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The application of AI in health and nutrition

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The AI nutritional research field is a research field that aims to apply information processing technology related to Artificial Intelligence (AI) to the fields of health and nutrition, just as the AI medical and drug discovery research field does, and was started at our institute in April 2020. In this section, we provide an overview of AI technology and its application to the fields of health and nutrition.

【Overview of AI】

Currently, the term "AI" is found everywhere, and it is used in a variety of contexts, ranging from simple data processing to advanced information and knowledge processing. In fact, there are many different definitions of AI, depending on the person, but how can human intelligence be reproduced in an artificial and computational manner? I would like to briefly describe the concept of AI from the point of view of the essentials.

Humans are equipped with various sensory functions to perceive the outside world, such as the five senses. How can we translate these sensations into numerical values for the computer as AI? For example, if we take up taste in the food sector, it is necessary to decompose the process of human understanding of taste and identify the elements to be applied in each phase based on the questions of what is understood and what is not. In other words, there are three phases: the taste sensing phase, taste memory and data accumulation phase, and taste classification and learning phase.

In this case, the AI technology elements required for each phase include data measurement (component, feature, and subjective evaluation and sensing), data accumulation and construction, and information processing (machine/deep learning and language processing), which are commonly required in other fields as well. However, this is an area of research that requires a wide range of perspectives, as it targets the reproduction of human abilities such as perception, understanding, prediction, and action, even when considering simple examples like this.

【Expansion into AI nutrition】

The above is just an example, but the goal of AI nutritional research is to address various issues in the field of health and nutrition by providing data measurement (component, feature, and subjective evaluation, and sensing), data integration and construction, and information processing (machine/deep learning and language processing) in each phase. We aim to contribute to precision nutrition and the extension of healthy life expectancy by starting from ”small” AI technology and eventually developing it into “big” AI. On the contrary, since the scope of AI nutrition research is diverse in terms of both subject matter and the technology required, it is essential to deepen cooperation with institutions both inside and outside the institute—such as the International Life Sciences Institute (ILSI Japan)—as well as with the industry. We want to move forward with an eye toward effectiveness as well.

Nutrient and food group intakes and skeletal muscle index (SMI) among the Japanese elderly: a secondary analysis of the National Health and Nutrition Survey, 2017

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【Introduction】

The elderly population is increasing globally, and one in four people is estimated to be 60 years and older in 2050, except Africa. In Japan, the proportion of those aged 65 years and older is rising dramatically, from 6.3% in 1965 to 26.6% in 2015. In order to promote healthy aging in this super aging society, maintaining muscle mass is one of the important factors, as well as adequate nutrition. In order to investigate the relationship between muscle mass and nutrition, we conducted this study using the National Health and Nutrition Survey 2017 data.

【Material and Methods】

Adults aged 60 years and over (797 men and 969 women), who participated in the 2017 National Health and Nutrition Survey, and had underwent the appendicular skeletal muscle mass measurement by a multi-frequency biomedical impedance apparatus (MC-780A), and completed both the dietary survey and the blood pressure measurements, were selected for analysis. Skeletal muscle mass index (SMI)was calculated as appendicular skeletal muscle mass divided by height squared. The subjects were grouped according to their SMI quartiles by sex.

【Results】

The subjects' general characteristics are shown in Table 1. In both men and women, subjects with higher SMI values were younger, with higher BMI, more likely to be habitual drinkers, and sleep less than 6 hours a day (all $p<0.01$).There were no differences in the proportion of current smokers or those with exercise habits. The nutrients and food groups that subjects in the highest quartile of SMI were consuming more compared to those in the lowest quartile, are shown in Table 2.

【Conclusions】

As in previous studies, protein intake as well as a balanced diet consisting of vegetables and meat were shown to be effective in maintaining muscle mass in the elderly. Although the current results are from a one-day dietary record survey, it is important that it produced similar results. However, we could not confirm whether improving dietary intakes enhances muscle mass in this study, and we could not compare the results with young adults. These issues should be addressed in future studies.

