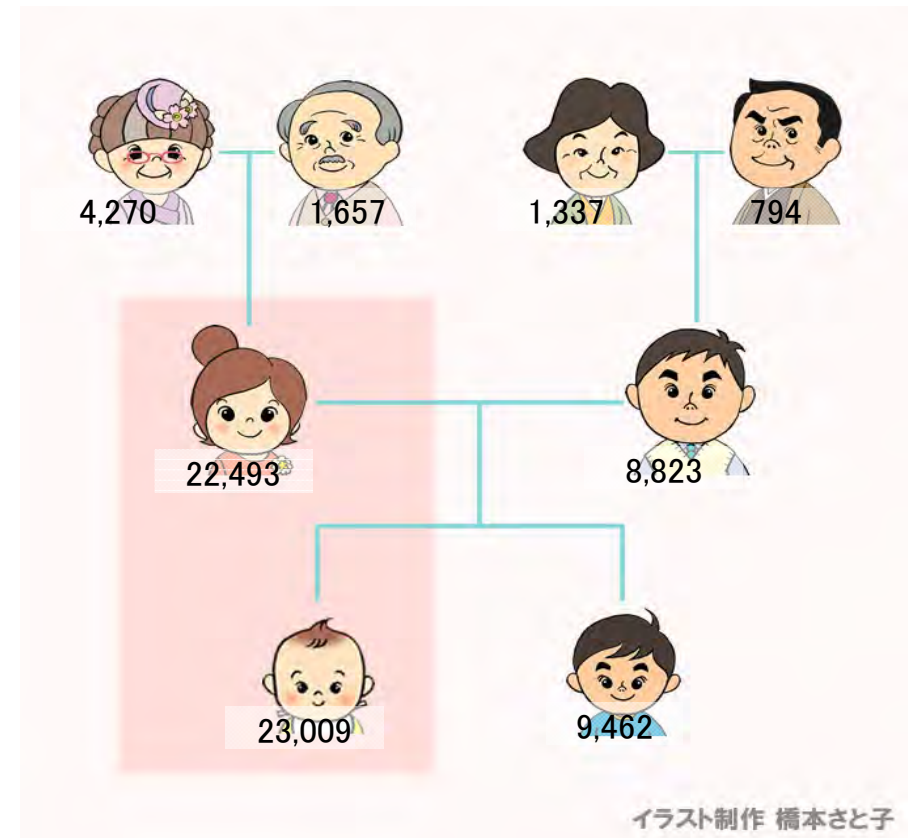
Recruit **80,000 residents** from coastal areas in Miyagi and Iwate provinces  
Recruit through joint session with health check by local government and use of seven regional support centers in the area

### ■ Birth & Three Generation Cohort

Recruit **70,000** people including offspring, parental and grandparental generations  
Request expectant mothers for cooperation in maternity hospitals



At March 31, 2016, we have finished recruit of **84,000** participants for Resident Cohort and at March 31, 2017, we have finished recruit of more than **73,000** for the Birth and Three Generation Cohort.

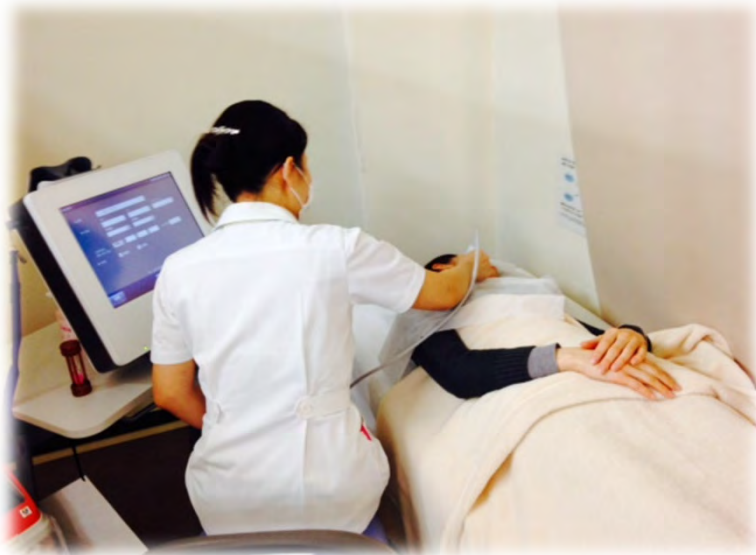


**We recruited more than 150,000 participants in total.**





# TMM Community Based Cohort Study



# Health Check-up

Depression  
Insomnia

Drinking  
Smoking

■ Increment of Life style related disease

■ Early detection of problem and counteraction

Monitor

- Monitoring of disease incidence
- Early intervention if risk factors are clarified

Prevention of secondary health damage

Follow-up

Prospective cohort study design

Clarify the causal relationship and elucidate risk factors of diseases.

