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Paradigm Change to Future Health Enhancement through Comprehending the Concept of Obesity Disease in Japan

Yuka Kohda*

Department of Pharmacotherapeutics, Osaka University of Pharmaceutical Sciences, Japan

***Corresponding author:** Yuka Kohda, Department of Pharmacotherapeutics, Osaka University of Pharmaceutical Sciences, 4-20-1 Nasahara, Takatsuki, Osaka 569-1094, Japan, Tel: +81-72-690-1081; Fax: +81-72-690-1081; E-mail: ykohda@gly.oups.ac.jp

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Abstract

The prevalence of obesity is rapidly increasing worldwide. Obesity greatly increases health care costs because of associated complications. Illnesses related to obesity include impaired glucose tolerance, hypertension, and cardiovascular disease. Obesity also increases the risk of developing type II diabetes. Mild obesity, as well as severe obesity, may result in development of obesity associated diseases, where a person suffers from health problems that are caused by or related to obesity. Obesity disease is differentiated from obesity, which is not accompanied by health problems that represent risk factors for various diseases. Development of obesity disease needs to be prevented or mitigated through a reduction in weight. For individuals who are obese, awareness of the concept of obesity disease could help in selecting appropriate treatment. The Japan Society for the Study of Obesity recommends that researchers and physicians fully comprehend the concepts of obesity and obesity disease. Treatment paradigms and therapeutic focuses are constantly changing, and this knowledge needs to be disseminated to individuals with obesity, regardless of whether they have health problems. This review discusses the concepts of obesity and obesity disease. The role of adipose tissue in metabolic complications due to obesity, as well as prevention and treatment of metabolic complications are also discussed with respect to improving health. The main aim of this review is to assist reader to determine the level of risk associated with obesity disease and obesity-related complications.

Keywords: Obese with health problems; Type II diabetes; Metabolic complications; Body mass index; Nagoya Declaration 2015; Adipocytes

Introduction

The term obesity implies excessive body fat for an individual's build [1,2]. The term body mass index (BMI) is used for assessment of the presence of overweight and obese individuals [3-5]. Obesity is a more extreme problem than overweight. BMI itself does not denote individuals who are overweight and obese. According to the World Health Organization (WHO) criteria for obesity, individuals who have a BMI of 25 to less than 30 kg/m^2 are pre-obese, and individuals who have a BMI of 30 kg/m^2 or greater are obese [1,2].

Table 1 shows the BMIs that correspond to individuals who are underweight compared with those that correspond to individuals who are morbidly obese. Without just applying WHO criteria, according to the Japan Society for the Study of Obesity, a BMI of greater than 25 kg/m^2 classifies the corresponding individual as obese [3]. Not only severe obesity, but also mild obesity, may easily result in development of obesity disease among the Japanese population [6-8]. The prevalence of obesity continues to markedly increase worldwide [9,10]. Recent data regarding the prevalence of obesity in Japan are listed in Table 2 [3,11].

In this report, the author provides an up-to-date and concise review of the concept of obesity and obesity disease, with the aim of guiding the reader through the Nagoya Declaration 2015 (Figure 1), where the concept of obesity disease has been globally proposed [12]. Prevention and control of obesity-related complications are also discussed with respect to enhancing future health.

WHO criteria	Body mass index (BMI) (kg/m^2)	Japan criteria
Underweight	Less than 18.5	Underweight
Normal range	18.5 to 24.9	Normal weight
Pre-obese	25.0 to 29.9	Obese (level 1)
Obese class 1	30.0 to 34.9	Obese (level 2)
Obese class 2	35.0 to 39.9	Obese (level 3)
Obese class 3	40.0 and greater	Obese (level 4)

Table 1: Body mass index (BMI) for pre-obesity and obesity (BMI>25 kg/m^2). The guidelines for the management of obesity disease 2016 by the Japan Society for the Study of Obesity [3].

Role of adipose tissue in metabolic complications due to obesity

Obesity is the leading cause of insulin resistance and a major contributing factor to metabolic complications [13,14]. Enlargement of fat cells and an increase in the number of fat cells are associated with obesity. Fat cells are present in adipose tissue distributed throughout the body. Adipose tissue is constructed from fat cells storing lipid droplets, interstitial tissue where fat progenitor cells exist, and the vascular system. Furthermore, adipose tissue comprises at least two types of fat cells, brown and white adipocytes, which have different morphology, distribution, and function [15]. Brown adipocytes perform oxidation of fatty acids derived from triglycerides within cells,

as well as function as energy consumption cells. White adipocytes store redundant energy as triglycerides.