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Table1. General characteristics of the study subjects by quartiles of SMI

	Men				Women			
Quartiles of SMI	First	Second	Third	Fourth	First	Second	Third	Fourth
N	199	199	200	199	242	242	243	242
Median of SMI* kg/m^2	6.6 (6.4-6.9)	7.4 (7.3-7.6)	8.0 (7.9-8.1)	8.7 (8.5-9.1)	5.8 (5.6-6.0)	6.3 (6.2-6.4)	6.6 (6.5-6.7)	7.1 (6.9-7.3)
Mean age (SE)	77.1 (0.5)	73.2 (0.5)	70.2 (0.4)	67.5 (0.4)	76.3 (0.5)	72.4 (0.4)	70.5 (0.4)	68.5 (0.4)
Mean BMI (SE), kg/m^2	21.9 (0.2)	23.4 (0.2)	24.1 (0.2)	25.7 (0.2)	21.3 (0.2)	22.5 (0.2)	23.5 (0.2)	25.2 (0.2)
Habitual drinkers (%)	65.3	73.9	80.5	80.9	26.3	43.3	44.0	48.8
Current smokers (%)	20.1	17.1	20.5	20.6	3.8	5.0	6.6	2.1
Exercise habits (%)	35.7	43.7	45.0	47.2	33.5	36.4	37.4	38.8
Sleep duration less than 6 hours per day (%)	21.6	22.1	24.5	29.6	30.2	38.0	38.7	43.0

* () : interquartile range

Table 2 . Nutrients and food groups consumed by subjects in the fourth quartile of SMI **

	Men	Women
Nutrients	Protein, fat, carbohydrates, <u>dietary fiber</u>, <u>vitamin A</u>, vitamin B2, niacin, <u>vitamin B6</u>, folate, pantothenic acid, <u>vitamin C</u>, sodium, <u>potassium</u>, <u>magnesium</u>, phosphorus, <u>iron</u>, zinc, <u>copper</u>	Protein, fat, carbohydrates, dietary fiber, vitamin A, vitamin E, vitamin B1, niacin, folate, pantothenic acid, vitamin C, sodium, potassium, magnesium, phosphorus, zinc
food groups	<u>Vegetables</u>, fruit, <u>Seasonings and spices</u>	Vegetables, Meat

**compared to the first quartile
The underlined nutrients and food groups were significantly higher after adjusting for age, drinking habits, smoking, sleep duration, exercise habits, occupation, and total energy intake.

Effective coverage of medical treatment for hypertension,diabetes, and dyslipidemia

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International Center for Nutrition and Information

【Introduction】

A metric for effective coverage of health interventions was proposed under a framework for benchmarking health system performance by the World Health Organization in the early 2000s. Effective coverage has been studied in recent years to assess universal health coverage (UHC) for the Sustainable Development Goals (SDGs). Hypertension, diabetes, and dyslipidemia are major metabolic risk factors for mortality and disability from noncommunicable diseases worldwide.[1] In this study, we assessed the effective coverage of medication for hypertension, diabetes, and dyslipidemia in the middle-aged and older population in Japan.[2]

【Methods】

We obtained cross-sectional data for individuals aged 40 - 74 years from the National Health and Nutrition Surveys of 2003 - 2017. We defined the treatment need for hypertension, diabetes, and dyslipidemia using biomarkers, such as systolic blood pressure (SBP), hemoglobin A1c (HbA1c), and non-high-density lipoprotein cholesterol (non-HDL-C), equal to or greater than diagnostic thresholds or self-reported medication use. For individuals needing treatment, we conducted matching to estimate treatment effects and effective coverage, defined as the fraction of potential reductions in biomarkers actually achieved in treated individuals.

