

Study Report on the Trends of Studies in Japan and Overseas Related to Nutrition/Diet and Physical Activity/Exercises in the Prevention and Treatment of Lifestyle Diseases

Summary Report

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1. Summary of study operations

1.1 Background and objective of this study

Background

- The Japan Agency for Medical Research and Development (AMED) has promoted integrated research and development from the foundation to practical implementation through the project for the practical implementation of measures against lifestyle diseases, including circulatory disorders and diabetes mellitus, with coverage of a variety of such themes as preventing the onset of lifestyle diseases through improvement of lifestyle habits, elucidating the pathology of lifestyle diseases, establishing the prevention/treatment methods, and maintaining and improving the quality of life of patients with lifestyle diseases.
- **Nutrition/diet and physical activity/exercise play an important role in the prevention/treatment of lifestyle diseases.** In improving the effect of prevention/treatment for lifestyle diseases, it is considered extremely important to improve dietary/exercise habits through clinical guidance that reflects the latest research in the applicable areas.
- Examples of advanced measures being taken in these areas include the establishment of a strategic plan regarding nutrition in the US.
- On the other hand, **there is a shortage of evidence regarding diet therapy and exercise therapy** in Japan. In order to promote research studies on nutrition/diet and physical activities/exercise in Japan, **there is a need to grasp the actual circumstances regarding research overseas and in Japan and clarify the differences, as well as to organize the information, including the environment of research.**



Objective

- This study was conducted to **identify the information on research studies in Japan and overseas, systems related to research promotion, and trends and organize these systematically for multifaceted verifications of the present issues with the aim of resolving these issues and utilization in future project design at AMED** as a part of the effort to promote medical research and development regarding nutrition/diet and physical activity/exercise for lifestyle diseases, such as circulatory disorders and diabetes mellitus.

1.2 Items implemented

- In this study, the research gap in medical research and development related to nutrition/diet and physical activity/exercise in the prevention/treatment of lifestyle diseases, such as circulatory disorders and diabetes mellitus, as well as the factors contributing to this gap, were identified and analyzed. The following steps (1) to (4) below were implemented with the aim of clarifying the areas and themes to be addressed by AMED.
 - Implementation item (1) Interview with the experts
 - Implementation item (2) Survey of the literature (including published information)
 - Implementation item (3) Trend survey
 - Implementation item (4) Organization and discussion on the necessary topics on the research gap
- In this study, *research gap* was defined as the “state of shortage or insufficiency in scientific evidence (evidence based on research articles) that is required for addressing the clinical issues in the prevention/treatment of disease (clinical question; CQ), resulting in a gap between these factors.” In addition, cases where scientific evidence was only available for a specific population (race, sex, age, pathology) were also regarded as the presence of a research gap (insufficiency in evidence required for addressing the clinical issues).

1. Summary of study operations

1.3 Overall structure of this study (1/2)

- This study summarized and discussed (a) the research gap and (b) factors contributing to the research gap in the area of nutrition/diet and the area of physical activity/exercise for prevention/treatment of lifestyle diseases in Japan. Also, implementation items (1) to (3) were conducted to investigate the themes and items to be addressed by the government and AMED going forward. (Refer to 1.2 “Items implemented” for the specific items to be implemented)

a. Study of the research gap in Japan

Implementation item (1) Interview with the experts

- Interview was conducted with the experts to collect their opinions on the actual circumstances of the research gap in Japan and the research themes to be addressed in Japan with consideration for these circumstances.

Implementation item (2) Survey of the literature (including published information)

- Literature survey was conducted on clinical guidelines on stroke, cardiac failure, and diabetes mellitus to compare the recommendations in the guideline in Japan and overseas as well as the evidence used as rationale for these recommendations to clarify the details of the research gap.

Implementation item (3) Trend survey

- Strategic plans in Japan and overseas were investigated and compared to clarify the research themes that are considered to require a particular focus in various overseas countries.

b. Factors contributing to the research gap

Implementation item (1) Interview with the experts

- Interviews were conducted with the experts to collect their opinions on the state of research personnel in Japan, issues regarding research/educational systems, and items expected by the government and AMED in research promotion.

Implementation item (3) Trend survey

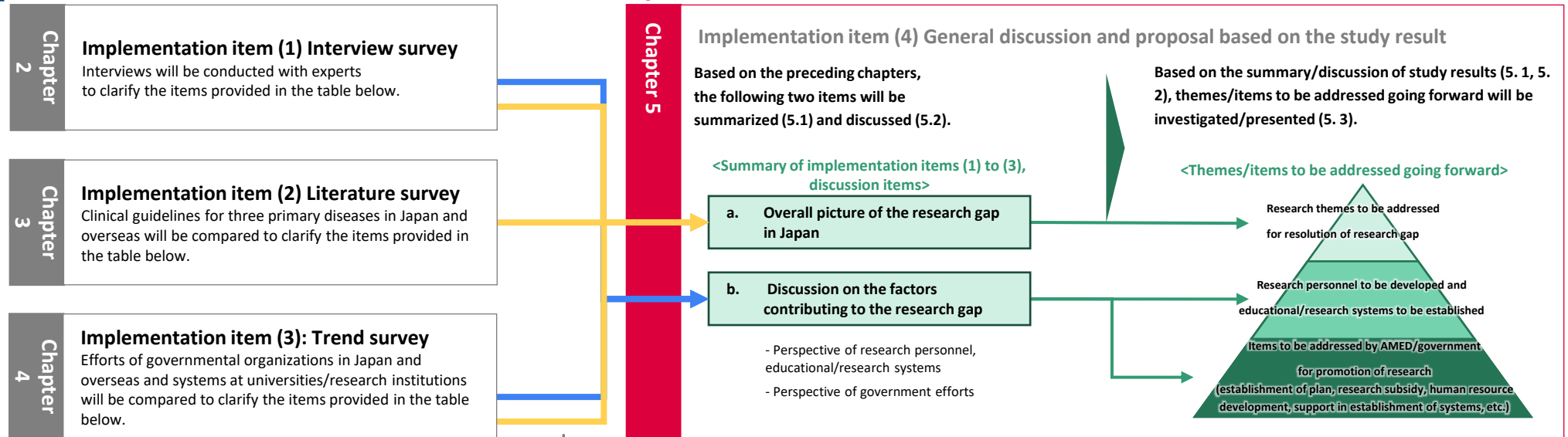
- Efforts for research promotion (such as establishment of strategic plans and subsidization system) in Japan and overseas as well as the education/research systems were investigated and compared to clarify the characteristics and issues related to research personnel and educational/research system in Japan, as well as the characteristics and issues regarding the efforts made by the Japanese government.

1. Summary of study operations

1.3 Overall structure of this study (2/2)

- This study was conducted under the following structure. In this summary report, the contents of Chapter 5 of the main text of the study report are provided.