Age (years)	Obesity prevalence (% of population)	
	Men	Women
20-29	0.218	0.107
30-39	0.254	0.133
40-49	0.349	0.148
50-59	0.311	0.219
60-69	0.287	0.215
≥ 70	0.276	0.271

Table 2: The prevalence of obesity in Japan. Data were modified from the National Health and Nutrition Survey 2015 by the Ministry of Health, Labour and Welfare [3, 11].

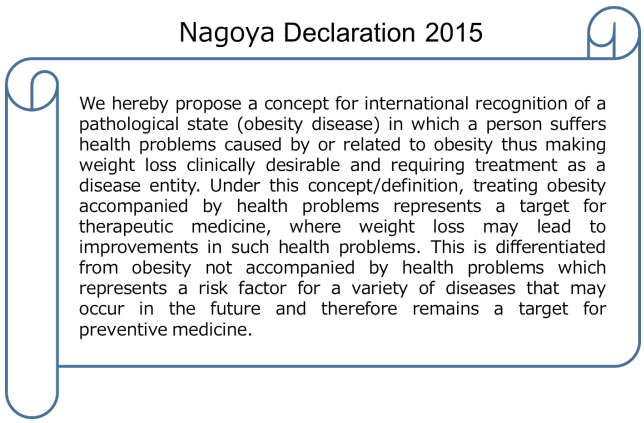

Figure 1: Nagoya Declaration 2015. The concept of obesity disease was globally proposed by the 8th Asia-Oceania Conference on obesity [12].

In the laboratory, rat white preadipocytes (Takara Bio Inc., Shiga, Japan) were cultured in Dulbecco's modified Eagle's medium with high glucose levels containing 10% fetal bovine serum at 37°C under 5% CO_2. The cells were subcultured after reaching 80% confluence. To induce adipogenesis, preadipocytes were cultured until confluence and the culture medium was changed to a differentiation and induction medium. We observed that lipid droplets reflecting the absence of accumulated triglycerides were increased during differentiation of preadipocytes into adipocytes (Figures 2 and 3).

Adipose tissue was once considered to be an inactive storage depot, but it shows a lot of metabolic activity. Fat is continuously being stored in and released from the adipose tissue. Insulin is responsible not only for moving glucose into muscle cells, but also for promoting glucose uptake by fat cells. Once glucose enters a fat cell, it can be converted to glycerol or fatty acids, which together form triglycerides. Therefore, fat cells affect the levels of triglycerides and free fatty acids, which partly explains why central obesity is a marker of impaired glucose tolerance and a risk factor for obesity-related disorders.

In addition to the function mentioned above, white adipocytes also function as endocrine cells and secrete signal molecules called adipocytokines. These adipocytokines include leptin, tumor necrosis factor, free fatty acids, and plasminogen activator inhibitor. An enlarged fat cell secretes adipocytokines after large quantities are produced, affecting signal transduction of insulin in the skeletal muscle and liver, which further result in the induction of insulin resistance. This situation occurs because of obesity-induced insulin resistance. Additionally, adipose tissue is not only an energy reservoir, but also a secretory endocrine organ that can produce cytokines, hormones, and proteins that affect cells and tissues throughout the body [16,17].

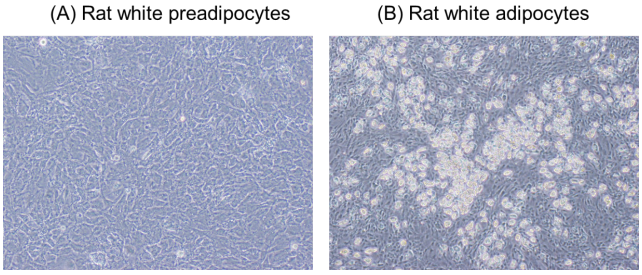

Figure 2: Photomicrographs of rat white preadipocytes (A) and adipocytes (B). White preadipocytes were isolated from the visceral fat of rats and cultured and passaged twice. With regard to morphology, most preadipocytes were fibroblast-like cells. Confluent cells were cultured in a differentiation medium. Kohda unpublished data.