【Results】

The age-standardized prevalence of treatment need for hypertension, diabetes, and dyslipidemia remained stable at around 40%, 7%, and 33%, respectively, from 2003 - 2017. Average treatment effects for those treated were 14.8 mmHg for SBP, 1.2 percentage points for HbA1c, and 57.9 mg/dL for non-HDL-C. The figure shows that effective coverage increased between 2003 and 2007 (hypertension: 48.4%, diabetes: 43.8%, dyslipidemia: 86.3%) and 2013 - 2017 (hypertension:76.2%, diabetes:74.7%, dyslipidemia:94.6%).

【Future research】

Effective medication coverage for metabolic risk factors has improved. Most of the potential reductions in non-HDL-C have been achieved, while further efforts are necessary to improve the effectiveness of antihypertensive and antidiabetic drugs in the Japanese health care system. In future research, we would like to apply effective coverage to examine the effects of health care interventions on the prevention of cardiovascular diseases.

【Acknowledgment】

This study was supported by the Japan Society for the Promotion of Science [grant numbers 24590785, 18H03063].

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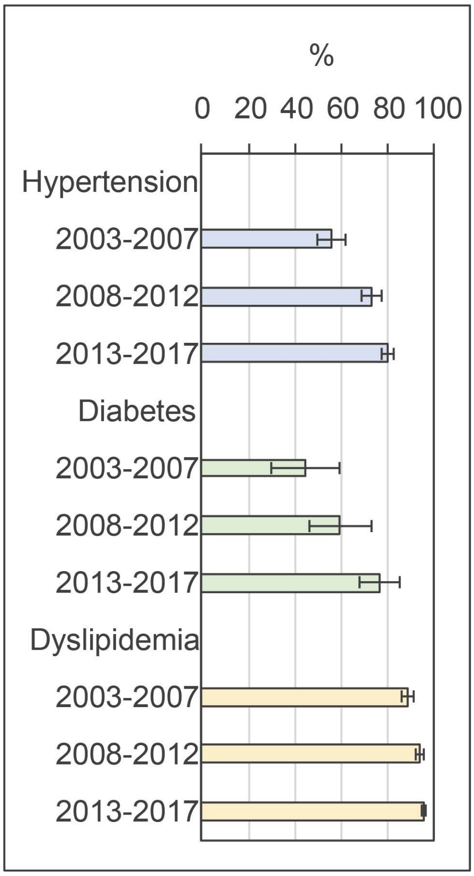

Figure. Effective coverage of medication for hypertension, diabetes and dyslipidemia in adults aged 40-74 years in Japan

Error bars indicate upper and lower bounds of 95% confidence intervals.

A study on the quality evaluation of health foods with functional claims

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【Introduction】

The extension of healthy life expectancy is one of the crucial issues of the super-aging society in Japan. The proper use of health foods (HF), including "Foods for Specified Health Uses", appears to be effective in extending healthy life expectancy. However, products that have not undergone proper efficacy and safety evaluations are being sold. Hepatic dysfunction and health damage due to estrogenic effects have been reported due to the consumption of certain HF. In 2018, the Food Sanitation Law was revised in part, and a system of "gathering information about health hazards from foods including ingredients needing special attention," was incorporated; four such plant-derived ingredients were established in 2019.

In 2015, the synergy research was initiated by National Institute of Health and Nutrition (NIH) in cooperation with Research Center for Medicinal Plant Resources, after NIH was combined with the National Institute of Biomedical Innovation. This study was conducted to confirm the safety and efficacy of HF and establish a quality evaluation method. Some parts of the study's findings are presented in this paper.

【Materials and methods】

First, we investigated the HF that showed high frequency of use as a health food ingredient (HFI) with limited scientific evidence. Herbal medicines (HM), HFI, and HF were assessed as follows: 1) differentiation of raw plant species by genetic analysis, 2) analysis of the functional (glabridin) and medicinal (glycyrrhizin) ingredients, 3) estrogen activity assay, and 4) effects on the activity of hepatic drug-metabolizing enzymes in normal female and post-menopausal model mice.