Gene-environmental interaction is not fully clarified

Gene X Environment

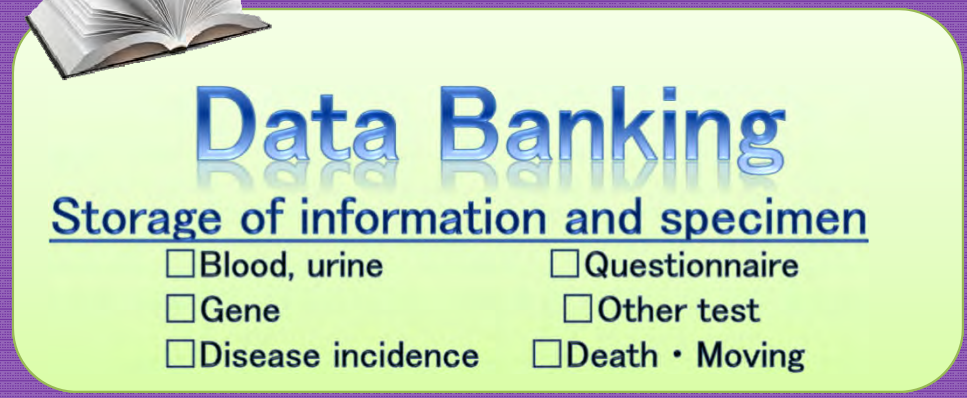
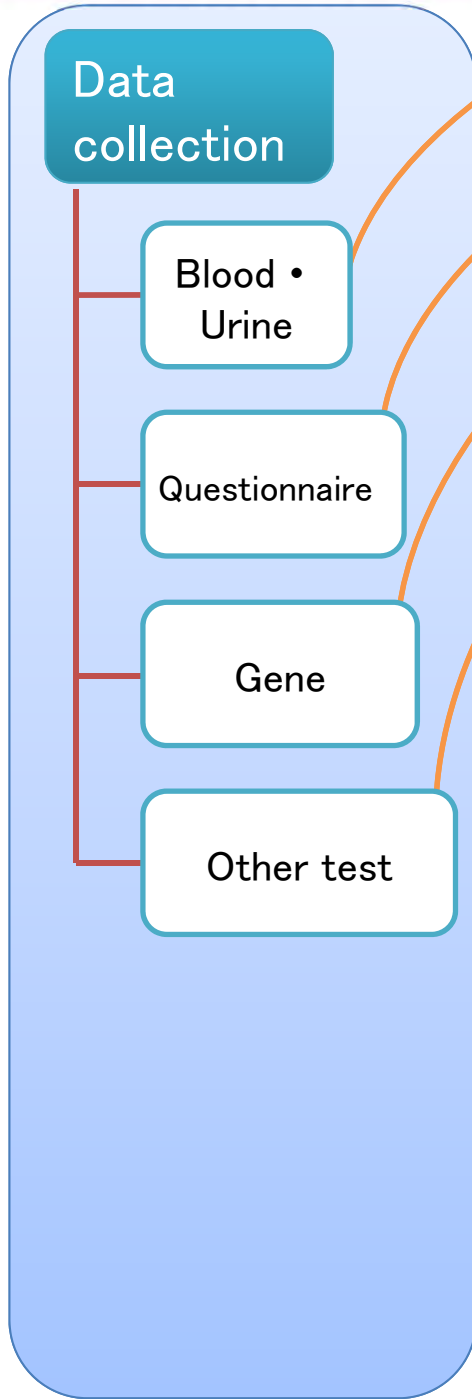
Establishment of personalized healthcare and medicine



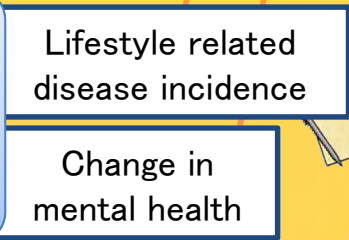
Baseline survey enabled us to assess the current condition



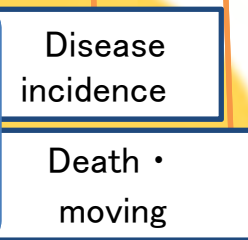
Tohoku University



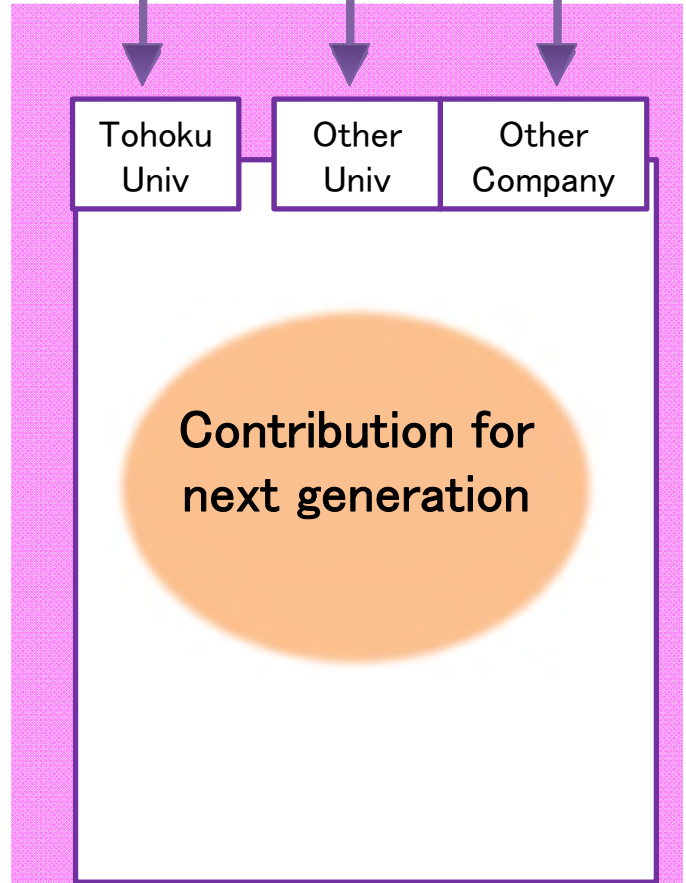
Short term follow-up



• Relation of gene, lifestyle, environmental factors with disease incidence



Long-term follow-up



# How participants were recruited ?

**Inclusion criteria: Aged > 20years and live in Miyagi and Iwate prefecture**

## **Type 1 survey based on municipal health check-up**

At the sites of annual health check-up in the local communities

- Trained staff approached and obtained additional blood sample and urine sample with informed consents
- Questionnaire was distributed

## **Type 2 survey based on assessment center-based survey**

Volunteer based recruitment at 7 community support centers

Participants voluntarily made appointments and visited community support centers nearby

# Data Collected from All Participants in TMM Cohort Studies

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## Baseline Measurements

- Height
- Weight
- Blood pressure
- Blood glucose
- Serum cholesterol
- Liver function
- Uric acid
- Renal function
- Specific Ig E (Allergy)
- Helicobacter pylori
- Pepsinogen I and II
- Microalbuminuria
- Urinary Na
- Urinary K

## Questionnaire-Based Data

- Smoking
- Alcohol consumption
- Physical activity
- Depression (CES-D)
- Psychological disorder (K6)
- Insomnia (Athene insomnia scale)
- Food Frequency Questionnaire
- Disaster related scale
- History of diseases
- Occupation
- Social connection



# Type1 recruitment, Miyagi prefecture

Recruitment period: 2013.5 – 2016.3



Pacific Ocean



About 63,000 participants participated in Miyagi and Iwate

<http://edit.freemap.jp/>







Compared with inland area, coastal area showed  
Higher prevalence of depression or psychological distress.  
Higher risk of withdrawing treatment for hypertension.  
Higher prevalence of metabolic disorder.



