Glycative Stress Research

Online edition : ISSN 2188-3610
Print edition : ISSN 2188-3602
Received : December 15, 2020
Accepted : May 18, 2021
Published online : June 30, 2021
doi:10.24659/gsr.8.2_115

Original article

Reduction of medical expenses by ingesting processed brown rice (sub-aleurone layer residual rinse-free rice, dewaxed brown rice)

Keiji Saika [1, 2)], Yoshikazu Yonei [3)]

1) Tokyo University of Agriculture, Tokyo, Japan
2) Toyo Rice Co., Ltd., Tokyo, Japan
3) Anti-Aging Medical Research Center and Glycative Stress Research Center, Faculty of Life and Medical Sciences, Doshisha University, Kyoto, Japan

Abstract

***Objectives*:** A financial crisis has been induced by the immense increase of national medical care expenditures in Japan, while investigations of causes and introductions of countermeasures have not yet been conducted. It has been reported that nutrients in brown rice and processed brown rice would contribute to the retention and promotion of health for citizens in Japan. The present study examined impacts of staple food replacement from polished rice to processed brown rice, concerning the reduction of public medical expenditures.

***Methods*:** Test sample products were a sub-aleurone layer residual rinse-free rice (SARFR) or a dewaxed brown rice (DBR). SARFR was a processed brown rice where sub-aleurone layer (white deep layer bran of brown rice) remains with a polished white rice-like appearance (patent number: 4708059). DER was a processed brown rice where only the wax bran layer was removed with a brown rice-like appearance (patent number: 6850526). Research targets were three companies located in Wakayama Prefecture and public medical expenditure information was obtained through medical expenditure information, which was issued by each company's health insurance society. Consumption rates were calculated with annual average rice consumption per person (2016), quantity of delivered processed brown rice and the number of subscribers. Control targets were medical expenses of residents in Wakayama Prefecture. The number of insured persons (subscribers) in 2018 fiscal year (FY) in health insurance societies were 169 (373) in Company T, 64 (98) in Company A, 53 (125) in Company B, and 170,939 (297,088) in Wakayama Prefecture. Mean age was 45.4 at Company T, 45.4 at Company A, and 44.5 at Company B. The number of subscribers is the total number of insured persons (staff) and dependents (family members).

***Results*:** At Company T, which had a large number of regular consumers of test sample products (consumption rate: 66.1% [DBR 14.3%, SARFR 85.7%]), annual medical expenses were 120,108 yen for the 2016 FY, 119,264 yen for the 2017 FY, and 127,248 yen for the 2018 FY. Average medical expenses in Wakayama Prefecture were 175,683 yen for the 2016 FY, 180,966 yen for the 2017 FY, and 183,372 yen for the 2018 FY. Average annual medical expenses in Company T were approximately 68% that in Wakayama Prefecture. After the introduction of the test product ingestion, Company A (consumption rate: 39.1% [DBR 13.5%, SARFR 86.5%]) reduced the average of annual medical expenses by approximately 40% to 224,335 yen for the 2017 FY and 134,354 yen for the 2018 FY. Company B (consumption rate: 29.4% [DBR 13.3%, SARFR 86.7%]) reduced expenses by approximately 39% to 198,892 yen for the 2017 FY and 121,172 yen for the 2018 FY.

***Conclusion*:** It was suggested that the ingestion of the test products would lead to the improvement in health condition, the decrease in disease incidence rates, and the reduction of public medical expenses through the increase of nutrient ingestion quantity, which is contained in the sub-aleurone layer and bran layer of Japanese short-grain rice.

***KEY WORDS*:** sub-aleurone layer residual rinse-free rice (SARFR), dewaxed brown rice (DBR), brown rice, medical expenses

Contact information: Professor Yoshikazu Yonei, PhD
Anti-Aging Medical Research Center / Glycative Stress Research Center,
Graduate School of Life and Medical Sciences, Doshisha University
1-3, Tatara Miyakodani, Kyotanabe-shi, Kyoto, 610-0321, Japan
TEL & FAX: +81-774-65-6394 e-mail: yyonei@mail.doshisha.ac.jp
Co-author: Saika K, somu@toyo-rice.jp

Introduction

Trends in national medical care expenditure indicate that the rate of increase had been approximately zero until 1955, but medical expenditure started to increase since then (***Fig.1***) [1].

An emergence of a new rice polishing method called "air-jet-polishing" was developed around that time, which was a major change that occurred to influence Japanese life. It is thought that the increase in medical care expenditure in Japan could be primarily related to the "air-jet-rice polishing method".

Another example of an emergence of a rice-polishing method can be shown for impacts on health conditions. Once toward the end of Edo period, during the days of the Tokugawa shogunate regime (around 1870), "sand-mixing rice mills" became widely operated and brown rice, which had been a staple food, was replaced by excessively polished rice. This polished rice, where the bran layer was completely removed from brown rice, led the prevalence of "a polished-white-rice-related disease". This disease, beriberi, was called "Ed-wazurai disease", which was caused by the deficiency of a vitamin group, particularly vitamin B1, due to the polised rice diet. It was recommended in 1919 that this sand-mixing polishing method should be banned, and polishing method should be improved [2]. The major purpose was not the improvement of health conditions but the prevention of lower quality of rice due to a sanitation problem of the mixing sand. As a result, "Ed wazurai disease" decreased and was temporarily contained.