【Results】

Although several HF were selected, we have discussed licorice in this section. Licorice has been sold as HM, HFI, HF, and imported HF. Glabridin was detected in HM, HFI, and HF made from *Glycyrrhiza glabra* or *G. inflata* (Figure 1). Likewise, glycyrrhizin was not detected in one HFI or in HF containing only one HFI (Figure 1). However, glycyrrhizin was detected in other HF, and it was found in almost all imported HF. Estrogenic activity was detected in some HM, HFI, and HF. The effects on the activity of the hepatic drug-metabolizing enzyme, and the weight of the reproductive organs and fat in post-menopausal model mice might be useful in evaluating the estrogenic activity of HFI.

【Future direction】

Since the recent revision of the Food Sanitation Law, prevention of health damage has become an important issue. Quality evaluation of HF, including their safety and efficacy, is required in the future. This study verified the safety and efficacy of HF, leading to the maintenance and promotion of safe and secure health in people. We will continue to provide evidence of safety and efficacy from this study the public widely.

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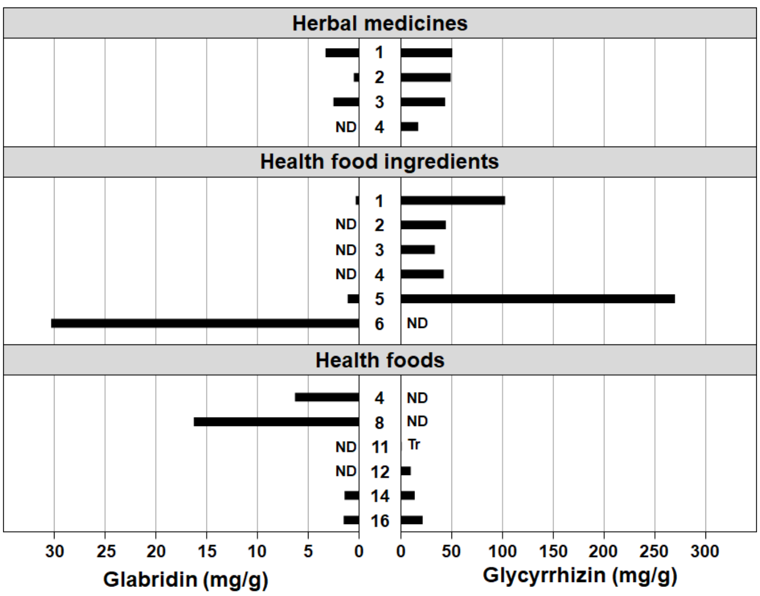

Figure 1. Glabridin and glycyrrhizin content in licorice-based products used as herbal medicines, health food ingredients, and health foods

Role of the Brain in the Regulation of Growth and Glucose Metabolism

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【Introduction】

In recent years, the prevalence of type 2 diabetes has increased considerably worldwide. Hence, it is crucial and imperative to develop strategies for preventing disease onset and minimizing its complications. Insulin receptor substrates (IRS) are activated by insulin and insulin–like growth factor (IGF)–1 receptors and allow docking of downstream effectors. Hence, they are essential for insulin and IGF signaling. In particular, IRS1 and IRS2 play a key role in glucose homeostasis. Our previous study demonstrated that IRS1 plays an important role in not only glucose metabolism but also growth in whole–body IRS1–knockout mice1). However, the underlying molecular mechanisms and tissues or organs responsible for IRS1–mediated growth and glucose homeostasis are unclear. Since recent studies have revealed that the brain, especially the hypothalamus, plays a crucial role in the regulation of food intake and glucose homeostasis, we investigated the role of IRS1 in hypothalamic neurons to elucidate the mechanism of IRS1–mediated growth and glucose homeostasis in the present study.