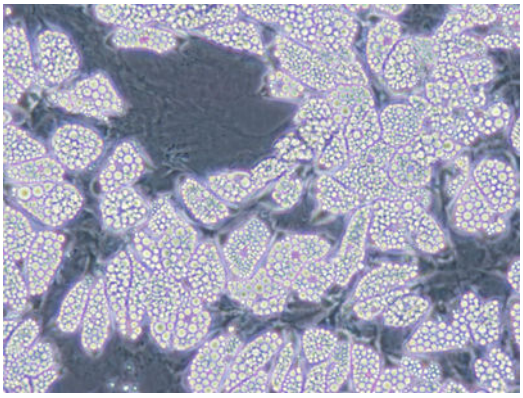

Figure 3: Photomicrograph of intracellular lipid droplets. Rat white adipocyte cells accumulated intracellular lipid droplets, which reflected the absence of accumulated triglycerides, when cultured in the differentiation medium. Kohda unpublished data.

We previously found that thiamine (vitamin B_1) treatment decreases not only body weight but also visceral fat mass and adipocytes size in obesity-related diabetic rats [18-20]. Absorption of food-derived thiamine, dietary supplements and medicines might be important in preventing and controlling obesity-related metabolic complications.

Obesity accompanied by health problems and medical economic impact

Obesity and metabolic syndrome significantly contribute to health care costs through their associated complications [21]. Some obesity-related illnesses are as follows: (1) type II diabetes, impaired glucose tolerance [22-27], (2) dyslipidemia [28,29], (3) hypertension [30,31], (4) gout [32,33], (5) cardiovascular disease [34-38], (6) cerebral brain infraction [39-41], (7) non-alcoholic fatty liver disease [42-45],

(8) menstrual disorder and infertility [46-48], (9) sleep apnea [49-51], (10) degenerative joint disease [52,53], (11) obesity-related chronic kidney disease [54,55], (12) cancer [56-59].

The global epidemic of obesity is also heralding an epidemic of type II diabetes, which is in turn escalating health care costs related to the burden of complications [21]. Obesity is linked with type II diabetes in terms of increasing the risk of developing this condition and its associated morbidity [21]. The annual cost of diabetes worldwide is $825 billion [60,61]. Furthermore, the medical cost soars when the individual is also pre-diabetic. Intensive management of diabetes from the time of diagnosis yields a reduction in the risk of metabolic complications. Changes in therapeutic lifestyle need to be advocated from the start. Prevention of metabolic complications is the most important aspect. Ideally, there needs to be a reduction in weight, as well as prevention of the development of obesity disease.

Closing Notes

The main aim of this review is to help readers determine the level of risk associated with obesity disease. Obesity affects every organ system in the body and may be the paradigm for obesity disease. The question can be asked whether obesity is a risk factor or a disease. Considering all of the types of obesity as equal is not scientifically appropriate. With regard to weight loss through improvements in lifestyle, such as starting to diet and exercise, considering obese individuals on a case-by-case basis is important from a medicoeconomic viewpoint (i.e., based on those who require a preventive intervention and those who should be medically treated). For individuals with obesity, making the concept of obesity disease widely available would contribute to selection of appropriate treatment. The prevalence of obesity disease is increasing worldwide. The Japan Society for the Study of Obesity recommends that doctors and researchers should fully understand the concepts of obesity and obesity disease. Because treatment paradigms and therapeutic focuses keep changing and evolving, this knowledge needs to be shared with individuals who are obese with or without health problems.

The true and scientific route to our future health enhancement is not only pharmaceutical medicine, but also preventive medicine against obesity disease and metabolic complications. A healthy diet, regular physical activity, and maintenance of healthy body weight can prevent or delay the onset of obesity-related complications.

Conflict of Interest

The author declares that there is no conflict of interest.