While a financial crisis has been induced by immensely increased national health care expenditures in Japan, investigations of causes and introductions of countermeasures have not yet been conducted. It is urgently required to identify factors for increasing life-style-related diseases including pre-symptomatic states, and to seek solutions to this problem.

Ministry of Economy, Trade and Industry (METI) established in 2013 "the Next-Generation Healthcare Industry Council" aiming to understand the situation of various products and services in health and longevity that the private sector provides, and analyze the issues and countermeasures from both demand and supply sides [3]. Wakayama Prefecture launched an associated project, "Platform for Wakayama Health Care Industry" [4]. We conducted research to validate effectiveness on the reduction of health care costs by the replacement of polished rice to processed brown rice as the staple diet. In the present study, reference materials were intended to be prepared for the investigation of causes and the establishment of countermeasures.

Methods

Test sample products for research were types of processed brown rice, sub-aleurone layer residual rinse-free rice (SARFR) [5, 6] or dewaxed brown rice (DBR) [7-10]. SARFR was a processed brown rice where sub-aleurone layer (deep layer bran of brown rice) remained (patent number: 4708059.) DER was a processed brown rice where only the wax bran

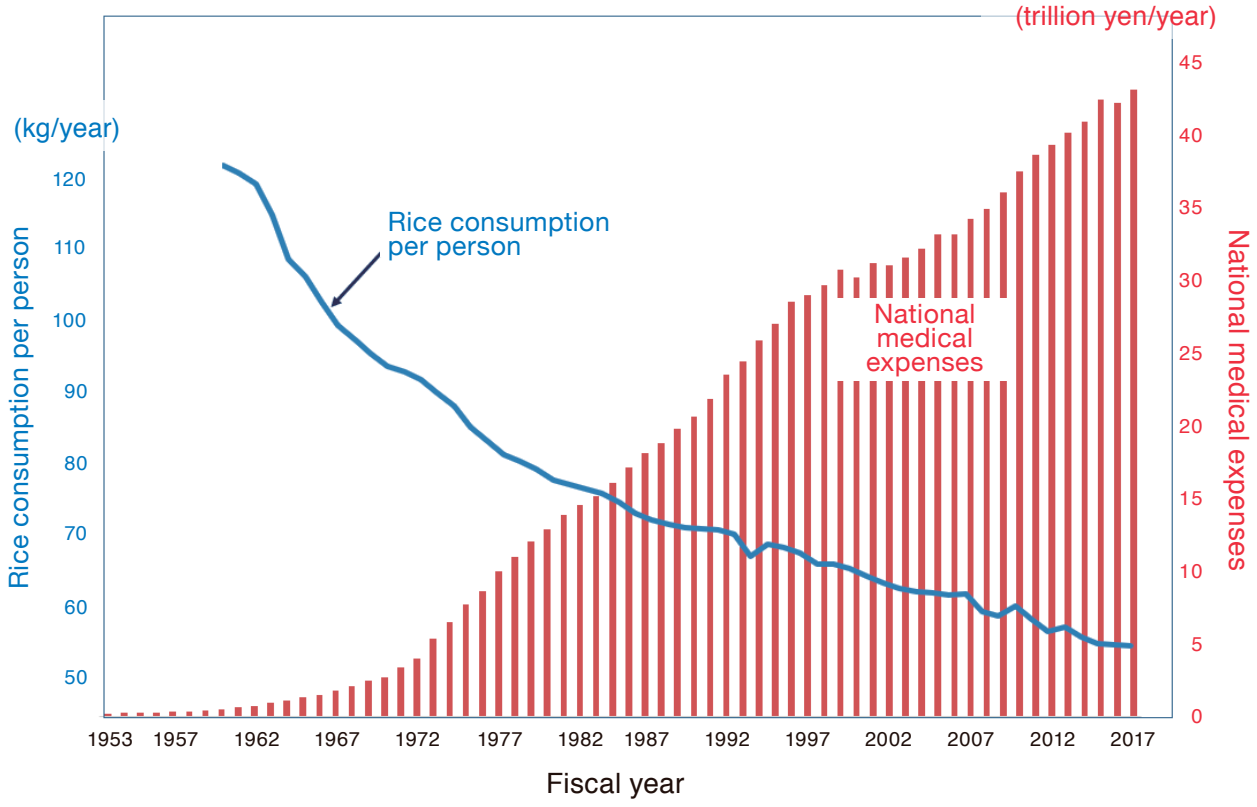

Fig.1. **National medical expense and rice consumption per person.**
The figure is quoted from **Reference 1)**.

layer was removed (patent number: 6850526.) Research targets were three cooperative companies located in Wakayama Prefecture (Company T, Company A, and Company B). The present study examined the consumption rates of test products and the total amounts of public medical expenses of each group. The average monthly medical expenses of the 2015 fiscal year (FY) for company T were compiled. Annual medical expenses were compiled for three years from the 2016 FY. The number of insured persons (members) in the 2018 FY in health insurance societies was 169 (373) at Company T, 64 (98) at Company A, 53 (125) at Company B, and 170,939 (297,088) in Wakayama Prefecture. Mean ages were 45.4 in Company T, 45.4 at Company A, and 44.5 at Company B.

