REVIEW ARTICLE

Reversing Type 2 Diabetes Through Functional Medicine

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ABSTRACT

Diabetes is one of the biggest global health emergencies of the 21st century. Overall, 425 million people worldwide are estimated to have diabetes, with India being home to the second largest number of people suffering with diabetes. A recent analysis showed that diabetes-related complications are continuously on the rise. These complications affect almost all systems of the body leading to retinopathy, neuropathy, nephropathy, cardiovascular disorders, diabetic foot, depression, anxiety and even eating disorders in diabetes patients, severely affecting the patient's quality-of-life. Traditional approach towards treating type 2 diabetes does not try to alter the course of diabetes at the prediabetes stage. It works on the symptoms, and as a result, the basic pathology keeps on getting intense and therefore, the number and dose of medicine keeps on increasing every few years. Functional medicine provides a holistic approach towards managing diabetes and reducing the complications associated with it. This review discusses the functional medicine approach, detailing the early diagnosis approach, preventive strategy, regular monitoring of blood glucose parameters and treatment approach of diabetes including diet management, exercise, functional foods, nutritional supplements and genetic and lifestyle interaction.

Keywords: Functional medicine, diabetes, reverse diabetes, diet, stress, exercise, nutritional medicine, functional foods

Diabetes is one of the largest global health emergencies of 21st century. Overall, 425 million people worldwide are estimated to have diabetes, with almost 79% living in low- and middle-income countries. India is home to the second largest number of adults living with diabetes worldwide, after China. In 2014, 8.5% of adults aged 18 years and older had diabetes. In 2016, diabetes was the direct cause of 1.6 million deaths and in 2012 high blood glucose was the cause of another 2.2 million deaths.

Diabetes is an ever-growing problem, primarily due to a lack of lifestyle education and physical activity as well as the consumption of high-calorie, low-nutrient, processed foods. Diabetes has various and often devastating complications such as heart disease, stroke, high blood pressure, nerve damage, kidney damage, eye damage, foot damage, hearing impairment, skin conditions such as bacterial and fungal infections and even Alzheimer's disease. With 1 out of 11 people suffering from diabetes, the disease disrupts all aspects of human physiology and increases the risk of cardiovascular disease, cancer, cognitive decline and virtually every other disease.

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Functional medicine plays a crucial role in managing and reversing diabetes by applying itself to laboratory testing, performing an extensive evaluation of the patients' overall lifestyle and health history leading to detection of issues, which can be reversed using intensive lifestyle changes. Functional medicine can control the blood glucose levels, as well as help in reducing many other linked health issues of the patient. Functional medicine is successful in not only optimizing glycosylated hemoglobin (HbA1c) and blood glucose levels, but also reversing diabetes completely.

CONVENTIONAL MEDICINE APPROACH

In conventional approach to diabetes treatment, inadequate time is spent on identifying the root cause of the disease. In traditional practice, the common approach is to wait till the patient is in later stages of diabetes and not much is done to alter the course of the disease in its early (insulin resistance) or prediabetes stage when the body is more responsive to diet and lifestyle changes.

FUNCTIONAL MEDICINE APPROACH TOWARDS DIABETES

Functional medicine approach works by applying itself to detailed laboratory testing, performing an extensive evaluation of the patient's overall lifestyle and health history leading to detection of issues, which can be

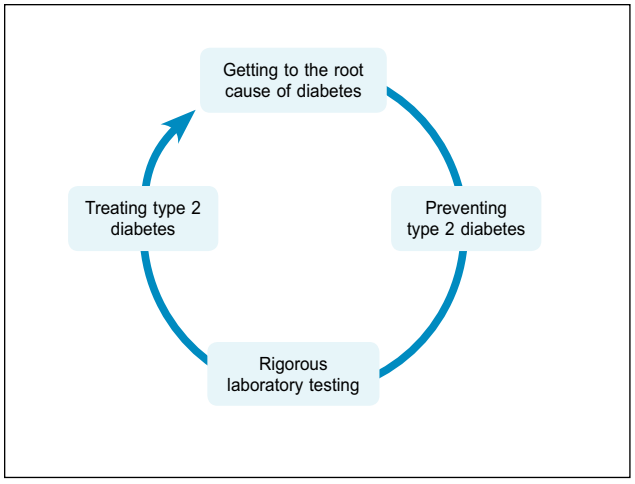


Figure 1. Functional medicine approach for diabetes management.

reversed using intensive lifestyle changes. In patients who are already diagnosed with type 2 diabetes, functional medicine approach tends to look for the root cause and correct it, thereby alleviating many (if not all) symptoms associated with diabetes (Fig. 1).