They might have higher risk of atherosclerotic disease,  
stroke or ischemic heart disease in future.

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They might have higher risk of atherosclerotic disease,  
stroke or ischemic heart disease in future.

Secondary damage from disaster might be occurred.

Government allowed us to measure change in subclinical  
atherosclerosis or other factors.



# Repeat assessment center-based survey during second period have just started 1 June 2017 -

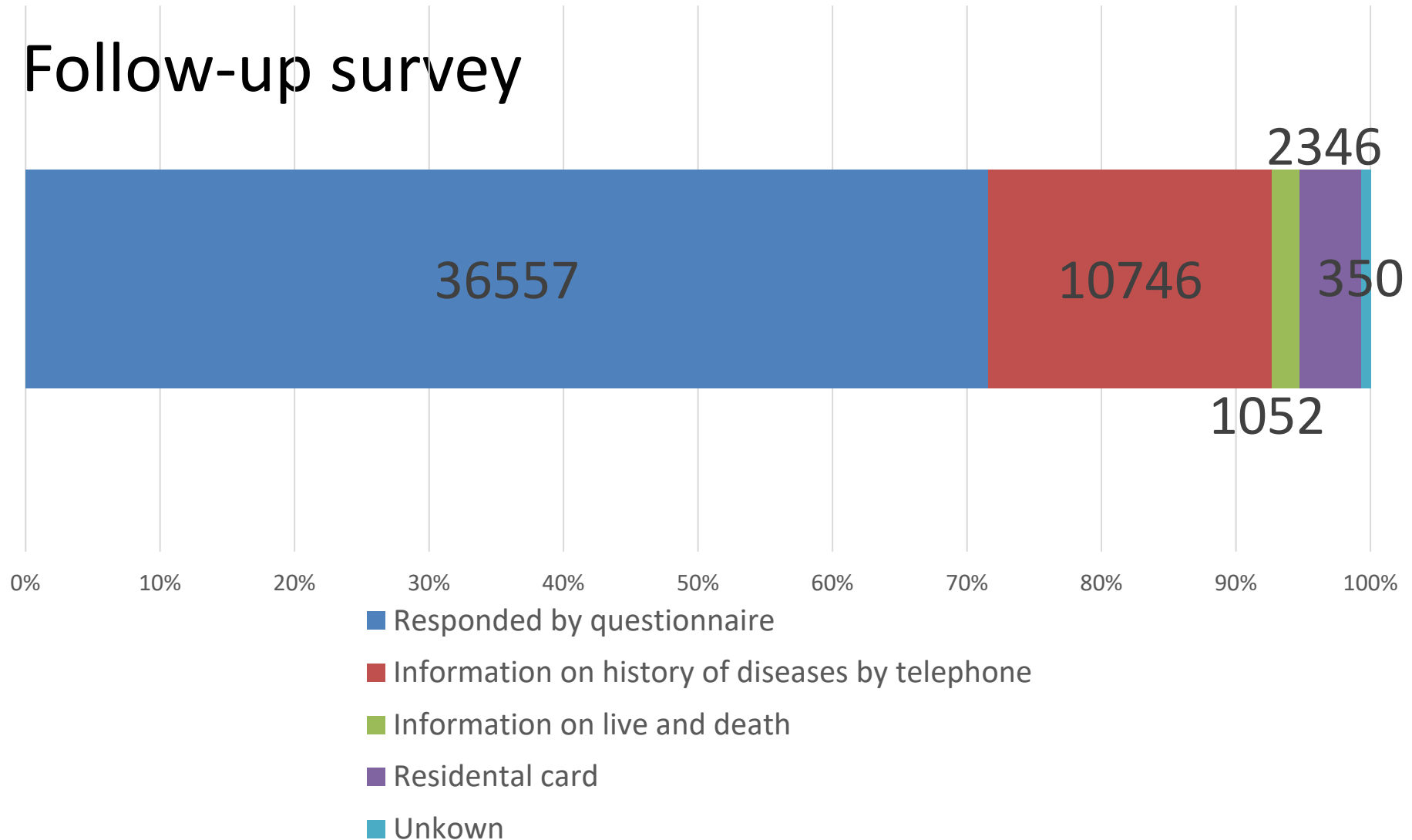
- Ask all participants to visit the community support centers nearby.

In Miyagi, more than 26,000 participants has already measured this repeated measurement within 3 year

- Questionnaire
- New devices measured at home (urine Na/K test, activity monitor, sleep monitor)

# Follow-up rate

- Follow-up survey



We confirmed 509 deaths until October 2018.

# ToMMo is an integrated biobank



Blood & Urine



Whole Blood, Serum, WBCs are stored  
→ metabolome & proteome



Genomic DNA

DNA extracted from blood is also stored  
→ genomics & transcriptome



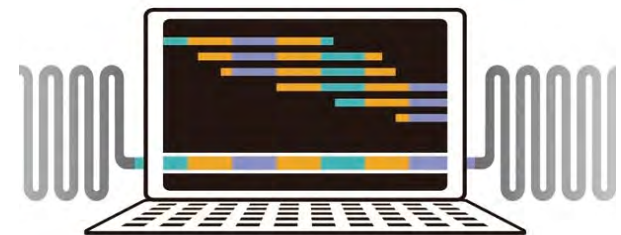
Questionnaire

Main part is for life style (including food), psychological condition, experiences of the disaster

+ MRI & more than 10 physiological examinations,  
and cognitive and psychological assessment