Intervention methods were as follows: SARFR and DBR were provided through the company cafeteria and a purchase-method for employees was provided. Additionally, dependents of employees were requested to ingest test products from June of 2014 (SARFR) and October of 2015 (added DBR) for Company T, November of 2018 for Company B, and February of 2018 for Company B. SARFR and DBR could be freely selected.

Analysis targets were Company T, A, B, and Wakayama Prefecture for insured persons and their dependents. Consumption rates were calculated based on the trend of rice consumption by the Ministry of Agriculture, Forestry and Fisheries, with average annual rice consumption per person (2016), quantity of delivered processed brown rice and the number of subscribers. The number of subscribers is defined as the total number of insured persons (staff) and dependents (family members). Mean data of public medical expenses were provided by each company's health insurance society. No personal information was included.

Ethical standards

This research was approved by each company and the research participants. No information regarding individual medical expense data was provided by health insurance societies and personally identifiable information of research targets was protected.

Results

Company T had started the ingestion of SARFR in June of 2014 and the ingestion of DBR in October of 2015. Average monthly medical expenses per insured person (0～74 at age) were compiled for 2015 FY (April 2015～March 2016) and the 2016 FY (***Table 1***). Average monthly medical expenses in 2015 FY were 13,909 yen for the national average, 14,124 yen for Wakayama Prefecture, 13,911 yen for employees with the same occupation in Wakayama (peer average), and 8,269 yen for Company T (154 insured persons). Compared with national average monthly medical expenses, Wakayama average was higher by 9.4% and Company T was lower by 35.9%. Company T continues to take SARFR and DBR, and the average annual medical expenses have remained at a low level since 2016.

Figure 2 shows aggregate results of average annual medical expenses per person from 2016 FY to 2018 FY. The number of survey subjects is shown in ***Table 2***.

Average annual medical expenses of Company T, which had many persons ingesting SARFR (consumption rate: 66.1% [DBR 14.3%, SARFR 85.7%]), showed average annual medical expenses of 120,108 yen for 2016 FY, 119,264 yen for 2017 FY, and 127,248 yen for 2018 FY. This was 68% of Wakayama average of 175,683 yen for 2016 FY, 180,966 yen for 2017 FY, and 183,372 for 2018 FY. After the commencement of the ingestion of SARFR, average annual medical expenses of Company A (consumption rate: 39.1% [DBR 13.5%, SARFR 86.5%]) decreased by 40%: 224,335 yen for 2017 FY and 134,354 yen for 2018 FY. Similarly, that of Company B (consumption rate: 29.4% [DBR 13.3%, SARFR 86.7%]) decreased by 39%: 198,892 yen for 2017 FY and 121,172 yen for 2018 FY.

Discussion

"National Medical Care Expenditure" is an estimate of expenditure spent on treatments for diseases and injuries at medical care institutions during the fiscal year. It includes medical expenditures for medical and dental treatment,

Table 1. Average monthly medical expenses per person.

Per subscriber	Number	medical expenses (total)	Hospitalization	Out of hospital	Dental
National average		14,202	4,038	8,596	1,568
Wakayama prefecture average		14,093	3,777	8,769	1,547
The peer average		14,198	4,339	8,259	1,600
Company T (2015FY)	389	9,266	1,628	6,108	1,531
(2016FY)	378	10,009	2,307	6,282	1,420
Per insured person					
National average		13,909	3,769	8,462	1,678
Wakayama prefecture average		14,124	3,568	8,881	1,675
The peer average		13,911	3,744	8,412	1,755
Company T (2015FY)	154	8,269	1,555	5,196	1,518
(2016FY)	155	9,340	2,836	5,261	1,243

FY, fiscal year.