Getting to the Root Cause of Diabetes

Blood glucose is a symptom of diabetes and not the cause of diabetes. Hence, it is important to understand that treating only the symptoms will not be helpful in alleviating diabetes. It thus becomes imperative to detect the primary cause of diabetes.

Insulin resistance

Insulin is an important hormone released by β-cells in the pancreas with one of its key functions being balancing the blood glucose levels in the body. To achieve blood glycemic control, insulin undergoes a process which allows the glucose floating in the blood to efficiently get absorbed into individual cells throughout the body (muscle, fat, liver, etc.). In the presence of insulin resistance, this process is disrupted, leading to a release of more insulin, to ensure that the glucose is absorbed in the body cells. However, as the blood glucose increases owing to lifestyle, genetics, toxins or mitochondrial function impairment, the β-cells are unable to produce more insulin, which causes an excess build-up of glucose in the blood. This excess glucose then damages cells throughout the body, and these symptoms present as diabetes complications in the body.

Chronic stress

Chronic stress is another factor leading to insulin resistance which in turn causes type 2 diabetes. Stress increases cortisol levels in the body, which increases blood glucose levels. In case, the stress is temporary, there is no problem; however, if the stress persists due to a high-stress work environment, or disturbed family life, then the persistently elevated cortisol causes persistently elevated blood glucose and the β-cells are unable to secrete adequate insulin. High perceived stress is associated with insulin resistance and a significantly increased risk of type 2 diabetes in adults.

Lack of sleep

Research has shown that sleep deprivation is also linked to insulin resistance. A study conducted among 9 healthy subjects (5 men and 4 women) has shown that partial sleep deprivation during only a single night induces insulin resistance in multiple metabolic pathways in healthy subjects. This physiological observation is of relevance for variations in glucose regulation in patients with type 2 diabetes. Sleep deprivation increased plasma nonesterified fatty acid levels.

Microbiome

Another theory suggests that an imbalance in the body's flora and fauna leads to an overgrowth of harmful bacteria carrying lipopolysaccharide. Lipopolysaccharide release has also been associated with insulin resistance. Research has also shown that patients with hypovitaminosis D are at higher risk of insulin resistance and the metabolic syndrome.

Methylation status

Epigenetic modifications, including DNA methylation, have been identified as one mechanism by which the environment interacts with the genome and there is evidence that alterations in DNA methylation may contribute to the increased prevalence of type 2 diabetes.

Smoking

Cigarette smoking is a well-known risk factor in many diseases, including diabetes. Many studies have reported the unfavorable effects of smoking on diabetes mellitus. Smoking increases the risk of developing diabetes, and aggravates the micro- and macrovascular complications of diabetes mellitus. Smoking is associated with insulin resistance, inflammation and dyslipidemia, but the exact mechanisms through which smoking influences diabetes mellitus are not clear. However, smoking cessation is one of the important targets for diabetes control and the prevention of diabetes complications.

Genetic propensity to diabetes

Type 2 diabetes has a strong link to family history and lineage, although it also depends on environmental

factors. The underlying genetic basis for mortality likely involves complex interactions with factors related to ethnicity, type 2 diabetes and body weight. Type 2 diabetes is partly genetically determined. Genetic factors that increase type 2 diabetes susceptibility may also raise mortality risk through type 2 diabetes or its related complications.

Preventing Type 2 Diabetes

Functional medicine takes a proactive approach in preventing type 2 diabetes. A detailed testing allows functional medicine practitioners to identify and initiate the reversal of problematic changes such as insulin resistance much sooner than the standard care in conventional approach of diabetes management. Functional medicine has laid down completely new standards for allowing early detection of diabetes so that it can be easily nipped in the bud.