Overall structure of this study



Corresponds to Summary of implementation items (1) to (3), discussion item "a."

Corresponds to Summary of implementation items (1) to (3), discussion item "b."

	Overall picture of the research gap in Japan and research themes to be addressed going forward	Current circumstances and issues regarding research personnel, educational/research systems	Current circumstances and issues regarding government efforts (establishment of strategic plans, research subsidies, etc.)
Chapter 2	<ul style="list-style-type: none"> Actual circumstances regarding the overall picture of the research gap in Japan Themes to be addressed in Japan going forward 	<ul style="list-style-type: none"> State of research personnel in Japan Issues regarding research/educational systems in Japan 	<ul style="list-style-type: none"> Items expected from AMED/government in research promotion
Chapter 3	<ul style="list-style-type: none"> Domestic research gap in evidence Global research gap in evidence Domestic research gap in recommendations 	-	-
Chapter 4	<ul style="list-style-type: none"> Themes that are considered to require a particular focus overseas 	<ul style="list-style-type: none"> Characteristics and issues regarding research personnel and educational/research systems in Japan 	<ul style="list-style-type: none"> Characteristics and issues regarding government efforts

1. Summary of study operations

(Reference) Summary of interview survey

- Summary of interview survey is as follows

Summary of interview survey**[Subjects of interview survey]**

- ✓ Interviews were conducted for primary members of working groups involved in the literature review for guideline preparation, young researchers, and directors of academic societies related to nutrition.
- ✓ Subjects of interview survey and status (interview arrangements and implementation status) were as follows:

Category	Name	Affiliation/title (at the time of interview)	Subject of interview	
			Before	After
Academic society guideline	Prof. Akira Fujiyoshi	Professor at the Department of Hygiene, School of Medicine, Wakayama Medical University	○	○
	Prof. Kazunori Utsunomiya	Executive Adviser at Jiseikai Nomura Hospital/Professor Emeritus at Jikei University		○
Regulatory authority guideline	Prof. Satoshi Sasaki	Professor at the Department of Social and Preventive Epidemiology, School of Public Health, Graduate School of Medicine and Faculty of Medicine, the University of Tokyo	○	○
	Prof. Fuminori Katsukawa	Professor at the Sports Medical Research Center, Keio University		○
Young researcher	Prof. Masamitsu Kamada	Lecturer of Health Sociology at the Department of Health Education and Sociology, School of Public Health, Graduate School of Medicine and Faculty of Medicine, the University of Tokyo	○	
Academic society related to nutrition	Prof. Yutaka Seino	Director of the Japan Society of Metabolism and Clinical Nutrition	○	
	Prof. Naoki Hiki	Director of the Japanese Society for Clinical Nutrition and Metabolism	○	
	Prof. Yoshihiko Kanno	Director of the Japanese Society of Clinical Nutrition	○	

1. Summary of study operations

1.4 Summary of the study results (1/2)

- Overall picture of the research gap in Japan (a) and research themes to be addressed going forward for resolution of research gap:

Research gap identified for each area from the results of this study and the research themes to be addressed (examples) are as follows:

Area	a. Overall picture of the research gap in Japan	Research themes to be addressed going forward for resolution of research gap (examples)
Nutrition/ diet	(1) Relationship between energy/nutritional intake and lifestyle diseases	<ul style="list-style-type: none"> • Research on dietary reference intake (ratio of energy/nutritional intake, intake of individual nutrition, etc.)
	(2) Individualization of diet therapy	<ul style="list-style-type: none"> • Research on what, when and how often to eat (dietary pattern, etc.) • Research on the design of diet therapy according to the characteristics of the subject (nutritional intervention by pathology, nutrition therapy, etc.)
	(3) Guidance by a registered dietitian on the practice of diet therapy	<ul style="list-style-type: none"> • (Handled by promoting human resource development for registered dietitians rather than research theme)
Physical activity/ exercise	(1) Exercise intensity/period/frequency in aerobic exercise	<ul style="list-style-type: none"> • Research on exercise intensity/period/frequency
	(2) Rehabilitation support using advanced technology	<ul style="list-style-type: none"> • Research on the development of exercise intervention method using advanced technology (monitoring technology, gaming device/VR, internet, robot, etc.)
	(3) Monitoring the amount of physical activity	
Other (Common)	(1) Observational study for data collection/accumulation and big data analysis based on this study	<ul style="list-style-type: none"> • Research by introduction of big data/analysis technology
	(2) Assessment on the utilization status of standard treatment specified by the guideline and verification on the effect of recommendations	<ul style="list-style-type: none"> • Research on the assessment of recommendations in the guideline
	(3) Research on practices that contribute to the realization of behavioral change	<ul style="list-style-type: none"> • Research on improvement of lifestyle diseases and contribution to presymptomatic state through behavioral change

1. Summary of study operations

1.4 Summary of the study results (2/2)

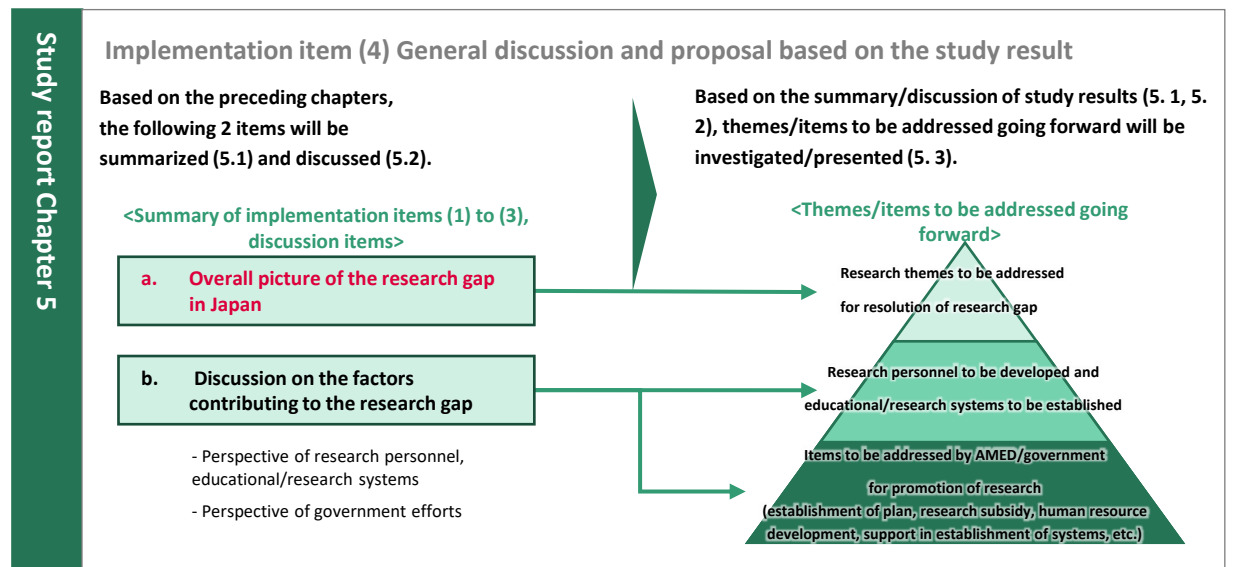
- Discussion on the factors contributing to the research gap (b) and efforts for research promotion, establishment of research/educational systems, and human resource development:

Factors contributing to research gap as identified from the result of this study, and the systems to be established, human resources to be developed, and items to be addressed by the government and AMED for promotion of research were as follows:

Area	b. Discussion on the factors contributing to the research gap	Efforts for research promotion, establishment of research/educational systems, and human resource development
Nutrition/ diet	<ul style="list-style-type: none"> • Lack of established systems for strategic investment for key themes 	<ul style="list-style-type: none"> • Strategic plans showing the goal and the road map for research and development need to be established (with consideration for the consistency with the mid- to long-term plan of National Institute of Health and Nutrition, National Institutes of Biomedical Innovation, Health and Nutrition). • Positioning of nutrition/diet in the broad context of environment and sustainability in food production is important (and is also effective from the perspective of promoting multidisciplinary research studies). • Research themes of particular importance in Japan should be determined within the area of nutrition/diet, and a system of subsidization with specific focus should be established.
	<ul style="list-style-type: none"> • Lack of established system on the joint research between the areas of nutrition and medicine 	<ul style="list-style-type: none"> • Multifaceted research promotion through involvement in the establishment of research systems related to these themes, centered around the government-affiliated research institutions.
	<ul style="list-style-type: none"> • Shortage of registered dietitians involved in medical research • Shortage of personnel who are able to engage in epidemiological research 	<ul style="list-style-type: none"> • Research/educational institutions involving nutrition epidemiological research should be established in graduate schools of medicine and graduate schools of public health to develop specialists in nutrition guidance who are able to engage in government policies on nutrition and preventive medicine/primary prevention. • Efforts required include the increase in the number of staff members with medicine as specialization and physicians in schools for development of registered dietitians, and inclusion of practical sessions on medical care in the clinical settings.
Physical activity/ exercise	<ul style="list-style-type: none"> • Lack of established systems for strategic investment for key themes 	<ul style="list-style-type: none"> • Strategic plans showing the goal and the road map for research and development need to be established (with consideration for the consistency with the mid- to long-term plan of National Institute of Health and Nutrition, National Institutes of Biomedical Innovation, Health and Nutrition).
	<ul style="list-style-type: none"> • Insufficient support for research studies utilizing advanced technology 	<ul style="list-style-type: none"> • (Reforms of systems required to lower the hurdles of having advanced technology approved and listed for insurance coverage as medical devices).
	<ul style="list-style-type: none"> • Shortage of personnel who are able to engage in epidemiological research 	<ul style="list-style-type: none"> • (Research/educational institutions involving epidemiological research should be established in graduate schools of medicine and graduate schools of public health to develop personnel who are able to engage in epidemiological research).

2. Summary of the study results

2.1 Overall picture of the research gap in Japan



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2.1 Overall picture of the research gap in Japan

2.1.1 Method of organizing the overall picture of the research gap in Japan

- Based on implementation item (1) Interviews with the experts and implementation item (2) Survey of the literature (including published information), [the areas/themes that should be addressed in Japan going forward as the overall picture of the research gap in Japan](#) were organized according to [Perspective 1] to [Perspective 3] below.
- Also, with consideration for implementation item (3) Trend survey, [research themes that are not included in the research gap in Japan below but considered to require a particular focus in the strategic plans of various overseas countries](#) were organized.

Perspectives for the organization of the research gap

[Perspective 1: Domestic research gap in evidence]

Cases where the evidence supporting the recommendations for CQ in the domestic clinical guideline are shown in “quotation of overseas literature”

[Perspective 2: Global research gap in evidence]

Cases where the evidence supporting the recommendations for CQ in the domestic clinical guideline are “lacking domestically and internationally”

[Perspective 3: Domestic research gap in recommendations]

Cases where the recommendations for CQ “are unavailable” in the domestic clinical guideline, specific examples are thought to include the following two cases:

- (1) If the recommendations for CQ are not unavailable in the domestic clinical guideline but available in the US or UK guideline
- (2) If the recommendations for CQ are not unavailable in the domestic clinical guideline but provided as a response to general question (Q)

* In this study, a *research gap* was defined as the “state of shortage or insufficiency in scientific evidence (evidence based on research articles) that are required for addressing the clinical issues in the prevention/treatment of disease (clinical question), resulting in a gap between these factors.” In addition, cases where scientific evidence is only available for a specific population (race, sex, age, pathology) were also regarded as the presence of a research gap (insufficiency in evidence required for addressing the clinical issues).

2.1 Overall picture of the research gap in Japan

2.1.2 Area of nutrition/diet: research gap in stroke area

- Research gap identified by implementation item (1) Interview survey and implementation item (2) Literature survey for area of nutrition/diet: Stroke area were as follows.

Perspective	Description	Source	
		Implementation item (1) Interview survey	Implementation on item (2) Literature survey
1. Domestic research gap in evidence	<ul style="list-style-type: none"> In the area of prevention, a gap is thought to exist in research studies regarding the avoidance of alcohol consumption in large amounts for the prevention of stroke. SR (systematic review) and MA (meta-analysis on overseas prospective cohort studies) have been quoted for consumption of alcohol in large amounts regarding the prevention of stroke onset. 		○
	<ul style="list-style-type: none"> In the area of treatment, a gap is thought to exist in research studies regarding nutrition intervention in patients with malnutrition. RCT has been conducted on these theme in 4,023 patients with stroke who are capable of swallowing as a part of FOOD Trial Collaboration in the UK, and some effects have been achieved. 		○
2. Global research gap in evidence	<ul style="list-style-type: none"> A gap is thought to exist in the research studies on screening tests for water drinking tests in the area of treatment and nutrition assessment in the area of treatment/rehabilitation. All four applicable studies were small-scale RCT and cohort studies conducted in Japan, and these were estimated to be in a supplementary position within the recommendations for CQ in the guideline, and the priority was therefore thought to be not high. 		○
3. Domestic research gap in recommendations	-		

Source

2.1 Overall picture of the research gap in Japan

2.1.2 Area of nutrition/diet: research gap in cardiac failure area

- Research gap identified by implementation item (1) Interview survey and implementation item (2) Literature survey for area of nutrition/diet: Cardiac failure area were as follows.