【Subjects and Methods】

We induced downregulation of IRS1 expression in a hypothalamic cell line by the addition of siRNA. We analyzed neurite outgrowth, neural proliferation, and mRNA expression levels in these cells, with or without the stimulation of insulin and IGF–1. We also investigated the phosphorylation of intracellular signaling proteins in these cells.

【Results】

Downregulation of IRS1 was associated with significant impairment of IGF–1–induced neurite elongation in these cells. GHRH mRNA expression levels after IGF–1 treatment were also significantly decreased in cells with downregulated IRS1. There were no differences in neural proliferation after IGF–1 administration between the control and IRS1–downregulated neurons.
Downregulation of IRS1 was associated with a decrease in Akt phosphorylation, but not Erk phosphorylation, induced by IGF–1 in these cells.

【Conclusion and Future Direction】

This study demonstrates that IRS1 plays a role in neurite outgrowth, but not in the proliferation of GHRH–producing hypothalamic neurons. Our findings suggest that brain IRS1 regulates both somatic growth and glucose metabolism via GHRH expression (Figure). We are now analyzing growth–related parameters and metabolic factors in brain–specific IRS1 knockout (NIrs1KO) mice. Further research is necessary to prevent and treat diabetes.

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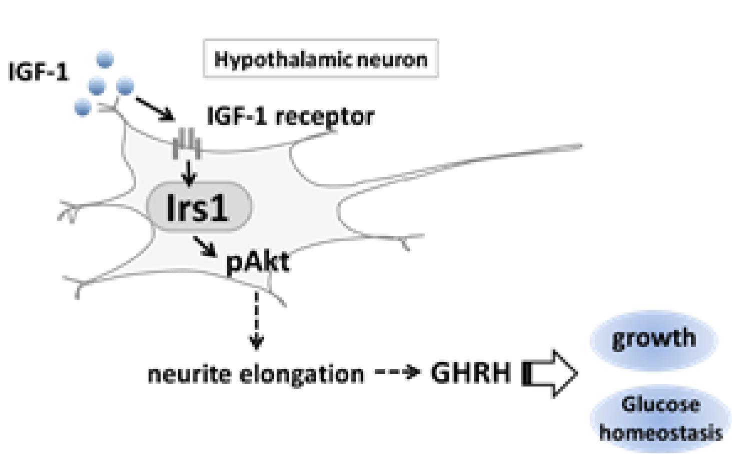
【Figure】 Role of Irs1 in hypothalamic neuron



Does breakfast skipping induce postprandial glucose excursion in lunch?

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【Introduction】

A well-balanced healthy diet is important for health and the prevention of chronic disease. However, recent studies indicate that not only "what we eat" but also "when we eat" is important and influences the physiological response and metabolism related to health outcomes [1, 2].

Our laboratory reported that a high-fat diet in the morning has a risk of increasing postprandial glucose level at lunch [2]. Unhealthy dietary habits can have various effects on cardiometabolic health markers, and skipping breakfast is a risk factor for diabetes and cardiometabolic disorders. One of such disorder is postprandial hyperglycemia. We examined the influence of breakfast-skipping on the postprandial glucose response[3]. (Meal timing and health were well documented by Dr. Yamasaki (the Number 61, February, 2019)).

【Subjects and method】

Nine young and healthy subjects (21.4±1.4 y) performed two different eating pattern trials: 1) three meals and 2) skipping breakfast. Blood glucose was measured continuously for 24-hours using a continuous glucose monitoring system (CGMS).

【Results and discussion】

Mean glucose values were not significantly different between the two trials. However, the peak postprandial glucose value in skipping breakfast trials was significantly higher than that in the three-meals trials. In the dinner, postprandial glucose responses were not significantly different between trials.

【Future research】

There are some variations of meal timing in the real world. We plan to examine and understand the effects of meal timing on health outcomes.