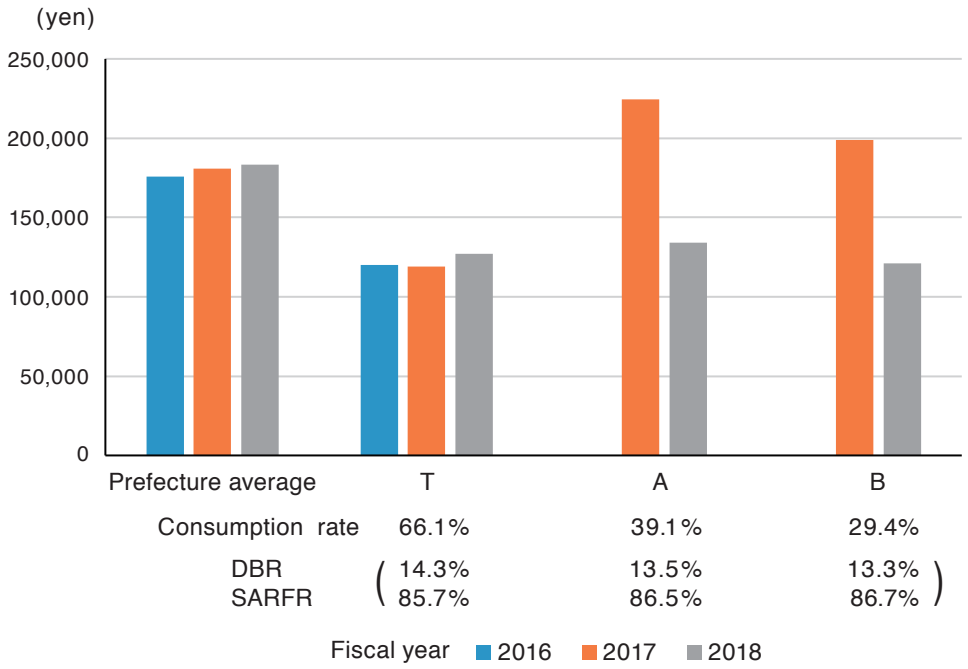

Fig. 2. **Intake of processed brown rice and average annual medical expenses per person.**
See **Table 2** for the number of subjects analyzed. DBR, dewaxed brown rice; SARFR, sub-aleurone layer residual rinse-free rice.

Table 2. Number of survey subjects.

	2016FY	2017FY	2018FY		
				The assured	Dependents
Wakayama	**293,861**	**296,774**	**297,088**	170,939 (46.0)	126,149 (26.7)
Company T	**389**	**378**	**373**	169 (45.4)	204 (28.5)
Company A			**98**	64 (45.4)	34 (24.2)
Company B	**128**	**126**	**125**	53 (44.5)	72 (22.9)

Blue letters indicate the analysis target, and parentheses show the average age. The turnover rate from 2017FY to 2018FY is Company T: 3.7%, Company A: 31.7%, Company B: 7.4%. Wakayama, average of Wakayama prefecture residence; FY, fiscal year

pharmacy dispensing medical expenditures, food and living care expenditures during admission, and home-visit nursing medical expenditure as well as transfer expenditures covered by health insurance.

National medical care expenditures are limited to treatments of diseases and injuries and excludes the following: (1) expenditure for uncomplicated pregnancies and deliveries, (2) expenditure for medical checkups and immunizations for maintenance and enhancement of health, and (3) expenditure for prosthetic devices for eyes and limbs, etc. required for established physical disabilities. It does not include optional medical treatments which are covered by patients such as extra charges for room fees during admission and dentistry.

National medical care expenditure for the 2019 FY (the first year of Reiwa era) was 43 trillion and 600 billion yen as an estimation calculated with receipt data, compared with 42 trillion 138 billion 100 million yen in the previous FY, an increase of 2.4%, one trillion ten billion yen. This was the highest figure ever for healthcare expenditure [11]. National medical expense per person was 339,900 yen for the 2019 FY. Compared with 332,000 yen of the previous FY, it increased by 7,900 yen, or 2.4%. Estimated medical care expenditure for the 2020 FY decreased by 1% compared with the previous FY. This was in an extraordinary situation due to the coronavirus pandemic [12].

Vaccination is an effective measure to reduce health care expenditures. It was reported that pneumococcal vaccination reduced the period of hospitalization and medical care expenses in comparison between pneumococcal vaccinators (310 subjects, 77.4 at mean age) and non-vaccinators (1,045 subjects, 77.5 at mean age) [13]. Covid-19 vaccination is being conducted in Japan at the time of this writing and it is expected that its efficacy evaluation will be

performed from the perspective of medical care expenditures.

Research has been increasingly reported regarding countermeasures and causative factors to reduce medical expenses, as cost reduction is an important issue. Geographic disparities in average medical care expenses have been recognized. Medical costs are high in western Japan and northern Japan (Hokkaido)[14]. This is associated with medical and economic disparities such as the number of long-term care beds and/or mental sickbeds per population, and accessibility to medical institutions for older adults. Analysis of medical expenses and nursing care have suggested that causative factors of increased costs were nursing care levels, period to death, and increased usage of medical and nursing resources[15]. Cognitive impairment is a serious problem as a factor which raises the nursing care burden.

Social burdens due to cognitive impairments increased from one trillion 196 billion 400 million yen for 2002 to two trillion 128 billion yen for 2011. According to an estimation employing the cost of illness methodology with a basis on Japanese official statistics, the cost increased 1.78 times over ten years[16]. Regional disparities were extensive from a viewpoint of dementia-related medical expenses and it was suggested that a higher ratio of hospitalization led to a huge rise in medical care expenses[17]. An analysis was reported on 1,736 subjects of aged patients with cognitive impairment (mean age: 71.6 ± 5.9 years old, females: 56.6%), which excluded serious-level cases[18]. Impairment degrees were classified into 40.3% of high-level group, 38.8% of upper mediate group, 16.8% of mediate group, 2.2% of lower mediate group, and 2.0% of low group. Medical and nursing care expenses (monthly average) were significant in the low and lower mediate group for five years. After eight years, expenses were the highest in the mediate group.