Detailed Laboratory Testing

Functional medicine follows a detailed lab testing and has more sensitive parameters than other conventional diagnostic methods. It is a well-known fact that conventional lab ranges for blood glucose and HbA1c which are considered by clinicians when screening for diabetes allow for quite high range of blood sugars before diabetes is diagnosed.

Current recommendations from the American Diabetes Association for laboratory values that qualify a patient for type 2 diabetes include:

- HbA1c: <7.0%
- Two-hour postprandial blood glucose: <180 mg/dL
- Fasting blood glucose: 80-130 mg/dL.

However, functional medicine looks for early warning signs such as mild elevations of glucose or of insulin resistance. Early markers for type 2 diabetes and related conditions in functional medicine are:

- Fasting glucose: 84 mg/dL
- Elevated triglyceride level
- Elevated uric acid level
- Low high-density lipoprotein (HDL)
- Elevated low-density lipoprotein (LDL)
- HbA1c: >5.4%
- Increased insulin or C-peptide levels (for long-term average insulin production)
- Antibodies such as glutamic acid decarboxylase (GAD65), pancreatic islet cells
- Increased waist size (>40 inches in men; >35 inches in women)
- Waist-to-hip ratio >0.85 in females and >0.90 in males
- Elevated blood pressure.

All these early warning signals, help in early diagnosis of diabetes or insulin resistance, hence curbing the progression to diabetes. Timely approach targeting the cause of this variation helps in completely reversing the condition and helps patients in regaining optimal health conditions.

Treatment of Type 2 Diabetes

In contrast to conventional medicine approach, functional medicine takes the path of supporting diet and lifestyle changes in the patient as the primary treatment for type 2 diabetes (Fig. 2) and optimizing the laboratory markers.

Under the vestiges of functional medicine, the patient is educated at length about food and nutrition, lifestyle changes and balancing laboratory markers through various scientific approaches, a typical visit averaging about between half an hour to 90 minutes.

Healthy gut

Research has shown that an altered, inflammatory gut microbiota is of utmost importance in the development of type 2 diabetes. A recent study showed that metformin has an effect on the gut microbiota; the drug increases levels of *Akkermansia muciniphila*, which is a commensal gut bacterium, associated with reduced inflammation and improved metabolic health. This supports the fact that the gut microbiota plays a pivotal role in type 2 diabetes.

Several prebiotics and probiotics have been investigated for their antidiabetic and gut health-promoting effect. A prebiotic fiber found in mushrooms and konjac root has been found to boost the blood glucose levels,

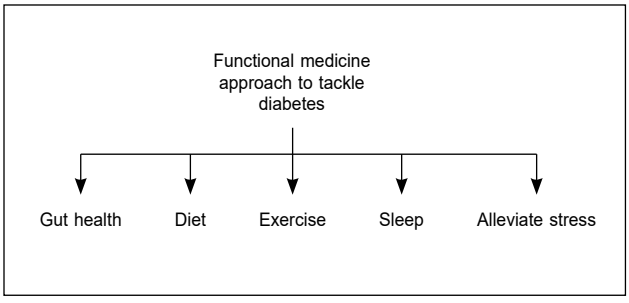


Figure 2. Components of functional medicine approach to manage diabetes.

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reducing effects of metformin. Similarly, inulin, a prebiotic found naturally in chicory, garlic, onions, leeks and asparagus, reduces fasting blood glucose and promotes a more metabolically healthy gut microbiota. Certain probiotic strains such as Lactobacilli and Bifidobacterium also improve biomarkers of inflammation and oxidative stress in type 2 diabetes and lower fasting blood glucose by promoting an anti-inflammatory gut microbiota.

Diet

Low-carbohydrate diet

A persistently growing body of research has indicated that low-carbohydrate diets are superior to high-carbohydrate diets for the treatment of type 2 diabetes. A recent systematic review and meta-analysis of 18 randomized controlled trials has found that reducing dietary carbohydrates produces significant-improvements in HbA1c, triglycerides and cholesterol, while also lowering patient's diabetes medication requirements.

Various large-scale clinical studies have compared the effectiveness of low-carbohydrate diet with high-carbohydrate diet to treat diabetes. The results of these studies have again reiterated that low-carbohydrate diets consistently outperform high-carbohydrate diets for the management of type 2 diabetes. In addition, it also produces more significant improvements in blood glucose stability and lipid profiles and significantly reduces the need for medications. Along with quantity, it is also important to refine the quality of carbohydrates being consumed by the patients.