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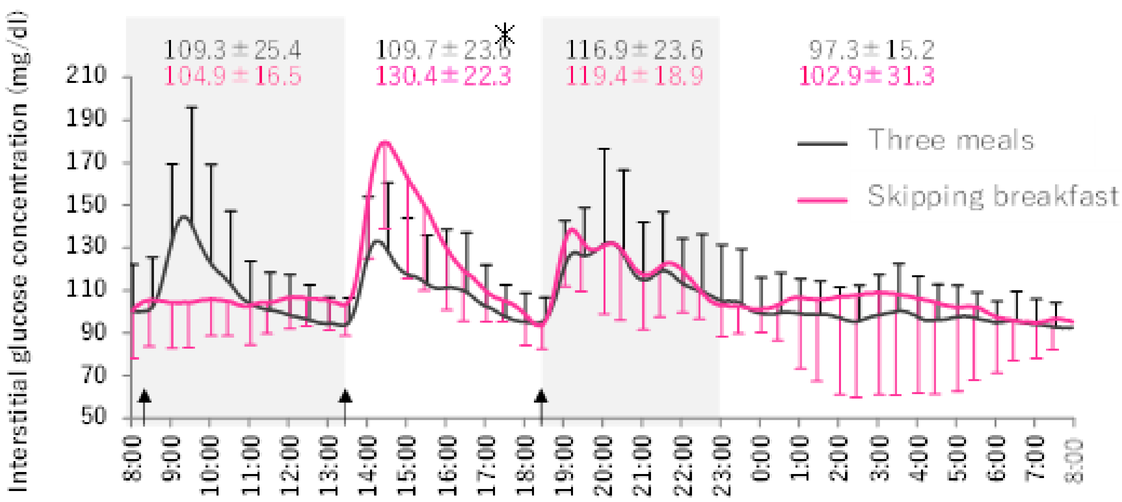

**Figure. Time course of interstitial glucose concentrations over 24 hours.
Data represents means with standard deviations represented by vertical bars (n=9).
Breakfast-skipping induced increased postprandial glucose levels at lunch.**

A U-Shaped Relationship between the Prevalence of Frailty and Body Mass Index in Community-Dwelling Japanese Older Adults: The Kyoto – Kameoka Study

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Department of Physical Activity Research

【Introduction】

Frailty is a condition in which the function of multiple physiological systems are impaired due to a decrease in homeostatic response to stress[1,2]. A cross–sectional British epidemiological study showed that body mass index (BMI) has a U–shaped relationship with the prevalence of frailty; it also showed that the BMI ranges associated with the lowest prevalence of frailty are 18.5 – 24.9[3,4] and 25 – 29.9 kg/m^2 [5]. Although the optimum BMI range may vary from study to study, the current state of knowledge points to the importance of maintaining a healthy BMI to prevent frailty. However, the mean BMI differs between Japanese and British people[6], and it is difficult to extrapolate the results of previous studies to account for Japanese people. With the use of two validated frailty assessment tools, the present study aimed to investigate the relationship between the prevalence of frailty and BMI in community–dwelling Japanese older adults.

【Methods】

This cross–sectional study used baseline data of 7191 individuals aged ≥65 years living in Kameoka City, Kyoto, Japan. BMI was calculated based on self–reported height and body weight and classified into six categories. The validity of "self–reported" BMI values was evaluated on a sub–cohort of 1169 subjects. No difference was observed between the BMI values calculated from actual height and weight measurements (22.6 kg/m^2 and 23.0 kg/m^2). A strong correlation was noted between these two BMI parameters (r = 0.915). Frailty was assessed using two validated assessment tools: the Fried phenotype (FP) model and the Kihon Checklist (KCL). The relationship between frailty and BMI was evaluated using multivariate, restricted spline logistic regression.