Lifestyle-related diseases were not only the biggest obstructive factor against health and longevity but also had an enormous impact on national medical care expenditures. Japan has the longest average life span and healthy life expectancy in the world. One causative factor is reported to be the low obesity rate in Japan, compared with other developed countries[19]. According to an analysis with 16,386 of Japanese male employees (48.2 at mean age) regarding the relationship between medical care expenses and physical index (body mass index [BMI], body weight, glyceride, high-density lipoprotein-cholesterol [HDL-C], blood glucose level), persons with the most expensive medical care expenses were those with both obesity and a metabolic disorder[20]. Analytical research regarding abdominal circumscription and medical expenses (88,556 subjects) recognized a positive correlation between these two factors. It was suggested that one centimeter decrease in abdominal circumscription was related to the reduction of the estimate of average annual medical expenses with 2,700 yen for men and 2,500 yen for women[21].

Average annual medical expense of patients with alcohol dependence (1,137 subjects of 63.1 at mean age) was 753,382 yen. Furthermore, medical expenses, even when one hospitalization was added, would rise drastically. Average annual medical expense (average period of hospitalization: 71.3 days) increased to 1,434,203 yen[22].

Diabetics largely account for metabolic diseases in the term of medical care expenses, and varied analyses were performed. In correlation analysis between medical expenses and medical examination index (798 subjects, 63.1 at mean age), positive correlations were indicated between medical expenses and both blood glucose levels and glycoalbumin levels. A relation was indicated with estimated glomerular filtration rates[23]. A five-year follow-up research study with 318 patients with type 2 diabetes (T2DM) suggested that average annual outpatient medical expenses per person significantly increased from 316 thousand ± 167 thousand to 379 thousand ± 209 thousand[24]. The volume of increase for medical care expenses had positive correlations with BMI and HbAlc, and negative correlations with hospital outpatient expense and HDL-C. Furthermore, administration of costly therapeutic agents for T2DM raised medical care expenses[25]. An awareness survey of pharmacists advocated an opinion that adjusting prescriptions by appropriately reusing leftover drugs could contribute to reduced medical care expenses[26].

T2DM has a characteristic of causing diverse complications, which is a factor for the rise of medical expenses. An examination with 1,099 subjects reported that average annual medical expenses were 42,461 yen for a group without nephropathy and 107,027 yen for a group with nephropathy. This was 2.52 times higher than non-nephropathy. Similarly, 44,819 yen for non-cardiac disease, and 68,458 yen for cardiac disease, which was 1.53 times higher; 43,900 yen for non-cerebrovascular, and 90,239 yen for cerebrovascular, which was 2.52 times higher[27]. When serious hypoglycemia is caused in T2DM management, medical care expenses are greatly increased. It is required to exert caution for medical treatments[28].

Furthermore, T2DM with obesity affects medical care expenditures. Research with 402 patients with T2DM (male: 66.2%, 66 mean age) in 165 subjects of obesity group and 237 subjects of non-obesity group reported that subjects in the obesity group had poorly controlled glycemia at a younger age than the non-obesity group and had higher rates of hypertension. Annual medical expenses of the obesity group were significantly higher than that of the non-obesity group[29].

Lifestyle-related diseases were not only the biggest obstructive factor against health and longevity but also had an enormous influence on national medical care expenditures. "Dietary education (*shokuiku*)" "physical education (*taiiku*)" and "intellectual education (*chiiku*)" are basic for teaching and training for the improvement of lifestyle. Physical and exercise therapy contributes to the reduction of medical care expenses.

A five-year follow-up research study for an exercise program reported a comparative survey regarding medical care expenses; 41 participants (65～84 at age) of the program for health promotion in Oizumi, Osaka from 2005 were compared with 54 control subjects[30]. The difference in total medical expenses widened from 299,911 yen in 2004 to 4,909,799 yen in 2009. The difference in annual average medical expenses per person was 92,647 yen.

An analytic study in Daisen-cho, Tottori Prefecture, was reported regarding 80 subjects, who participated in the following exercise program once or more a week for years[31]. The exercise was a 30-minute program consisting of two units (12 minutes × 2) of muscular strength exercises (12 types, 30 seconds) and aerobic exercise (30 seconds) in turn, followed by cool down stretching. Persons with a tendency toward

obesity significantly reduced BMI and persons with risks of high blood pressure, hyperglycemia and/or lipid abnormality improved these indexes. However, the effectiveness of the medical cost reduction was not confirmed.

A comparative result between an intervention group (296 subjects of 67.0 at mean age) and a control group (882 subjects of 66.8 at mean age), which examined the effectiveness of walking on medical care expenses employing a pedometer with information communication technology (ICT) monitoring system, demonstrated that medical expenses were reduced but significant differences between groups were not confirmed [32].