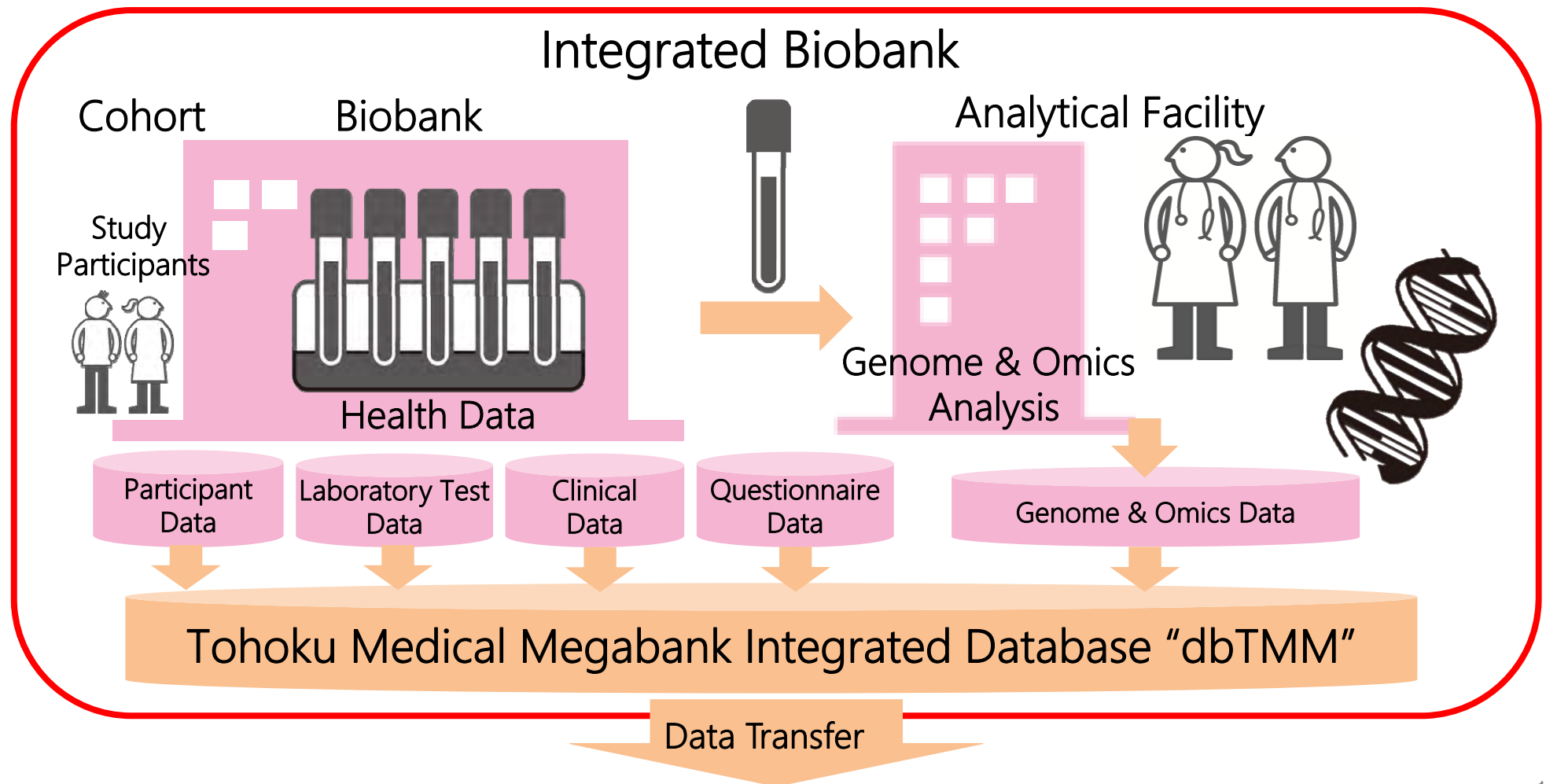
## Integrated biobank

- ToMMo sets up an analytical center that executes standard analyses of samples
- To avoid rapid depletion of samples, ToMMo distributes analysis information first, and then bio-samples



# Integrated biobank and database

Tohoku Medical Megabank (TMM) is an integrated biobank retaining both Biobank and Genome / Omics Analytical Facilities



Scientists in Academia and Industry



# Follow-up measurements

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- As well as detailed survey, we sent brief questionnaire every 1–2 years.
- We also have obtained mortality data from residence card.
- We have already linked our data to cancer registry.
- Furthermore, we have obtained insurance data regarding medical cost and long term health care.
- From these resources, we are collecting the information on stroke or MI incidence of our participants.

# Outlines of our dataset

## Lifestyle

Smoking  
Physical activity  
Diet, nutrition

## Gene

Whole genome  
SNP array

## Damage from Disaster

House destruction  
Loss of family or kin

## Follow-up

Physiological data  
Disease incidence  
Mortality

## Physiological data

Blood pressure  
Atherosclerosis  
Lung function

## Metabolome data

# Examples of biobank data

- We have started data distribution of type 1 recruitment data (about 67,000 participants).
- The data set consists of following data.
- We confirmed relation of blood pressure with traditional risk factors, such as BMI, alcohol, and NaCl.

- Height
- Weight
- Blood pressure
- Blood glucose
- Serum cholesterol
- Liver function
- Uric acid
- Renal function
- Specific Ig E (Allergy)
- Helicobacter pylori
- Pepsinogen I and II
- Microalbuminuria
- Urinary Na
- Urinary K

- Smoking
- Alcohol consumption
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# Examples of add-on cohort in ToMMo

As a cooperative study with industrial companies, we have added several component to our detailed survey.