Low glycemic index diet

A meta-analysis of six small studies (n = 202) with short duration, revealed that overweight or obese people on low glycemic index diets lost more weight and had better improvement in lipid profiles than those receiving other diets.

Cyclic ketogenic diet

Cyclic ketogenic diet has emerged as an effective alternative diet that relies less on medication, and may even be a preferable option when medications are not available. This form of keto diet helps patients follow it more consistently and reap best and long-term results. The ketogenic diet substantially reduces the glycemic response that results from dietary carbohydrate as well as improves the underlying insulin resistance. Results of a study demonstrated that low-carbohydrate, keto diet resulted in significant improvement of glycemia, as measured by fasting glucose and HbA1c in patients with type 2 diabetes. An important point to note here is that this improvement was observed while diabetes medications were reduced or even discontinued. Along with this, participants also experienced moderate reductions in body weight, waist circumference and percent body fat. Another study has also shown that Mediterranean diet was associated with better glycemic control and cardiovascular risk factors than control diets, including a lower fat diet, suggesting that it is suitable for the overall management of type 2 diabetes.

Mediterranean diet

In a randomized, single-blind controlled trial, it was shown that a Mediterranean-style diet might be effective in reducing the prevalence of the metabolic syndrome.

Nutraceuticals in insulin resistance syndrome

Nutraceuticals or functional foods such as plant proteins have been shown to improve insulin resistance and reduce triglyceride secretion. Pro- and prebiotics, that are able to modify intestinal microbiome, reduce absorption of specific nutrients and improve the metabolic handling of energy rich foods. Lastly, specific nutraceuticals have proven to be of benefit such as red-yeast rice, berberine, curcumin, acai, berry antioxidants, *Ginkgo biloba*, green tea as well as vitamin D. All these can improve lipid handling by the liver as well as ameliorate insulin resistance.

Micronutrients

Micronutrient recommendations for a diabetes patient include chromium, vitamin D, magnesium, CoQ10 and alpha-lipoic acid. Alpha-lipoic acid has been shown to be beneficial in the treatment of peripheral diabetic neuropathy. Benefits of magnesium supplementation on metabolic profile in diabetes patients have been found in many clinical studies.

Exercise

It is a well-known fact that a sedentary lifestyle is a significant risk factor for type 2 diabetes, so exercise should be a central part of any treatment plan for the disease. Research has indicated that walking for just 30 minutes a day reduces the risk of type 2 diabetes by approximately 50%. High intensity interval training also appears beneficial as it reduces fasting blood sugar, HbA1c and cardiovascular complications in type 2 diabetes and is more effective than continuous aerobic activity for improving blood sugar control.

In addition to increased exercise, reducing sedentary time in daily life is also essential. Alternate sitting with working at a standing desk or treadmill desk, breaking

up prolonged sitting with standing or walking has been shown to improve the post-meal blood glucose response in those at risk for diabetes.

Maintaining sleep hygiene

Research has shown that short sleep duration or sleep loss may promote type 2 diabetes by interfering with energy metabolism and increasing insulin sensitivity. Sleep loss also impairs satiety, triggering cravings and overconsumption of sugary processed foods that increase the risk of diabetes. Obstructive sleep apnea, a common cause of sleep loss, promotes type 2 diabetes by inducing hypoxia, which in turn impairs insulin production by pancreatic β-cells.

Functional medicine focusses on strategies that correct obstructive sleep apnea, reduces severity of apnea and improves sleep quality and duration.

Stress management

Research has shown that reducing psychological stress can improve blood sugar management in type 2 diabetes. Functional medicine adopts an approach to alleviate patient's chronic stress and improve his overall health as well as reverse diabetes condition. Meditation, yoga, laughter therapy and breathing exercises have been found to reduce fasting blood glucose and post-meal glucose hike in diabetes patients. Functional medicine practitioners offer guided meditation, breathing exercises and relaxation techniques to the patients to alleviate stress.