Perspective	Description	Source	
		Implementation item (1) Interview survey	Implementation item (2) Literature survey
1. Domestic research gap in evidence	-		
2. Global research gap in evidence	<ul style="list-style-type: none"> A gap is thought to exist in the research studies on salt reduction in the area of treatment. A gap is thought to exist, in which the Japanese guideline quotes the EU guideline as evidence supporting the recommendations for CQ but only a description “target for salt reduction in chronic cardiac failure is set as < 6 g daily in this guideline with consideration for the current circumstance of diet in the Japanese population” is provided. 		○
3. Domestic research gap in recommendations	-		

Source

2.1 Overall picture of the research gap in Japan

2.1.2 Area of nutrition/diet: research gap in type 2 diabetes mellitus area

- Research gap identified by implementation item (1) Interview survey and implementation item (2) Literature survey for area of nutrition/diet: Type 2 diabetes mellitus area were as follows.

Perspective	Description	Source	
		Implementation item (1) Interview survey	Implementation item (2) Literature survey
1. Domestic research gap in evidence	<ul style="list-style-type: none"> In the area of treatment, a gap is thought to exist in research studies regarding the correction of lifestyle habits with a focus on diet therapy, as well as the individualization of diet therapy. Among the reference literature extracted, the Diabetes Prevention Program in the US conducted a lifestyle intervention study in 2,766 patients with a 10-year follow-up survey thereafter. Look AHEAD study was quoted as a representative study in patients with diabetes mellitus with long-term research with an observation period spanning 9.6 years. 		○
	<ul style="list-style-type: none"> In the area of nutrition/diet, it was pointed out that a research gap exists in nutrition therapy for patients with lifestyle diseases by pathology due to the historical background of advancement in the research studies involving this area. 	○	
	<ul style="list-style-type: none"> A gap is thought to exist in the research studies on guidance provided by registered dietitians in the practice of diet therapy. 		○
2. Global research gap in evidence	-		
3. Domestic research gap in recommendations	<ul style="list-style-type: none"> A research A gap is thought to exist in the ratio of nutritional intake, relationship between total fat intake and risk of diabetes mellitus onset, impact on artificial sweetener on the risk of diabetes mellitus onset and blood glucose control, relationship between carbohydrate intake and the risk of onset and management of diabetes mellitus, and the impact of vitamins/minerals on management of diabetes mellitus in the area of prevention/treatment of type 2 diabetes mellitus. Overseas literature was quoted for the ratio of nutritional intake, total fat intake, and artificial sweeteners, and no clear evidence was shown to be available for the response to Q in the guideline. For carbohydrate intake, multiple studies from Japan were quoted; however, these were limited to small-scale RTC and cohort studies as well as a diet survey. Furthermore, while a cross-sectional study in Japan was quoted for vitamins/minerals, the relationship with the management of diabetes mellitus has not been confirmed. 		○

2.1 Overall picture of the research gap in Japan

2.1.3 Area of physical activity/exercise: research gap in stroke area

- Research gap identified by implementation item (1) Interview survey and implementation item (2) Literature survey for area of physical activity/exercise: Stroke area were as follows.

Perspective	Description	Source	
		Implementation item (1) Interview survey	Implementation item (2) Literature survey
1. Domestic research gap in evidence	<ul style="list-style-type: none"> A gap is thought to exist in the research studies on rehabilitation support using robots in the area of rehabilitation. In addition to studies with high evidence levels being conducted internationally, 160 clinical studies (100%) found at Clinical Trials.gov included 69 studies (43.1%) on exercise therapy, 48 studies (30.0%) on digital devices, and 25 studies (15.6%) on robot rehabilitation, suggesting the progression of development in this area globally. 		○
2. Global research gap in evidence	-		
3. Domestic research gap in recommendations	A gap is thought to exist in the research studies on exercise intensity/period/frequency of aerobic exercise in the area of prevention/treatment for stroke and type 2 diabetes mellitus.		○

Source

2.1 Overall picture of the research gap in Japan

2.1.3 Area of physical activity/exercise: research gap in cardiac failure area

- Research gap identified by implementation item (1) Interview survey and implementation item (2) Literature survey for area of physical activity/exercise: Cardiac failure area were as follows.

Perspective	Description	Source	
		Implementation item (1) Interview survey	Implementation on item (2) Literature survey
1. Domestic research gap in evidence	<ul style="list-style-type: none"> A gap is thought to exist in the research studies on exercise intensity/period/frequency of aerobic exercise in the area of prevention. Within the reference literature extracted, the HF-ACTION (Heart Failure: A Controlled Trial Investigating Outcomes of Exercise Training) study as the largest RCT that involves exercise training in patients with cardiac failure in the US, is quoted not only in CQ for recommendations on the amount/frequency/intensity of physical activity but also in cardiac rehabilitation and exercise assessment (6-minute walk test). 		○
2. Global research gap in evidence	<ul style="list-style-type: none"> Exercise therapy with the aim of improving exercise tolerability was thought to be applicable to the research gap. The experts have pointed out the shortage of evidence related to exercise therapy as a global research gap, suggesting that there is no evidence available on the appropriate frequency, intensity, and conditions of exercise for individual subjects. 	○	○
	<ul style="list-style-type: none"> In addition to the above, a gap is thought to exist in the research studies on remote rehabilitation practice using the internet and support involving the use of gaming devices and VR in the area of rehabilitation. 		○
3. Domestic research gap in recommendations	-		

2.1 Overall picture of the research gap in Japan

2.1.3 Area of physical activity/exercise: research gap in type 2 diabetes mellitus area

- Research gap identified by implementation item (1) Interview survey and implementation item (2) Literature survey for area of physical activity/exercise: Type 2 diabetes mellitus area were as follows.

Perspective	Description	Source	
		Implementation item (1) Interview survey	Implementation item (2) Literature survey
1. Domestic research gap in evidence	<ul style="list-style-type: none"> A gap is thought to exist in the research studies on exercise intensity/period/frequency of aerobic exercise in the area of treatment. All 41 reference literatures extracted were SR or MA, indicating the accumulation of research with high evidence levels internationally. 		○
2. Global research gap in evidence	-		
3. Domestic research gap in recommendations	-		

Source

2.1 Overall picture of the research gap in Japan

2.1.4 Other research gaps

- Research gap identified by implementation item (1) Interview survey and implementation item (2) Literature survey for other research gaps were as follows.