# First example, survey regarding dairy products containing probiotics

2017.07.28 | 成果

乳酸菌摂取の保健効果を明らかにする共同研究を開始 ～数万人以上の規模

東北大学東北メディカル・メガバンク機構と株式会社ヤクルト本社が共同で、数万人を対象とした調査を実施することを発表しました。

本研究では、腸内細菌叢と健康状態との関連性を明らかにすることを目的として、乳酸菌飲料の摂取の有無や摂取量、発酵乳の摂取の有無や摂取量について調査を行います。対象者は、東北大学東北メディカル・メガバンク機構の調査対象者の中から、年齢、性別、地域を考慮して抽出されます。

2018.04.12 | 成果

東北メディカル・メガバンク機構、疾病罹患・生理機能低下と腸内細菌叢との関連性を明らかにする共同研究を開始【プレスリリース】

国立大学法人東北大学東北メディカル・メガバンク機構（機構長 山本 雅之、以下、ToMMo）と株式会社ヤクルト本社（社長 根岸 孝成、以下、ヤクルト）は、腸内細菌叢<sup>\*1</sup>を標的とした新規の疾病予防法や治療法の創出、予防医学に基づく乳酸菌飲料および発酵乳の生理的意義を明らかにすることを目的とした共同研究を開始しましたのでお知らせします。

# Add on cohort with Yakult.

- **Questionnaire survey (Started on August 2017)**

Investigate detailed information on dairy products containing probiotics.  
About 40,000 participants answered the questionnaire.



- **Study regarding intestinal flora (Started on April 2018).**

The first wave collection has completed (about 2700 samples).

# Second example, survey regarding Na/K ratio using handy size device.

- **Potassium** (vegetables and fruits etc.) intake is **inverse blood pressure** (INTERSALT Co-operative Research Group. *BMJ* 1988)
- The balance between sodium intake and potassium intake (sodium to potassium ratio: **Na/K ratio**) has been drawing attention recently

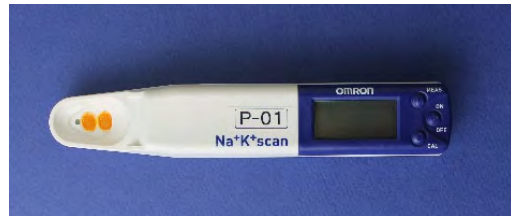
# Aim of collaborative study

OMRON



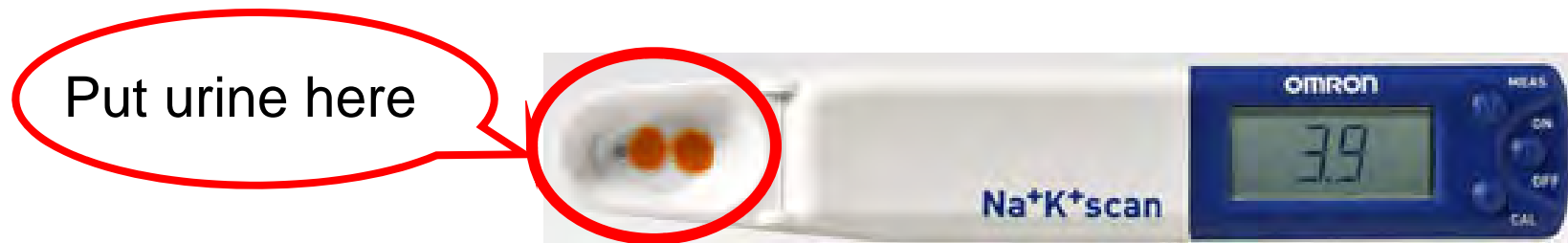
## Collaboration

Add physical activity monitor,  
Na/K ratio monitor, and  
Sleep monitor on our second  
wave study.



# Na/K ratio

- OMRON Healthcare Co., Ltd. developed a handy-sized urinary Na/K ratio monitor
- It can **quickly and easily** measure Na/K ratios from urine sample for **long-term**