Pharmacological management

Although currently there are no Food and Drug Administration (FDA) approved medications specifically for the treatment of insulin resistance, the pharmacological agents that are often prescribed for insulin resistance in some patients include metformin and thiazolidinediones. Insulin is also used for some cases of insulin resistance. Metformin is a biguanide insulin sensitizer that is used as a first-line drug.

CONCLUSION

Poor diet, a sedentary lifestyle, inadequate sleep, chronic stress, gut dysfunction and environmental toxins, genetics, toxic thoughts and disturbed mitochondrial function play a significant role in causing diabetes. Functional medicine is a science-based approach to preventing and treating diabetes that is focused on diet and lifestyle changes, and is the most effective first-line strategy for managing type 2 diabetes. It is an effective way to prevent, treat and manage type 2 diabetes. Reversing type 2 diabetes is no more a dream now.

SUGGESTED READING

1. Tay J, Thompson CH, Luscombe-Marsh ND, Wycherley TP, Noakes M, Buckley JD, et al. Effects of an energy-restricted low-carbohydrate, high unsaturated fat/low saturated fat diet versus a high-carbohydrate, low-fat diet in type 2 diabetes: a 2-year randomized clinical trial. Diabetes Obes Metab. 2018;20(4):858-71.
2. Tay J, Luscombe-Marsh ND, Thompson CH, Noakes M, Buckley JD, Wittert GA, et al. Comparison of low- and high-carbohydrate diets for type 2 diabetes management: a randomized trial. Am J Clin Nutr. 2015;102(4):780-90.
3. Huntriss R, Campbell M, Bedwell C. The interpretation and effect of a low-carbohydrate diet in the management of type 2 diabetes: a systematic review and meta-analysis of randomised controlled trials. Eur J Clin Nutr. 2018;72(3):311-25.
4. Bansal A, Pinney SE. DNA methylation and its role in the pathogenesis of diabetes. Pediatr Diabetes. 2017;18(3):167-77.
5. Owen N, Healy GN, Matthews CE, Dunstan DW. Too much sitting: the population health science of sedentary behavior. Exerc Sport Sci Rev. 2010;38(3):105-13.
6. Hamasaki H. Daily physical activity and type 2 diabetes: a review. World J Diabetes. 2016;7(12):243-51.
7. Chang SA. Smoking and type 2 diabetes mellitus. Diabetes Metab J. 2012;36(6):399-403.
8. Leong A, Porneala B, Dupuis J, Florez JC, Meigs JB. Type 2 diabetes genetic predisposition, obesity, and all-cause mortality risk in the U.S.: a multiethnic analysis. Diabetes Care. 2016;39(4):539-46.
9. Francois ME, Pistawka KJ, Halperin FA, Little JP. Cardiovascular benefits of combined interval training and post-exercise nutrition in type 2 diabetes. J Diabetes Complications. 2018;32(2):226-33.
10. Henson J, Davies MJ, Bodicoat DH, Edwardson CL, Gill JM, Stensel DJ, et al. Breaking up prolonged sitting with standing or walking attenuates the postprandial metabolic response in postmenopausal women: a randomized acute study. Diabetes Care. 2016;39(1):130-8.
11. Wu H, Esteve E, Tremaroli V, Khan MT, Caesar R, Mannerås-Holm L, et al. Metformin alters the gut microbiome of individuals with treatment-naive type 2 diabetes, contributing to the therapeutic effects of the drug. Nat Med. 2017;23(7):850-8.
12. De la Cuesta-Zuluaga J, Mueller NT, Corrales-Agudelo V, Velásquez-Mejía EP, Carmona JA, Abad JM, et al. Metformin is associated with higher relative abundance of mucin-degrading *Akkermansia muciniphila* and several short-chain fatty acid-producing microbiota in the gut. Diabetes Care. 2017;40(1):54-62.
13. Zheng J, Li H, Zhang X, Jiang M, Luo C, Lu Z, et al. Prebiotic mannan-oligosaccharides augment the hypoglycemic effects of metformin in correlation with modulating gut microbiota. J Agric Food Chem. 2018;66(23):5821-31.