"Dietary education" encourages the practice of a well-balanced diet at appropriate calorie levels and contributes to the prevention and improvement of lifestyle-related diseases.

A prospective study with 139 patients with lifestyle-related diseases (70.2 at mean age) was conducted to examine how effective nutrition education was on high blood pressure, dyslipidemia, T2DM, and obesity [33]. A six-month nutrition education program for target subjects showed that HbAlc and body weight were significantly decreased and low-density lipoprotein-cholesterol (LDL-C) had a declining tendency, while no significant change was observed in blood pressure.

There have been a large number of reports that "dietary education" improved glycolipid metabolism. However, there have not yet been reports that interventions with dietary education leads to a medical care cost reduction. The present study of an intervention with staple food replacement from polished rice to test sample products of processed brown rice (SARFR and DWR), has suggested remarkable results. Through this intervention, medical expenses decreased by approximately 40% in one year, without any further interventions.

These types of processed brown rice for the present study, contained brown-rice-derived nutrients, while ordinary polished rice contained them only at a negligible extent. Their components were dietary fiber, vitamin B1, B2, B6, magnesium, nicotinic acid, pantothenic acid, inositol, choline, vitamin B group such as folate, γ-oryzanol, ferulic acid, phytic acid, γ-aminobutyric acid, and lipopolysaccharide (LPS) [10]. The present investigation indicated that these nutrient components were related to the medical cost reduction.

Antioxidant vitamin, ferulic acid [34], and phytic acid [35] are characterized as participating components that exert antioxidative effects.

As participating components to affect carbohydrate and lipid metabolism, dietary fiber decreases postprandial blood glucose. Furthermore, γ-oryzanol leads to a breakaway from addiction to animal-fat based food and improves insulin resistance [36]. Triterpene alcohol, which is contained in the lipid-soluble fraction of rice bran, as well as sterol fraction decreases postprandial blood glucose [37]. Probiotics activities of dietary fiber lead to the increase of bacteria production for organic acid and short-chain fatty acids (SCFA), such as bifidobacteria bifidus, lactic acid bacteria, and butyrate-producing bacteria. This promotes basal metabolism when excessive calories are ingested, namely, the elevation of body temperature and the increase of heart rate [38]. Thus, brown rice, including processed brown rice, is effective for the prevention of obesity and the loss of weight, compared with ordinary polished rice [39]. Glycative stress reduction is promoted by these activities.

As participating components for immune function, dietary fiber (probiotics) enhances the retention of intestinal flora and LPS promotes intestinal immunostimulatory activities [40]. Furthermore, brown rice ingredients promote the secretion of IgA in breast milk [41].

To name another participating component, γ-aminobutyric acid (GABA) relieves physical and psychological stress [42]. Furthermore, it was demonstrated that brown-rice-derived components could help retain cognitive functions and prevent the progress of Alzheimer's disease [43].

It is recognized that these participating components function in an integrated and coordinated manner. Unidentified components could exist. Further research is required to explore accurate mechanisms.

Results of the investigation of the present study included dental care expenses. ***Table 2*** shows dental care reduction in Company T for 2016 FY. Maintenance of oral functions contributes to the reduction of the increasing health care expenditures. An analytical survey with 4,700 elderly subjects living in Mie Prefecture (2,745 subjects of 75 at age, 1,955 subjects of 80 at age) indicated that the period of hospitalization was shorter in subjects who had more remaining teeth and health care expenses were lower in these subjects [44]. Further research is required to examine relationships with processed brown rice and oral functions.

Conclusion

The present study examined the impacts on medical care expenditures of corporate health insurance societies by the replacement of staple food from polished rice to processed brown rice. The investigation results demonstrated that the medical expense of Company located in Wakayama Prefecture was lower by 32% than the prefecture average. Companies which had newly introduced the processed brown rice diet decreased medical expenses by 39%～40%. The present study suggested that the ingestion of nutrients contained in the sub-aleurone layer and bran layer could improve health conditions, decrease disease incident rates, and consequently reduce public medical care expenditures.

Conflict of interest

Research support was provided by Toyo Rice Corporation.

Acknowledgements

Support was provided for the present study by "*Ishokudogen Shouyaku-Kenkyu Zaidan*", the Research Foundation of Crude Drug gained from the same source of Medicine & Food (IDF#21006). Outline of the present study was reported at the first anniversary seminar of Platform for Wakayama Health Care Industry (February 4th, 2019), the 61th Conference of the Japan Association for the Integrated Study of Dietary Habits (held online, November 28th, 2020), and the 22nd Glycative Stress Academic Meeting /ifia Japan 2021 (May 15th, 2021).