References

1. WHO (2017) Fact sheet fs311 Obesity and overweight, updated June 2016. Geneva: World Health Organization.
2. World health statistics (2016) Geneva; World Health Organization
3. Guidelines for the management of obesity disease (2016) The Japan Society for the Study of Obesity.
4. Gallagher D, Visser M, Sepúlveda D, Pierson RN, Harris T, et al. (1996) How useful is body mass index for comparison of body fatness across age, sex, and ethnic groups? See comment in PubMed Commons belowAm J Epidemiol 143: 228-239.
5. NCD Risk Factor Collaboration (NCD-RisC) (2016) Trends in adult body-mass index in 200 countries from 1975 to 2014: a pooled analysis of 1698 population-based measurement studies with 19.2 million participants. Lancet 387:1377-1396.
6. Chan JC, Malik V, Jia W, Kadowaki T, Yajnik CS, et al. (2009) Diabetes in Asia: epidemiology, risk factors, and pathophysiology. JAMA 301: 2129-2140.
7. Hu FB (2011) Globalization of diabetes: the role of diet, lifestyle, and genes. Diabetes Care 34: 1249-1257.
8. Misra A, Shrivastava U (2013) Obesity and dyslipidemia in South Asians. Nutrients 5: 2708-2733.
9. Afshin A, Forouzanfar MH, Reitsma MB, Sur P, Estep K, et al. (2017) GBD 2015 Obesity Collaborators. Health Effects of Overweight and Obesity in 195 Countries over 25 Years. N Engl J Med 377: 13-27.
10. Ng M, Fleming T, Robinson M, Thomson B, Graetz N, et al. (2014) Global, regional, and national prevalence of overweight and obesity in children and adults during 1980-2013: a systematic analysis for the Global Burden of Disease Study 2013. Lancet 384: 766-781.
11. National Health and Nutrition Survey (2015) The Ministry of Health, Labour and Welfare.
12. The 8th Asia-Oceania Conference on Obesity, Nagoya Declaration 2015.
13. de Luca C, Olefsky JM (2008) Inflammation and insulin resistance. FEBS Lett 582: 97-105.
14. de Luca C, Olefsky JM (2006) Stressed out about obesity and insulin resistance. Nat Med 12:41-42.
15. Gómez-Hernández A, Beneit N, Díaz-Castroverde S, Escribano Ó (2016) Differential role of adipose tissues in obesity and related metabolic and vascular complications. Int J Endocrinol Article 2016: 1216783.
16. Aldhahi W, Hamdy O (2003) Adipokines, inflammation, and the endothelium in diabetes. Curr Diab Rep 3: 293-298.
17. Mathieu P, Lemieux I, Després JP (2010) Obesity, inflammation, and cardiovascular risk. Clin Pharmacol Ther 87: 407-416.
18. Kohda Y, Tanaka T, Matsumura H (2012) Role of thiamine in obesity-related diabetes: Modification of the gene expression. Food and Nutritional Components in Focus No.4 B Vitamins and Folate: Chemistry, Analysis, Function and Effects. The Royal Society of Chemistry 580-591.
19. Tanaka T, Kono T, Terasaki F, Yasui K, Soyama A, et al. (2010) Thiamine prevents obesity and obesity-associated metabolic disorders in OLETF rats. J Nutr Sci Vitaminol 56: 335-346.
20. Kohda Y, Tanaka T, Matsumura H (2012) Effect of thiamine repletion on cardiac fibrosis and protein *O*-glycosylation in diabetic cardiomyopathy. J Diabetes Metab S7: 001.
21. Zhou B, Lu Y, Hajifathalian K, Bentham J, Di Cesare M, et al. (2016) NCD Risk Factor Collaboration (NCD-RisC). Worldwide trends in diabetes since 1980: a pooled analysis of 751 population-based studies with 4.4 million participants. Lancet 387:1513-1530.
22. Tuomilehto J, Lindström J, Eriksson JG, Valle TT, Hämäläinen H, et al. (2001) Prevention of type 2 diabetes mellitus by changes in lifestyle among subjects with impaired glucose tolerance. N Engl J Med 344: 1343-1350.
23. Knowler WC, Barrett-Connor E, Fowler SE, Hamman RF, Lachin JM, et al. (2002) Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. N Engl J Med 346:393-403.
24. Chiasson JL, Josse RG, Gomis R, Hanefeld M, Karasik A, et al. (2002) Acarbose for prevention of type 2 diabetes mellitus: the STOP-NIDDM randomised trial. Lancet 359: 2072-2077.
25. Kawamori R, Tajima N, Iwamoto Y, Kashiwagi A, Shimamoto K, et al. (2009) Voglibose for prevention of type 2 diabetes mellitus: a randomised,

double-blind trial in Japanese individuals with impaired glucose tolerance. Lancet 373: 1607-1614.