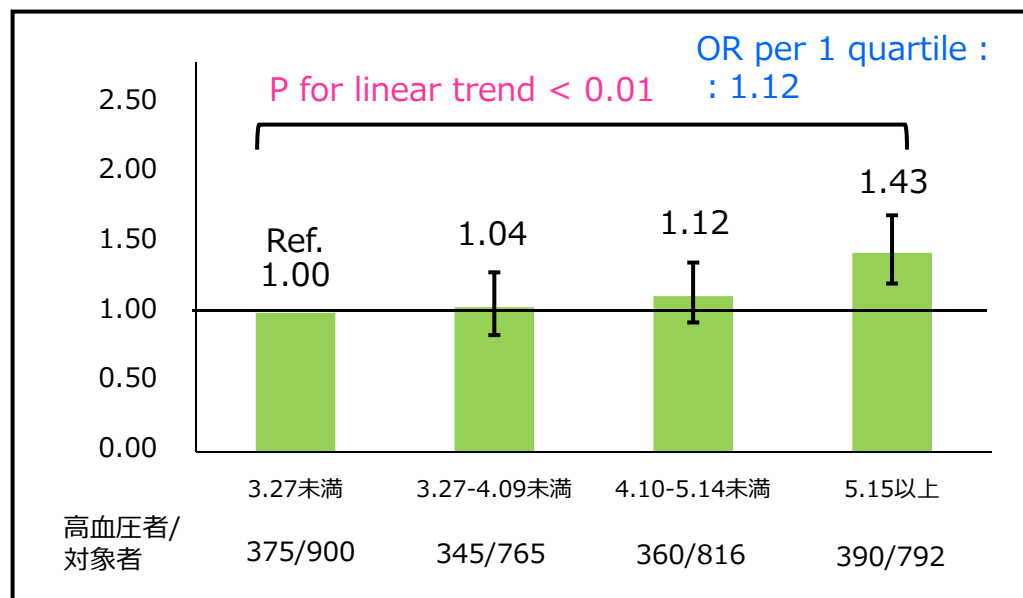
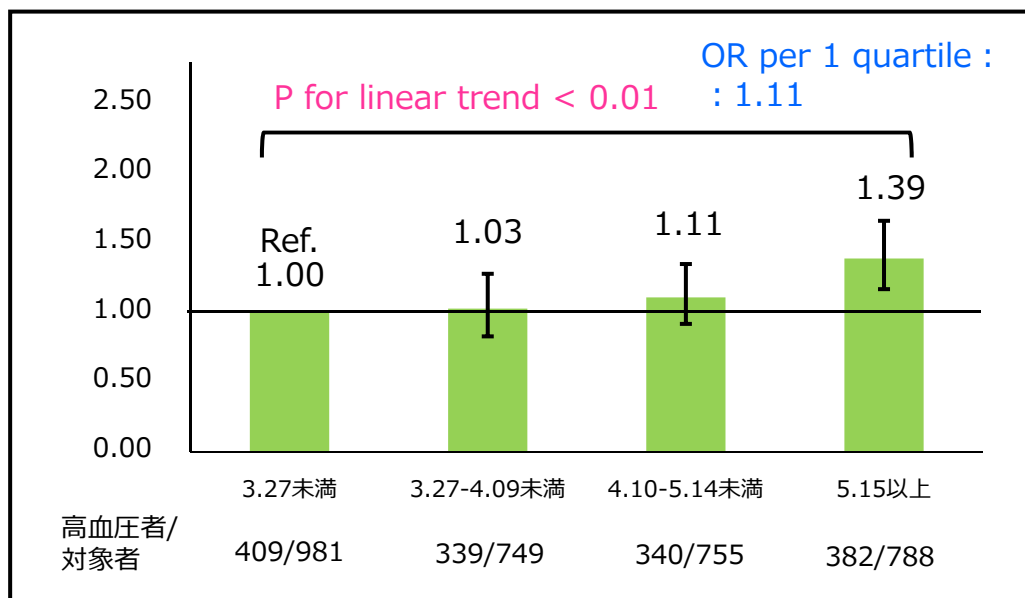
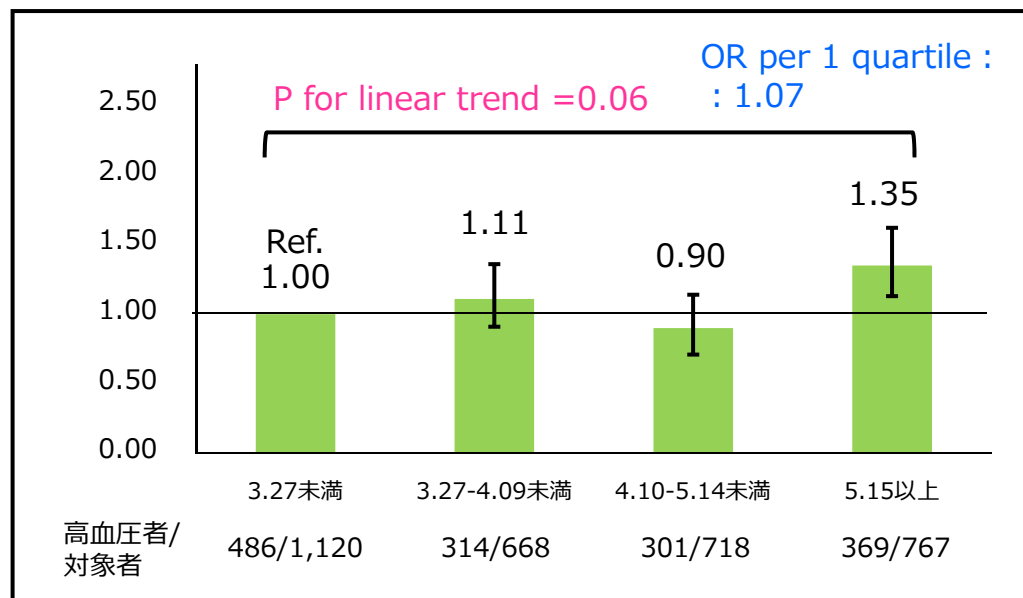
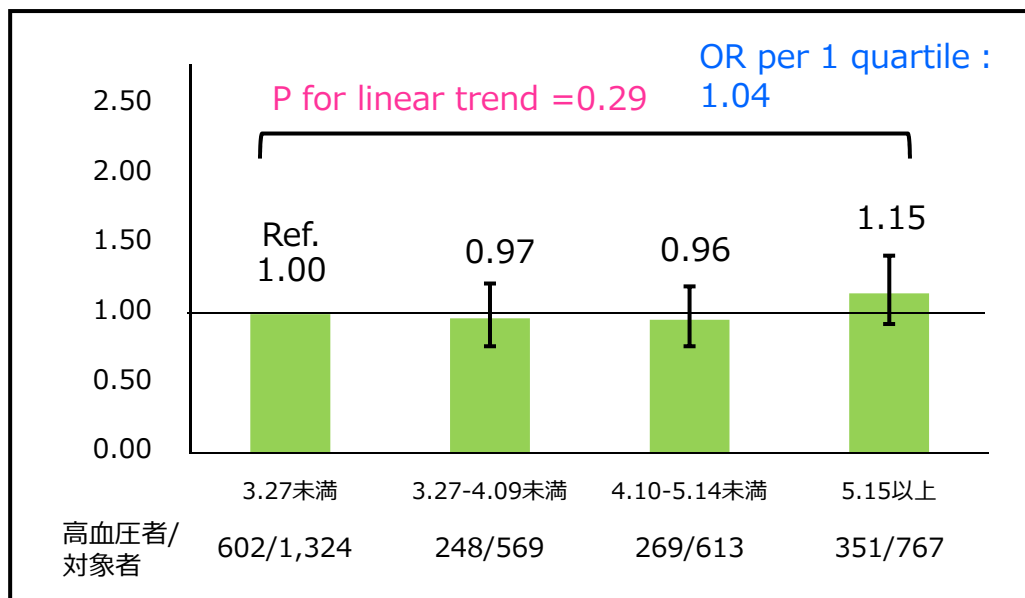


(HEU-001F, OMRON, Kyoto)