Reference

1) Newspaper article. Big difference in processing method: Rice that promotes health. Japan Agricultural Communications. Oct 29th, 2019. https://www.jacom.or.jp/kome/news/2019/10/191029-39490. php (in Japanese)
2) Hochi newspaper article. Urgent need to prohibit the mixed sand rice milling method. Hochi newspaper 1919.6.12. Research Institute for Economics and Management, Kobe University, Newspaper article library: Rice (18-230). http://www.lib.kobe-u.ac.jp/das/jsp/ja/ContentViewM.jsp?METAID=00734287&TYPE=IMAGE_FILE&POS=1 (in Japanese)
3) Ministry of Economy, Trade and Industry (METI). The Next- Generation Healthcare Industry Council. https://www.meti.go.jp/policy/mono_info_service/healthcare/health_care_industry_council.html (in Japanese)
4) Wakayama Prefecture. Platform for Wakayama Health Care Industry. https://www.pref.wakayama.lg.jp/prefg/061000/d00202983.html (in Japanese)
5) Kyo H, Suzuki N, Enomoto T, et al. Influence of the special processing rice on the factors of lifestyle related disease. *Japanese Journal of Complementary and Alternative Medicine*. 2018; 15: 103-108. (in Japanese)
6) Wickramasinghe UPP, Uenaka S, Tian Z, et al. Effects on skin by sub-aleurone layer residual rinse-free rice (Kinmemai rice): An open label test. *Glycative Stress Res*. 2020; 7: 248-257.
7) Inagawa H, Saika T, Nishizawa T, et al. Dewaxed brown rice contains a significant amount of lipopolysaccharide pointing to macrophage activation via TLRs. *Anticancer Research* (*International Journal of Cancer Research and Treatment)*. 2016; 36: 3599-3536
8) Inagawa H, Saika T, Nishiyama N, et al. Improvement effect of dewaxed brown rice on constipation in antibiotic-treated mice. In Vivo. 2017; 31: 573-577.
9) Inagawa H, Saika T, Nishiyama N, et al. Dewaxed brown rice feed improves fatty liver in obese and diabetic model mice. *Anticancer Research*. 2018; 38: 4339-4345.
10) Yonei Y, Uenaka S, Yagi M, et al. Effects on skin by dewaxed brown rice: An open label test. *Glycative Stress Res*. 2021; 8: 29-38.
11) Ministry of Health, Labor and Welfare. Survey for estimates of national medical care expenditure: 2019FY. https://www.mhlw.go.jp/topics/medias/year/19/dl/iryouhi_data.pdf (in Japanese)
12) Ministry of Health, Labor and Welfare. Survey for estimates of national medical care expenditure: June, 2020FY. https://www.mhlw.go.jp/topics/medias/month/20/dl/gaisan_iryou_data_06.pdf (in Japanese)
13) Naito T, Suzuki M, Kanazawa A, et al. Pneumococcal vaccination reduces in-hospital mortality, length of stay and medical expenditure in hospitalized elderly patients. *J Infect Chemother*. 2020; 26: 715-721.
14) Awashima M, Itagaki T, Sugano S, et al. Geographic disparities in the average cost of medical care for adults aged 75 years or older in secondary medical areas and their association with medical, socioeconomic, and lifestyle-related indicators. *Niigata Journal of Health and Welfare*. 2020; 20: 16-24. (in Japanese)
15) Mori H, Ishizaki T, Takahashi R. Association of long-term care needs, approaching death and age with medical and long-term care expenditures in the last year of life: An analysis of insurance claims data. *Geriatr Gerontol Int*. 2020; 20: 277-284.
16) Hanaoka S, Matsumoto K, Kitazawa T, et al. Social burden of dementia in Japan: Time-lapse analysis using government statistics. *The Journal of Japan Society for Health Care Management*. 2016; 17: 8-13. (in Japanese)
17) Tashiro A, Shobugawa Y, Saito R. Regional differences in dementia based on receipt data: Examination by all late-stage elderly in Niigata Prefecture. *Journal of Health and Welfare Statistics*. 2020; 67(3), 1-5. (in Japanese)
18) Taniguchi Y, Kitamura A, Ishizaki T, et al. Association of trajectories of cognitive function with cause-specific mortality and medical and long-term care costs. *Geriatr Gerontol Int*. 2019; 19: 1236-1242.
19) Miyamoto K, Imai T, Sezaki A, et al. International comparative study on the difference between life expectancy and healthy life expectancy. *Nagoya Journal of Nutritional Sciences*, 2018; 4: 1-7. (in Japanese)
20) Nishikawa K, Yamamoto M. Combined associations of body mass index and metabolic health status on medical and dental care days and costs in Japanese male employees: A 4-year follow-up study. *J Epidemiol*. 2020; 30: 201-207.
21) Funayama K, Tobita Y, Azuma K, et al. Relationship between abdominal circumference and average annual medical expenses using specific medical examination results and receipt data. *Journal of Health and Welfare Statistics*. 2016; 63: 20-25. (in Japanese)
22) Yuzuriha T, Den R, Azuma K, et al. Burden of illness for alcohol dependence using health insurance claims database in Japan. *Japanese Journal of Alcohol Studies & Drug Dependence*. 2019; 54: 181-197. (in Japanese)
23) Funayama K, Tobita Y, Azuma K, et al. Relationship between abdominal circumference and average annual medical expenses using specific medical examination results and receipt data. *Journal of Health and Welfare Statistics*. 2016; 63: 20-25. (in Japanese)
24) Tanaka M, Ito H, Omoto T, et al. An analysis of the factors affecting the changes in nedical expenses over the past 5 years in the management of out-patients with type 2 diabetes mellitus. *J Japan Diab Soc*. 2016; 59: 188-195. (in Japanese)
25) Kurosaki H, Yoshimura K. Medical expenses for diabetes care in Japan: Analysis of inter-prefecture differences. *Nihon Koshu Eisei Zasshi*. 2020; 67: 501-508. (in Japanese)
26) Shimizu Y, Nagatomo T. Survey of pharmacists' attitudes toward patient residual drug problems. *Pharmacometrics*. 2020; 98: 43-47. (in Japanese)
27) Suzuki H. Analysis of medical expenses for diabetes and complications in municipalities in Miyagi prefecture. *The Journal of Sendai Shirayuri Women's College*. 2020; 24: 69-82. (in Japanese)
28) Ikeda Y, Kubo T, Oda E, et al. Retrospective analysis of medical costs and resource utilization for severe hypoglycemic events in patients with type 2 diabetes in Japan. *J Diabetes Investig*. 2019; 10: 857-865.
29) Kusunoki-Tsuji C, Araki SI, Kume S, et al. Impact of obesity on annual medical expenditures and diabetes care in Japanese patients with type 2 diabetes mellitus. *J Diabetes Investig*. 2018; 9: 776-781.