Perspective	Description	Source	
		Implementation item (1) Interview survey	Implementation item (2) Literature survey
1. Domestic research gap in evidence	<ul style="list-style-type: none"> A gap is thought to exist in the research studies on smoking abstinence and avoidance of passive smoking. With regard to the investigation on smoking abstinence and avoidance of passive smoking in the prevention of stroke, a prospective cohort study involving more than 10,000 patients has been conducted in the US and China. 		○
	<ul style="list-style-type: none"> The experts mentioned the research studies utilizing big data and the observational studies that act as the foundation of data collection and accumulation for such study as the research gap across different diseases and as a common factor between nutrition/diet and physical activity/exercise areas. 	○	
	<ul style="list-style-type: none"> From the perspective of the utilization status and effect verification of the guideline, expectations were expressed regarding the research studies on standard treatment in the guidelines with regard to the assessment of utilization status in the actual clinical practice and effect verification of guideline recommendations. 	○	
2. Global research gap in evidence	<ul style="list-style-type: none"> For areas/themes to be address in Japan going forward, the experts pointed out the global shortage of research studies on nutritional therapy in elderly patients with various disorders. In particular, research studies on nutrition therapy for sarcopenia and frailty were named as important themes in the research studies on nutrition therapy common to the areas of surgery/lifestyle disease. Other individual themes included assessment of energy/nutrition intake, nutrition absorption, mechanism of intestinal flora/endocrine system control by nutrition, continuous blood glucose level, and relationship between eating patterns and diseases. 	○	
	<ul style="list-style-type: none"> The experts pointed out the necessity for research studies on the amount of physical activity and the technology for monitoring this in preparation for the implementation of physical activity. 	○	
	<ul style="list-style-type: none"> The experts suggested research on the practical application contributing to the realization of behavioral change in people within the society as the common theme between the areas of nutrition/diet and physical activity/exercise. 	○	
3. Domestic research gap in recommendations	<ul style="list-style-type: none"> A gap is thought to exist in the research studies on eating pattern/sodium restriction across different diseases in the area of prevention/treatment. Mediterranean diet is recommended for eating pattern. 		○
	<ul style="list-style-type: none"> A research gap is thought to exist in behavioral change program for type 2 diabetes mellitus. 		○

2.1 Overall picture of the research gap in Japan

2.1.5 Summary of the overall picture of the research gap in Japan

- Based on the results above, the research gap in the areas of nutrition/diet and physical activity/exercise in Japan are summarized as follows.

Area	Research gap identified in this study (examples)	Remarks
Nutrition/diet	(1) Relationship between energy/nutritional intake and lifestyle diseases	Not available in domestic clinical guidelines for CQ
	(2) Individualization of diet therapy (patients with nutrition, elderly people, and others)	A research gap exists not only in Japan but globally regarding research studies on nutrition therapy in elderly people
	(3) Guidance by a registered dietitian on the practice of diet therapy	
Physical activity/exercise	(1) Exercise intensity/period/frequency in aerobic exercise	Not available in domestic clinical guidelines for CQ, although there are differences between diseases/areas
	(2) Rehabilitation support using advanced technology (robots, internet, gaming devices, VR, etc.)	
	(3) Monitoring the amount of physical activity	
Other (Common)	(1) Observational study for data collection/accumulation and big data analysis based on this study	
	(2) Assessment of the utilization status of standard treatment specified by the guideline and verification on the effect of recommendations	
	(3) Research on practices that contribute to the realization of behavioral change	

2.1.6 Research gap in Japan as identified in the trend survey

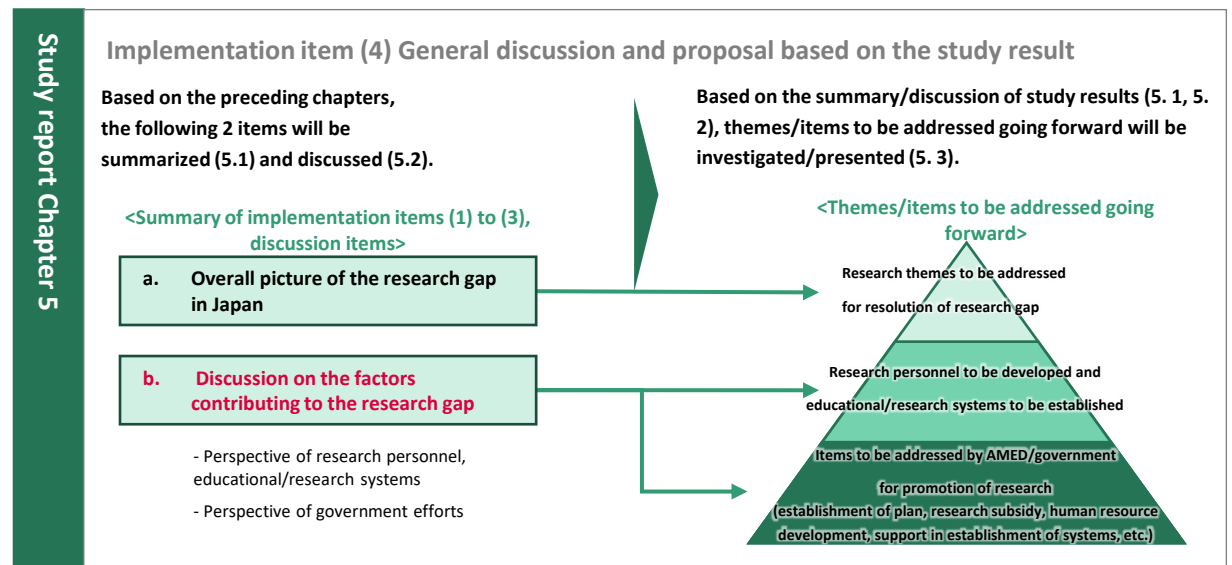
- In addition to the research gaps organized in [Perspective 1] to [Perspective 3], research themes considered to require a particular focus in the strategic plans of various overseas countries and are considered to be the research gap in Japan were as follows:

Themes mentioned in the strategic plans of various overseas countries that are considered to be research gaps in Japan

	Themes mentioned in the strategic plans of various overseas countries
U.S.	Bioinformatics research on nutrition-related genes and pathways
	Research on epigenetics
	Research in sensory nutrition and eating behavior
	Research on the microbiome (microbes in the digestive tract)
	Search for biomarkers
Finland	Research on the interaction between symptoms/drugs/nutrition
	Study on the functions of plant-based food
	Research on nutritional potential of alternative protein and raw materials used
	Research on the interaction between microbial flora, immune system, inflammation, inflammation, and intestinal tract barrier function

2. Summary of the study results

2.2 Discussion on the factors contributing to the research gap



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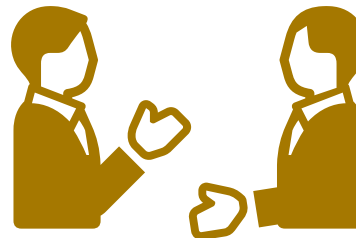
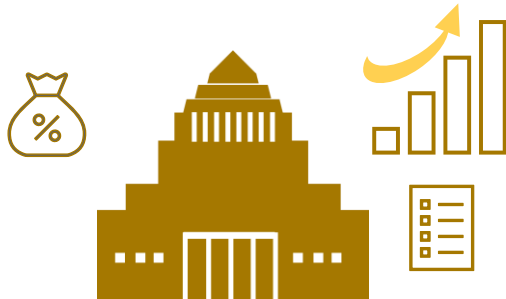
2.2 Discussion on the factors contributing to the research gap

2.2.1 Discussion on the factors contributing to the research gap in the area of nutrition/diet

- Factors that were thought to contribute to the research gap in the area of nutrition/diet were identified to be (1) Lack of established systems for strategic investment for key themes, (2) Lack of established system on the joint research between the areas of nutrition and medicine, and (3) Shortage of registered dietitians involved in medical research.