26. DeFronzo RA, Tripathy D, Schwenke DC, Banerji M, Bray GA, et al. (2011) Pioglitazone for diabetes prevention in impaired glucose tolerance. N Engl J Med 364: 1104-1115.
27. Muramoto A, Matsushita M, Kato A, Yamamoto N, Koike G, et al. (2014) Three percent weight reduction is the minimum requirement to improve health hazards in obese and overweight people in Japan. Obes Res Clin Pract 8: e466-475.
28. Lamon-Fava S, Wilson PW, Schaefer EJ (1996) Impact of body mass index on coronary heart disease risk factors in men and women. The Framingham Offspring Study. Arterioscler Thromb Vasc Biol 16: 1509-1515.
29. Shirai K, Saiki A, Oikawa S, Teramoto T, Yamada N, et al. (2013) The effects of partial use of formula diet on weight reduction and metabolic variables in obese type 2 diabetic patients--multicenter trial. Obes Res Clin Pract 7: e43-54.
30. Jamerson K, Weber MA, Bakris GL, Dahlöf B, Pitt B, et al. (2008) Benazepril plus amlodipine or hydrochlorothiazide for hypertension in high-risk patients. N Engl J Med 359: 2417-2428.
31. Weber MA, Jamerson K, Bakris GL, Weir MR, Zappe D, et al. (2013) Effects of body size and hypertension treatments on cardiovascular event rates: subanalysis of the ACCOMPLISH randomised controlled trial. Lancet 381: 537-545.
32. Yamashita S, Matsuzawa Y, Tokunaga K, Fujioka S, Tarui S (1986) Studies on the impaired metabolism of uric acid in obese subjects: marked reduction of renal urate excretion and its improvement by a low-calorie diet. Int J Obes 10: 255-264.
33. Matsuura F, Yamashita S, Nakamura T, Nishida M, Nozaki S, et al. (1998) Effect of visceral fat accumulation on uric acid metabolism in male obese subjects: visceral fat obesity is linked more closely to overproduction of uric acid than subcutaneous fat obesity. Metabolism 47: 929-933.
34. Hubert HB, Feinleib M, McNamara PM, Castelli WP (1983) Obesity as an independent risk factor for cardiovascular disease: a 26-year follow-up of participants in the Framingham Heart Study. Circulation 67: 968-977.
35. Chei CL, Iso H, Yamagishi K, Inoue M, Tsugane S (2008) Body mass index and weight change since 20 years of age and risk of coronary heart disease among Japanese: the Japan Public Health Center-Based Study. Int J Obes (Lond) 32: 144-151.
36. Berlin JA, Colditz GA (1990) A meta-analysis of physical activity in the prevention of coronary heart disease. Am J Epidemiol 132: 612-628.
37. Lu Y, Hajifathalian K, Ezzati M, Woodward M, Rimm EB, et al. (2014) Metabolic mediators of the effects of body-mass index, overweight, and obesity on coronary heart disease and stroke: a pooled analysis of 97 prospective cohorts with 1.8 million participants. Lancet 383:970-983.
38. Peirson L, Douketis J, Ciliska D, Fitzpatrick-Lewis D, Ali MU, et al. (2014) Treatment for overweight and obesity in adult populations: a systematic review and meta-analysis. CMAJ Open 2: E306-317.
39. Rexrode KM, Hennekens CH, Willett WC, Colditz GA, Stampfer MJ, et al. (1997) A prospective study of body mass index, weight change, and risk of stroke in women. JAMA 277: 1539-1545.
40. Bodenant M, Kuulasmaa K, Wagner A, Kee F, Palmieri L, et al. (2011) Measures of abdominal adiposity and the risk of stroke: the MOnica Risk, Genetics, Archiving and Monograph (MORGAM) study. Stroke 42: 2872-2877.
41. Bazzano LA, Gu D, Whelton MR, Wu X, Chen CS, et al. (2010) Body mass index and risk of stroke among Chinese men and women. Ann Neurol 67: 11-20.
42. Promrat K, Kleiner DE, Niemeier HM, Jackvony E, Kearns M, et al. (2010) Randomized controlled trial testing the effects of weight loss on nonalcoholic steatohepatitis. Hepatology 51: 121-129.