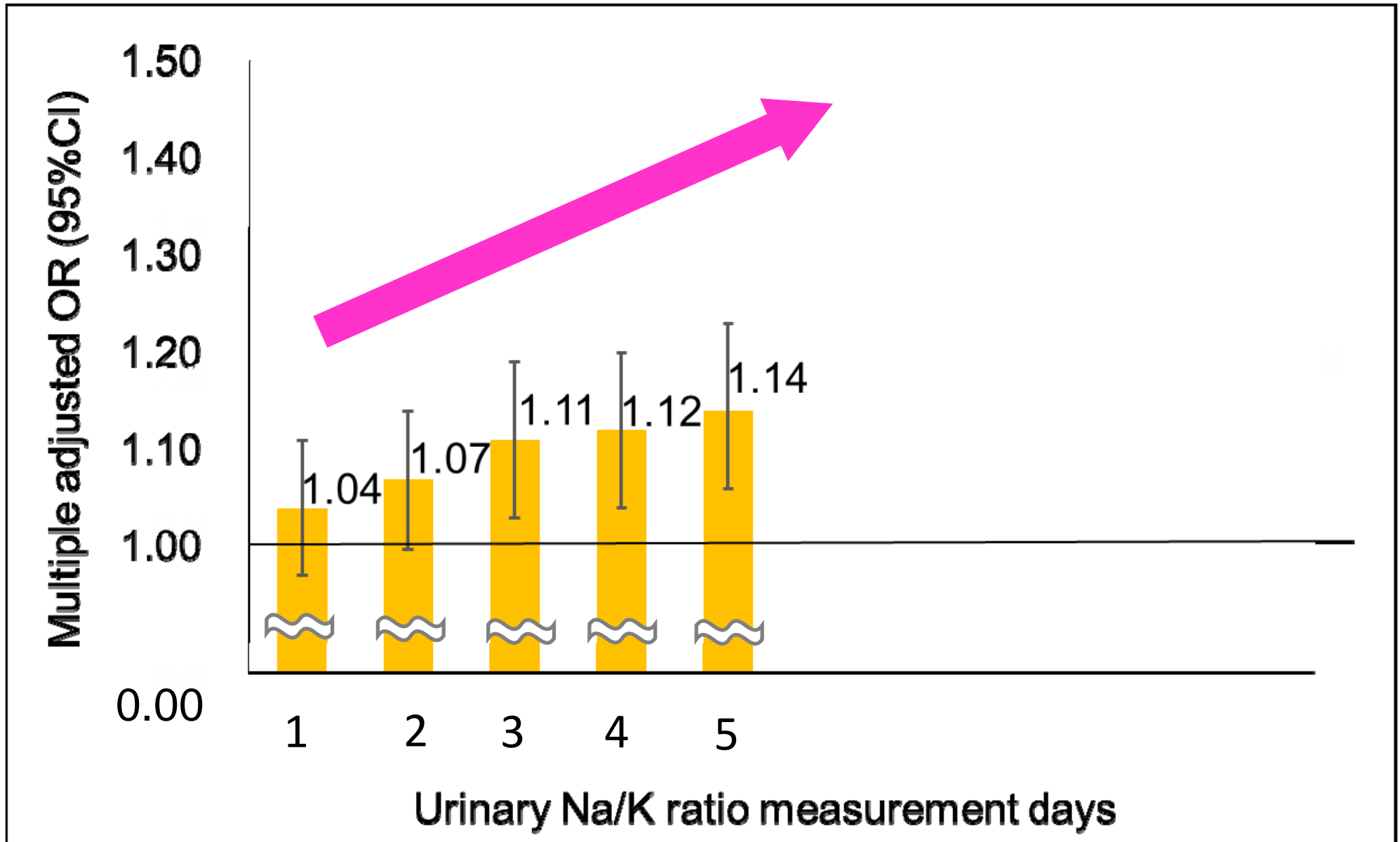
- ToMMo began a collaborative study in June 2017 with OMRON Healthcare Co., Ltd.