Study result	Study result	Study result
<p>Failure to set national strategic target and effective provision of research subsidy</p> <ul style="list-style-type: none"> While research goals in the area of nutrition/diet have been set in the mid- to long-term plan of the National Institutes of Biomedical Innovation, Health and Nutrition, research goals have not been set or announced clearly by the entire government. Although the Project for the General Research on Measures Against Lifestyle Diseases Including Circulatory Disorders and Diabetes Mellitus by the Ministry of Health, Labour and Welfare has promoted subsidization for the research in this area, the subsidization system does not focus on the area of nutrition/diet or the research in the specific area unlike the system in the UK. 	<p>Failure to establish systems to facilitate multidisciplinary research studies compared to overseas countries</p> <ul style="list-style-type: none"> While the majority of the research/educational systems in Japan are established by units of laboratory, those overseas are made of a larger organizational structure in units of faculty and specialization with inclusion of multiple laboratories. In addition, there are examples overseas where government research centers being established in universities with government making efforts to establish systems for multidisciplinary research. 	<p>Many registered dietitians have no interest in working in medical setting</p> <ul style="list-style-type: none"> For the following reasons, role models of registered dietitians working in medical settings have not been established, which leads to human resources with specialist education in nutrition not engaging in medical research: <ul style="list-style-type: none"> Shortage of staff members with medical qualifications in the schools for the development of registered dietitians in Japan Shortage of registered dietitians flourishing in the area of medical care

Factor (1)	Factor (2)	Factor (3)
Lack of established systems for strategic investment for key themes	Lack of established systems on joint research between the areas of nutrition and medicine	Shortage of registered dietitians involved in medical research*



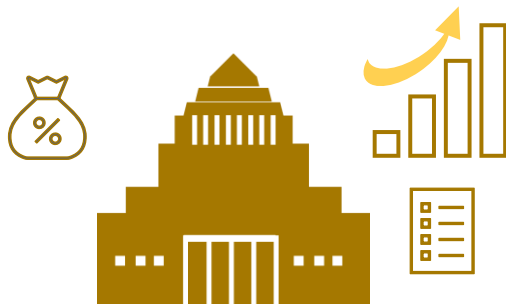
*From the perspective of the personnel shortage, insufficiency in personnel who are able to engage in epidemiological research is also considered a contributing factor in the research gap.

2.2 Discussion on the factors contributing to the research gap

2.2.2 Discussion on the factors contributing to the research gap in the area of physical activity/exercise

- Factors that were thought to contribute to research gap in the area of physical activity/exercise were identified to be (1) Lack of established systems for strategic investment for key themes, (2) Insufficient support for research studies utilizing advanced technology, and (3) Shortage of personnel who are able to engage in epidemiological research.

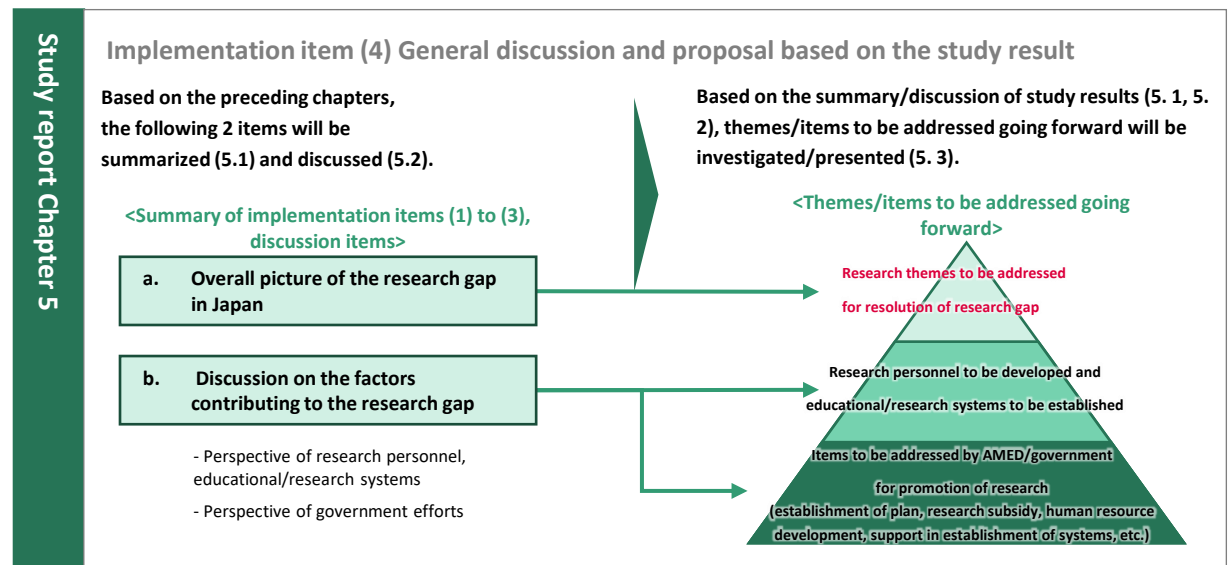
Study result	Failure to set national strategic target and effective provision of research subsidy	Study result	High hurdles in utilizing advanced technology as medical device	Study result	Shortage of personnel with specialist education on epidemiology
<ul style="list-style-type: none"> While research goals in the area of nutrition/diet have been set in the mid- to long-term plan of the National Institutes of Biomedical Innovation, Health and Nutrition, research goals have not been set or announced clearly by the entire government. Although the Project for the General Research on Measures Against Lifestyle Diseases Including Circulatory Disorders and Diabetes Mellitus by the Ministry of Health, Labour and Welfare has promoted subsidization for the research in this area, the subsidization system does not focus on the area of nutrition/diet or the research in the specific area unlike the system in the UK. 		<ul style="list-style-type: none"> In the US, advancements in approval by the Food and Drug Administration (FDA) have led to the establishment of an environment to promote research and development of robot technology in the area of medical care. However, the high hurdle in approval and listing for insurance coverage as medical devices is thought to have resulted in delays in Japan. 		<ul style="list-style-type: none"> Shortage in human resources with epidemiological knowledge who are capable of comparing the best studies from observational studies to carefully examine the study design and methodology. 	
Factor (1)	Lack of established systems for strategic investment for key themes	Factor (2)	Insufficient reform in systems to promote research that utilizes advanced technology	Factor (3)	Shortage of personnel who are able to engage in epidemiological research



2. Summary of the study results

2.3 Themes to be addressed in the research area going forward

* Please be advised that the themes to be addressed going forward that are discussed in this section have been investigated based on the results obtained in the survey of “1. Themes with insufficiency in evidence required (research gap)” in Japan with regard to the recommendations in the clinical guideline. In practice, “2. Themes with evidence available but require further studies” (e.g., long-term, precise cohort study on local residents) are included as important research themes in addition to the research gap from the perspective of prevention/treatment of lifestyle diseases, and the details in this section is, therefore, thought to require additional investigation in the future.