43. Lee YM, Low HC, Lim LG, Dan YY, Aung MO, et al. (2012) Intragastric balloon significantly improves nonalcoholic fatty liver disease activity score in obese patients with nonalcoholic steatohepatitis: a pilot study. Gastrointest Endosc 76: 756-760.
44. Oza N, Eguchi Y, Mizuta T, Ishibashi E, Kitajima Y, et al. (2009) A pilot trial of body weight reduction for nonalcoholic fatty liver disease with a home-based lifestyle modification intervention delivered in collaboration with interdisciplinary medical staff. J Gastroenterol 1203-1208.
45. de Luis DA, Aller R, Izaola O, Gonzalez Sagrado M, Conde R (2010) Effect of two different hypocaloric diets in transaminases and insulin resistance in nonalcoholic fatty liver disease and obese patients. Nutr Hosp 25: 730-735.
46. Rowland AS, Baird DD, Long S, Wegienka G, Harlow SD, et al. (2002) Influence of medical conditions and lifestyle factors on the menstrual cycle. Epidemiology 13: 668-674.
47. Hartz AJ, Barboriak PN, Wong A, Katayama KP, Rimm AA (1979) The association of obesity with infertility and related menstural abnormalities in women. Int J Obes 3: 57-73.
48. Douchi T, Kuwahata R, Yamamoto S, Oki T, Yamasaki H, et al. (2002) Relationship of upper body obesity to menstrual disorders. Acta Obstet Gynecol Scand 81: 147-150.
49. Jordan AS, McSharry DG, Malhotra A (2014) Adult obstructive sleep apnoea. Lancet 383: 736-747.
50. Peppard PE, Young T, Palta M, Dempsey J, Skatrud J (2000) Longitudinal study of moderate weight change and sleep-disordered breathing. JAMA 284: 3015-3021.
51. Peppard PE, Young T, Barnet JH, Palta M, Hagen EW, et al. (2013) Increased prevalence of sleep-disordered breathing in adults. Am J Epidemiol 177: 1006-1014.
52. Kutzner I, Heinlein B, Graichen F, Bender A, Rohlmann A, et al. (2010) Loading of the knee joint during activities of daily living measured in vivo in five subjects. J Biomech 43: 2164-2173.
53. Jiang L, Tian W, Wang Y, Rong J, Bao C, et al. (2012) Body mass index and susceptibility to knee osteoarthritis: a systematic review and meta-analysis. Joint Bone Spine 79: 291-297.
54. Foster MC, Hwang SJ, Larson MG, Lichtman JH, Parikh NI, et al. (2008) Overweight, obesity, and the development of stage 3 CKD: the Framingham Heart Study. Am J Kidney Dis 52: 39-48.
55. Thomas G, Sehgal AR, Kashyap SR, Srinivas TR, Kirwan JP, et al. (2011) Metabolic syndrome and kidney disease: a systematic review and meta-analysis. Clin J Am Soc Nephrol 6: 2364-2373.
56. Kainz A, Hronsky M, Stel VS, Jager KJ, Geroldinger A, et al. (2015) Prediction of prevalence of chronic kidney disease in diabetic patients in countries of the European Union up to 2025. Nephrol Dial Transplant 30: 113-118.
57. Renehan AG, Tyson M, Egger M, Heller RF, Zwahlen M (2008) Body-mass index and incidence of cancer: a systematic review and meta-analysis of prospective observational studies. Lancet 371: 569-578.
58. Berrington de Gonzalez A, Hartge P, Cerhan JR, Flint AJ, Hannan L, et al. (2010) Body-mass index and mortality among 1.46 million white adults. N Engl J Med 363: 2211-2219.
59. Renehan AG, Soerjomataram I, Tyson M, Egger M, Zwahlen M, et al. (2010) Incident cancer burden attributable to excess body mass index in 30 European countries. Int J Cancer 126: 692-702.
60. Nakamura K, Okamura T, Kanda H, Hayakawa T, Murakami Y, et al. (2008) Health Promotion Research Committee of the Shiga National Health Insurance Organizations. Public Health 122:1226-1228.
61. Seuring T, Archangelidi O, Suhrcke M (2015) The Economic Costs of Type 2 Diabetes: A Global Systematic Review. Pharmacoeconomics 33: 811-831.