30) Ohsaka N, Michikawa M, Yamamoto S, et al. Evaluation of long-term preventive care activities for the elderly: 10-year tracking survey of fitness tests. *Journal of Rehabilitation and Health Sciences*. 2018; 15: 41-45.
31) Kato T, Nishimura M, Yamashita H, et al. Effectiveness of long-term combined aerobic and resistance training circuits on physical function, medical examination, and cost of medical care among middle-aged women. *The Journal of the Yonago Medical Association*. 2020; 71: 1-11. (in Japanese)
32) Yamashita T, Yamashita K, Sato M, et al. Effect of walking on depression prevalence for diabetes using information communication technology: Prospective study. *Geriatr Gerontol Int*. 2019; 19: 1147-1152.
33) Takeichi Y, Narita K, Yokoyama K, et al. Study of therapeutic effect determinants of nutritional guidance for lifestyle-related diseases. *The Journal of Metabolism and Clinical Nutrition*. 2016; 19: 291-297. (in Japanese)
34) Ogiwara T, Satoh K, Kadoma Y, et al. Radical scavenging activity and cytotoxicity of ferulic acid. *Anticancer Res*. 2002; 22: 2711-2717.
35) Schlemmer U, Frølich W, Prieto RM, et al. Phytate in foods and significance for humans: Food sources, intake, processing, bioavailability, protective role and analysis. *Mol Nutr Food Res*. 2009; 53: S330-S375.
36) Masuzaki H, Kozuka C, Yonamine M, et al. Brown rice-specific γ-oryzanol-based novel approach toward lifestyle-related dysfunction of brain and impaired glucose metabolism. *Glycative Stress Res*. 2017; 4: 58-66.
37) Shimotoyodome A, Okahara F. Anti-obese and Anti-hyperglycemic effects of dietary triterpene alcohols and sterols from rice bran oil. *Journal of Oleo Science*. 2017; 17: 269-276. (in Japanese)
38) Shimizu H, Ohue-Kitano R, et al. Regulation of host energy metabolism by gut microbiota-derived short-chain fatty acids. *Glycative Stress Res*. 2019; 6: 181-191.
39) Sawada K, Takemi Y, Murayama N, et al. Relationship between rice consumption and body weight gain in Japanese workers: white versus brown rice/multigrain rice. *Appl Physiol Nutr Metab*. 2019; 44: 528-532.
40) Nakata K, Inagawa H, Nishizawa T, et al. Specific messenger RNA expression for signal transduction molecules by lipopolysaccharide in intestinal macrophages. *Clin Exp Immunol*. 2006; 143: 484-493.
41) Sakamoto S, Hayashi T, Hayashi K, et al. Pre-germinated brown rice could enhance maternal mental health and immunity during lactation. *Eur J Nutr*. 2007; 46: 391-396.
42) Thanapreedawat P, Kobayashi H, Inui N, et al. GABA affects novel object recognition memory and working memory in rats. *J Nutr Sci Vitaminol* (*Tokyo*). 2013; 59: 152-157.
43) Kuroda Y, Matsuzaki K, Wakatsuki H, et al. Influence of Ultra-High Hydrostatic Pressurizing Brown Rice on Cognitive Functions and Mental Health of Elderly Japanese Individuals: A 2-Year Randomized and Controlled Trial. *J Nutr Sci Vitaminol* (*Tokyo*). 2019; 65(Supplement): S80-S87.
44) Saito M, Shimazaki Y, Nonoyama T, et al. Associations of number of teeth with medical costs and hospitalization duration in an older Japanese population. *Geriatr Gerontol Int*. 2019; 19: 335-341.