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2.3 Themes to be addressed in the research area going forward

2.3.1 Area of nutrition/diet

- Examples of themes to be addressed going forward in the area of nutrition/diet include 1) "Research on dietary reference intake", 2) "Research on what, when and how often to eat", and 3) "Research on the design of diet therapy according to the characteristics of the subject"

Themes to be addressed going forward as identified in this study (examples) (area of nutrition/diet)

Category	Perspective of the research gap	Details of the research gap	Themes to be addressed going forward as identified in this study (examples)	Target disease
[Nutrition/diet-1]	1. Domestic research gap in evidence	Research on dietary reference intake	[Treatment] Ratio of nutritional intake	Type 2 diabetes mellitus
			[Treatment] Individual nutrition intake (fat, artificial sweeteners, carbohydrates, vitamins, minerals)	
			Sodium restriction (salt reduction)	Across different diseases
[Nutrition/diet-2]	1. Domestic research gap in evidence	Research on what, when and how often to eat	[Treatment] Correction of lifestyle habits with focus on diet therapy	Type 2 diabetes mellitus
			Eating pattern	Across different diseases
			[Prevention] Avoidance of alcohol consumption in large amount	Stroke
[Nutrition/diet-3]	1. Domestic research gap in evidence	Research on the design of diet therapy according to the characteristics of the subject	[Treatment] Individualization of diet therapy	Type 2 diabetes mellitus
			Nutrition intervention and nutrition therapy (including sarcopenia/frailty) by pathology for patients with lifestyle disease/elderly people	Across different diseases
			Standard for total energy intake and ratio of nutrition intake by target (elderly people, dementia patients, young people, and others) and life stage (prevention/treatment/rehabilitation)	

2.3 Themes to be addressed in the research area going forward

2.3.2 Area of physical activity/exercise

- Broad examples of themes to be addressed going forward in the area of physical activity/exercise are **1) “Research on exercise intensity/period/frequency”** and **2) “Research on the development of exercise intervention method using advanced technology.”**

Themes to be addressed going forward as identified in this study (examples) (area of physical activity/exercise)

Category	Perspective of the research gap	Details of the research gap	Themes to be addressed going forward as identified in this study (examples)	Target disease
[Physical activity/exercise-1]	2. Global research gap in evidence	Research on exercise intensity/period/frequency	Exercise intensity/period/frequency in aerobic exercise	Across different diseases
			Exercise therapy with the aim of improving exercise tolerability	Cardiac failure
[Physical activity/exercise-2]	2. Global research gap in evidence	Research on the development of exercise intervention method using advanced technology	Monitoring technology	Across different diseases
			[Rehabilitation] Support using gaming devices/VR	Cardiac failure
	[Rehabilitation] Remote rehabilitation care using the internet			
1. Domestic research gap in evidence	[Rehabilitation] Rehabilitation support using robot	Stroke		

2.3.3 Other areas (common)

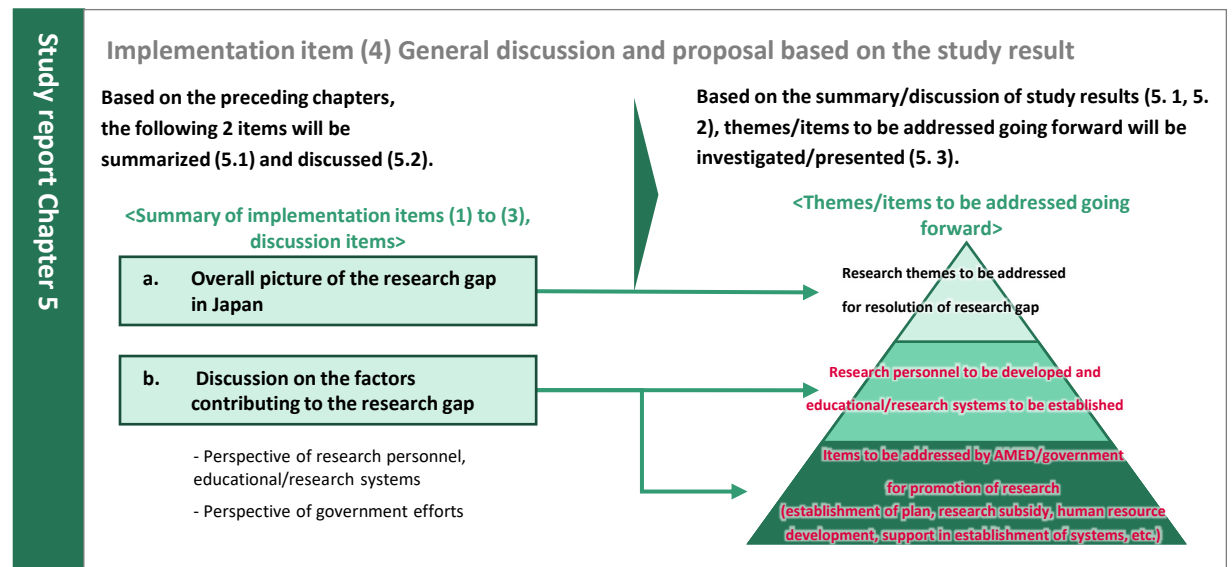
- Broad examples of themes to be addressed going forward in other areas (common) include 1) “Research by introduction of big data/analysis technology”, 2) “Research on the assessment of recommendations in the guideline”, and 3) “Research contributing to the prevention of onset/severe development of lifestyle diseases through behavioral change.”