【Results】

The prevalence of frailty defined using the FP model and KCL for each BMI category (<18.5, 18.5 – 19.9, 20.0 – 22.4, 22.5 – 24.9, 25.0 – 27.4, and ≥27.5 kg/m^2) were 25.3% and 55.5%, 19.6% and 37.7%, 14.3% and 34.2%, 12.4% and 32.6%, 12.6% and 34.3%, and 19.4% and 49.2%, respectively. The spline model showed a significant U–shaped relationship between BMI and the prevalence of frailty defined using both the KCL and FP models. The BMI range corresponding to the lowest prevalence of frailty was found to be 21.4 – 25.7 kg/m^2 (Figure 1).

【Future direction】

The results indicate that a healthy BMI may reduce the prevalence of frailty, and the risk of frailty should be evaluated in underweight and overweight people. Middle–aged and older individuals with obesity and metabolic syndrome may already experience frailty. Therefore, adding BMI–related items to the tools currently used for evaluating frailty among middle–aged and older individuals could potentially lead to a more robust diagnosis of frailty. The National Institute of Health and Nutrition is focused on the "prevention of frailty from working generations" and is working in cooperation with Osaka Prefecture to aim for social implementation.

Please refer the article below for details.

Watanabe, D., Yoshida, T., Watanabe, Y., Yamada, Y., Kimura, M., and Kyoto–Kameoka Study Group. A U–Shaped Relationship Between the Prevalence of Frailty and Body Mass Index in Community–Dwelling Japanese Older Adults: The Kyoto–Kameoka Study. J. Clin. Med. 2020, 9, E1367. doi: 10.3390/jcm9051367.

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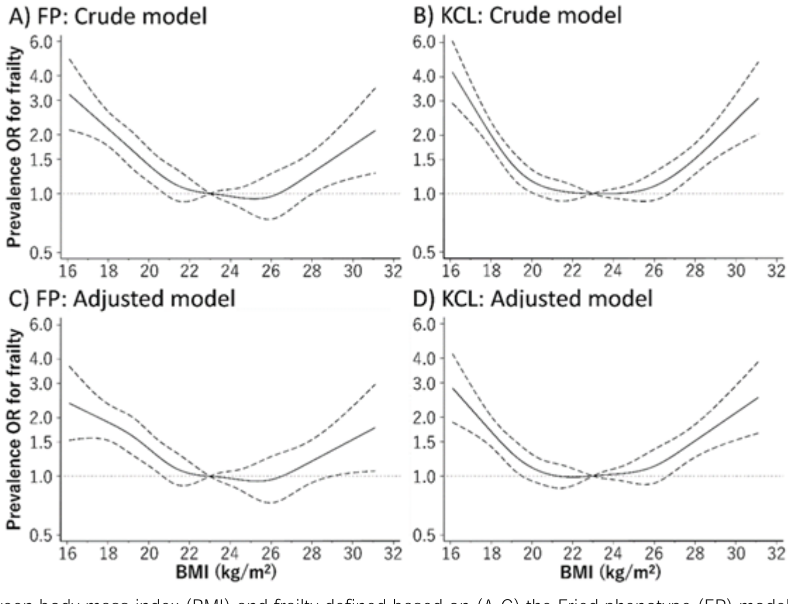

Figure 1. Relationship between body mass index (BMI) and frailty defined based on (A,C) the Fried phenotype (FP) model and (B,D) the Kihon Checklist (KCL), using a restricted cubic spline logistic regression model. Frailty according to the KCL was defined as a score ≥7 out of 25 points, whereas frailty according to the FP model was defined as a score ≥3 out of 5 points. Solid lines represent odds ratios (ORs) and dashed lines represent 95% confidence intervals (CIs). The OR was calculated using a BMI reference value of 23.0 kg/m^2. The analysis was adjusted for age, sex, region, smoking habit, alcohol consumption, education history, number of drugs taken, family composition, economic status, physical activity, presence/absence of dentures, and history of hypertension, stroke, heart disease, diabetes, and dyslipidemia.