# Relationship between Hypertension and day1 to day1-4 Na/K ratio

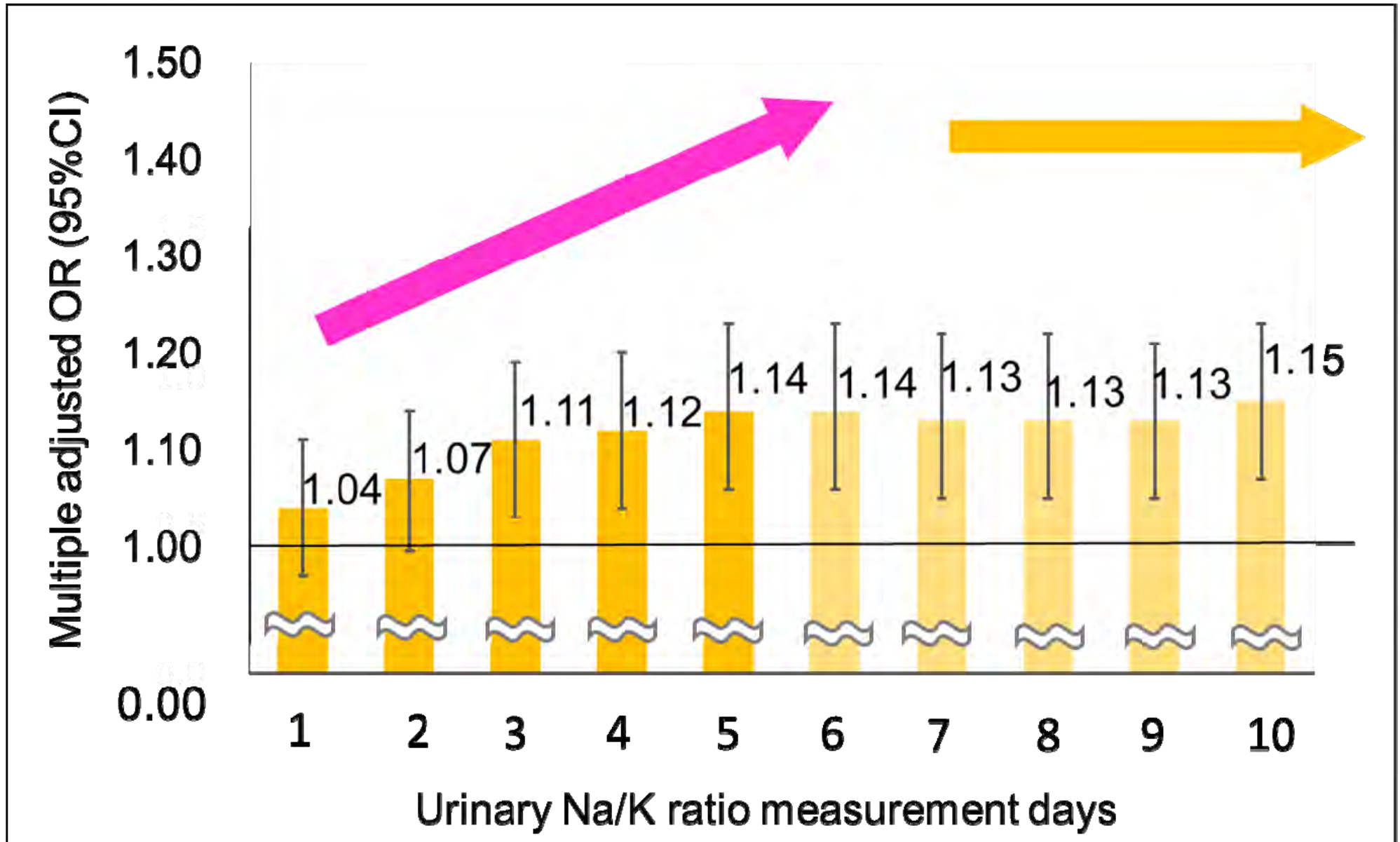


# Prevalence of home hypertension per one unit increase in urinary Na/K ratio from 1day to 10days about 3000 data



*The aOR of home hypertension per one unit increase in urinary Na/K ratio increased from 1 days to around 5 days*

# Prevalence of home hypertension per one unit increase in urinary Na/K ratio from 1day to 10days

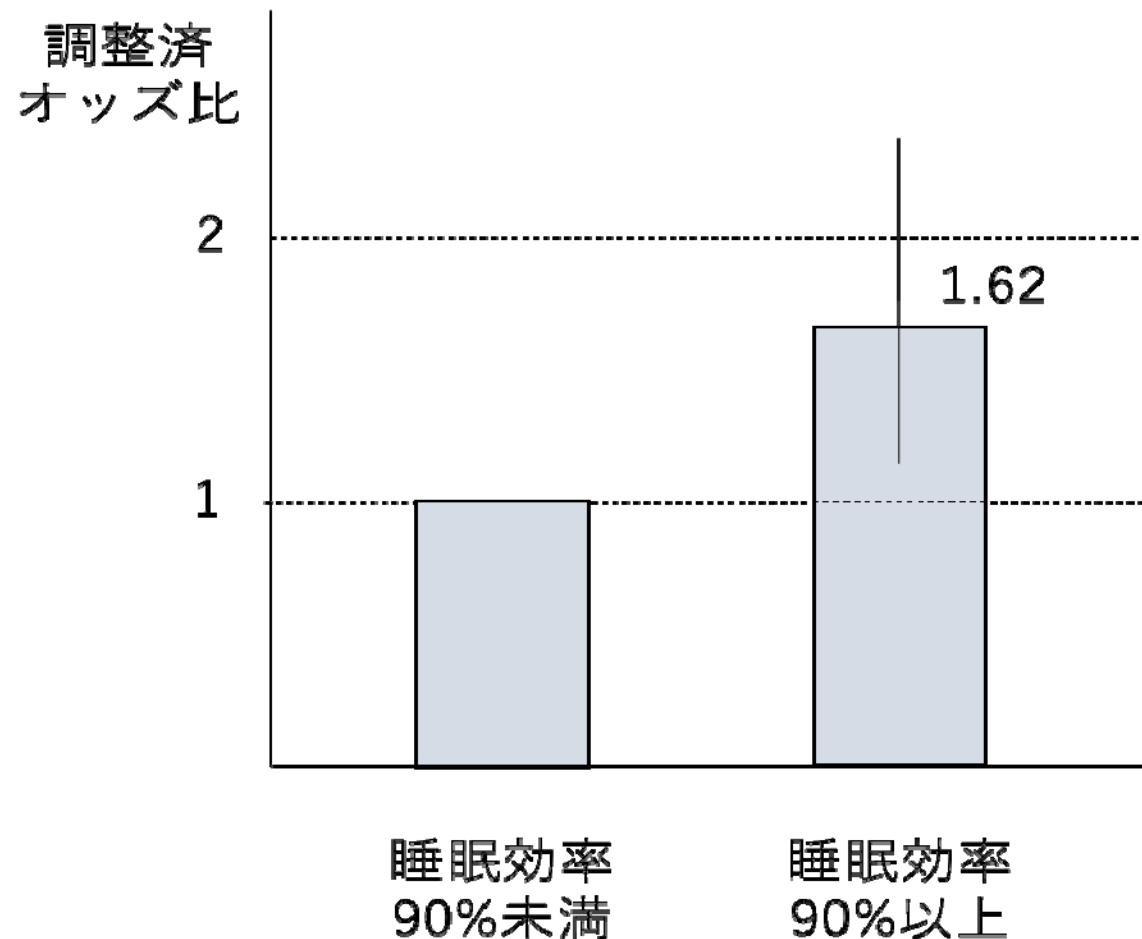


***The aOR of home hypertension per one unit increase in urinary Na/K ratio was stable after around 6 days***

Kogure M, et al Hypertension Research 2020.

We also published sleep efficiency and hypertension.

Poor sleep efficiency associated with higher prevalence of hypertension.



# Conclusion

- We have established community-based and three generation cohorts after Great Eastern Japan Earthquake.
- We have reported several effect of damage from GEJE on community health.
- We have also collected information on genome metabolome, and several add-on measurements.
- We have started several set of data distribution.
- We have collaborated with industrial companies.
- We consider that using our data accelerate health information.
- We would like to ask your good practice.