Themes to be addressed going forward as identified in this study (examples) (other areas (common))

Category	Perspective of the research gap	Details of the research gap	Themes to be addressed going forward as identified in this study (examples)	Target disease
[Other-1]	1. Domestic research gap in evidence	Research by introduction of big data/analysis technology	Research utilizing advanced technology, such as big data and AI	Across different diseases
[Other-2]	1. Domestic research gap in evidence	Research on the assessment of recommendations in the guideline	Utilization status and verification on the effect of standard treatment and recommendations in the guidelines	Across different diseases
[Other-3]	2. Global research gap in evidence	Research on improvement of lifestyle diseases and contribution to presymptomatic state through behavioral change	Research on practices that contribute to the realization of behavioral change	Across different diseases
	1. Domestic research gap in evidence		Behavior change program	Type 2 diabetes mellitus
			Smoking abstinence and avoidance of passive smoking	Stroke

2. Summary of the study results

2.4 Items to be addressed for promotion of research going forward (systems/strategies)



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2.4.1 Efforts for research promotion (1/2)

1) Establishment of strategic plans*

a. Area of nutrition/diet

● Need for strategic plans

- In promoting the research studies in the area of nutrition/diet for prevention/treatment of lifestyle diseases in Japan, **it is necessary to first establish a strategic plan to specify the goals and road maps of the research and development involved.**
- This should be established **with reference to the existing strategic plans overseas and with consideration for the consistency with the mid- to long-term plan of the National Institute of Health and Nutrition, National Institutes of Biomedical Innovation, Health and Nutrition** to support the construction of a national research system that allows the creation of outcomes with high levels of evidence.

● Importance of the perspective of environment and sustainability in food production in the strategic plan

- Perspectives that are thought to be important in the establishment of a strategic plan not only include the US-based direction of **improvement in the effect of nutrition/diet in the prevention/treatment of lifestyle diseases for individuals** but also the **positioning of nutrition/diet in the broad context of the environment and sustainability in food production as adopted in such countries as the Netherlands and Finland.**
- The experts have also pointed out that **research studies related to sustainability should be regarded with more importance going forward**, and there is a demand for the government to take the initiative in these research studies. For these reasons, research studies on sustainability should be considered as an important direction for the strategic plan.
- In particular, the educational/research system for the area of nutrition/diet in Japan is thought to have weaknesses in the multidisciplinary perspective; therefore, the positioning of sustainability in food production as agricultural/environmental areas together with the realization of health through nutrition/diet as a medical/public health area is considered to be effective from the viewpoint of promoting multidisciplinary research studies.

* Strategic plan must fulfill the following conditions: (1) it must be a long-term plan with a span of about 10 years, and (2) it must specialize in the promotion of research in the area of nutrition/diet and physical activity/exercise contributing to the prevention/treatment of lifestyle diseases with identification of the target vision, research issues, and specific research themes.

2.4.1 Efforts for research promotion (2/2)

1) Establishment of strategic plans*

b. Area of physical activity/exercise

● Need for strategic plans

- Considering that the establishment of research/educational systems in the area of physical activity/exercise in Japan is thought to have reached a certain standard and that there are historically many research studies in the Western countries of the US, UK, and Australia involving the perspective of intervention for health issues of obesity, there is a demand in **Japan to become a global pioneer in the establishment of a strategic plan in the physical activity/exercise area not limited to the issue of obesity.**

2) Other efforts for research promotion (research subsidy and support in system establishment)

- In the provision of research subsidies, it is expected that subsidies are not only provided in the broad setting of themes, such as prevention/treatment of lifestyle disease, but to **identify the research themes to be addressed in Japan within the areas of nutrition/diet and physical activity/exercise and establish the subsidization system with the focus on these themes.**
- In addition to the establishment of the subsidization system, **multifaceted research promotion should be implemented through involvement in the establishment of research systems related to these themes, centered around the government-affiliated research institutions.** The efforts made in the UK should be used as a reference with regard to this perspective.

* A strategic plan must fulfill the following conditions: (1) it must be a long-term plan with a span of about 10 years, and (2) it must specialize in the promotion of research in the area of nutrition/diet and physical activity/exercise contributing to the prevention/treatment of lifestyle diseases with identification of the target vision, research issues, and specific research themes.

2.4.2 Establishment of research/educational systems and human resource development

- The important measures for the establishment of research/educational system was organized as follows based on the opinions of the experts:

1) Area of nutrition/diet

- In order to promote multidisciplinary research, **research/educational institutions involving nutrition epidemiological research should be established in graduate schools of medicine and graduate schools of public health (SPH) to develop specialists in nutrition guidance who are able to engage in government policies on nutrition and preventive medicine/primary prevention.**
- While registered dietitians play an important role in multidisciplinary medicine, **the number of registered dietitians engaging in work/research in the clinical setting is limited, and such personnel should be increased in number.** In order to realize the increase in the number of registered dietitians, it is important to develop personnel who become role models for registered dietitians flourishing in the clinical field. For this reason, **efforts, such as the increase in the number of staff members with medicine as specialization and physicians in schools for development of registered dietitians, and inclusion of practical sessions on medical care in the clinical settings are necessary.**

2) Area of physical activity/exercise

- Historically, research studies in the area of physical activity/exercise in the US and other overseas countries have been mainly promoted from the perspective of measures against obesity, and this was thought to have resulted in the difference to Japan from the viewpoint of research systems, as well as being possibly reflected in the difference in previously conducted research studies. **It is important to continue the development of a research base and utilize the strengths we have in promoting research on exercise therapy as a global research gap.**

2. Summary of the study results

2.5 Limitations of this study project and the true intention

2.5 Limitations of this study project and the true intention

- This research project is associated with the following limitations and true intentions.

- **Limitations of this study project**
 - It should be noted that, in the themes that should be addressed as summarized from the result of this research, **there are themes not mentioned due to the limitation in the methodology of this study, and a comprehensive organization of themes to be addressed in Japan is not provided as a result.**
 - The specific limitations in the methodology of this study include the following three points. Efforts were made to supplement for the three items listed below through interviews with the experts.
 - i. Since this is the extraction of themes based on the recommendations for CQ in the Japanese guidelines as well as the literature quoted in these guidelines, **themes that are lacking globally, including Japan, are not covered.**
 - ii. **Research gaps related to lifestyle diseases other than the three disorders included (stroke, cardiac failure, type 2 diabetes mellitus) have not been clarified.**
 - iii. The study was conducted on the guidelines in the area of treatment, and **while this includes some results on research gaps in the prevention area, no comprehensive coverage was provided for these.**

- **True intentions of this study project**
 - In AMED's Project for the Research on Practical Implementation of Measures Against Lifestyle Diseases Including Circulatory Disorders and Diabetes Mellitus, personnel involved in the project from various standpoints have collected information from relevant authorities and academic societies and identified the latest research trends and needs in medical care to establish the research plan that is considered optimal. However, **the creation of evidence in the areas of nutrition/diet and physical activity/exercise was not considered sufficient, both from the quantity and quality point of view.**
 - The true intentions of this study project were to resolve the gaps present through **comprehensive and systematic analysis of the current circumstances and exploration of a better way to promote research studies.** We hope that AMED will take the strong initiative and implement effective measures in promoting the research studies in the area of nutrition/diet and physical activity/exercise in Japan, thereby leading to health promotion for citizens and academic advancement in the areas involved.