14. Chiu KC, Chu A, Go VL, Saad MF. Hypovitaminosis D is associated with insulin resistance and beta cell dysfunction. Am J Clin Nutr. 2004;79(5):820-5.
15. Yancy WS Jr, Foy M, Chalecki AM, Vernon MC, Westman EC. A low-carbohydrate, ketogenic diet to treat type 2 diabetes. Nutr Metab (Lond). 2005;2:34.
16. Westman EC, Tondt J, Maguire E, Yancy WS Jr. Implementing a low-carbohydrate, ketogenic diet to manage type 2 diabetes mellitus. Expert Rev Endocrinol Metab. 2018;13(5):263-72.
17. Esposito K, Marfella R, Ciotola M, Di Palo C, Giugliano F, Giugliano G, et al. Effect of a Mediterranean-style diet on endothelial dysfunction and markers of vascular inflammation in the metabolic syndrome: a randomized trial. JAMA. 2004;292(12):1440-6.
18. Esposito K, Maiorino MI, Bellastella G, Chiodini P, Panagiotakos D, Giugliano D. A journey into a Mediterranean diet and type 2 diabetes: a systematic review with meta-analyses. BMJ Open. 2015;5(8):e008222.
19. Foster TS. Efficacy and safety of alpha-lipoic acid supplementation in the treatment of symptomatic diabetic neuropathy. Diabetes Educ. 2007;33(1):111-7.
20. Barbagallo M, Dominguez LJ. Magnesium metabolism in type 2 diabetes mellitus, metabolic syndrome and insulin resistance. Arch Biochem Biophys. 2007;458(1):40-7.
21. Shan Z, Ma H, Xie M, Yan P, Guo Y, Bao W, et al. Sleep duration and risk of type 2 diabetes: a meta-analysis of prospective studies. Diabetes Care. 2015;38(3):529-37.
22. Wang N, Khan SA, Prabhakar NR, Nanduri J. Impairment of pancreatic β-cell function by chronic intermittent hypoxia. Exp Physiol. 2013;98(9):1376-85.
23. Steiropoulos P, Papanas N. Continuous positive airway pressure to improve insulin resistance and glucose homeostasis in sleep apnea. World J Diabetes. 2011;2(1):16-8.
24. Donga E, van Dijk M, van Dijk JG, Biermasz NR, Lammers GJ, van Kralingen KW, et al. A single night of partial sleep deprivation induces insulin resistance in multiple metabolic pathways in healthy subjects. J Clin Endocrinol Metab. 2010;95(6):2963-8.
25. Yan YX, Xiao HB, Wang SS, Zhao J, He Y, Wang W, et al. Investigation of the relationship between chronic stress and insulin resistance in a Chinese population. J Epidemiol. 2016;26(7):355-60.
26. Harris ML, Oldmeadow C, Hure A, Luu J, Loxton D, Attia J. Stress increases the risk of type 2 diabetes onset in women: a 12-year longitudinal study using causal modelling. PLoS One. 2017;12(2):e0172126.
27. Priya G, Kalra S. Mind-body interactions and mindfulness meditation in diabetes. Eur Endocrinol. 2018;14(1):35-41.
28. Marcovecchio ML, Chiarelli F. The effects of acute and chronic stress on diabetes control. Sci Signal. 2012;5(247):pt10.
29. Terrie YC. Insulin resistance: recognizing the hidden danger. Pharmacy Times. Oct 2012.
30. Yanovski JA, Krakoff J, Salaita CG, McDuffie JR, Kozlosky M, Sebring NG, et al. Effects of metformin on body weight and body composition in obese insulin-resistant children: a randomized clinical trial. Diabetes. 2011;60(2):477-85.
31. Weickert MO. Nutritional modulation of insulin resistance. Scientifica (Cairo). 2012;2012:424780.
32. Sirtori CR, Pavanello C, Calabresi L, Ruscica M. Nutraceutical approaches to metabolic syndrome. Ann Med. 2017;49(8):678-97.
33. Derosa G, Limas CP, Macías PC, Estrella A, Maffioli P. Dietary and nutraceutical approach to type 2 diabetes. Arch Med Sci. 2014;10(2):336-44.
34. Bird SR, Hawley JA. Update on the effects of physical activity on insulin sensitivity in humans. BMJ Open Sport Exerc Med. 2017;2(1):e000143.
35. Pot GK, Battjes-Fries MCE, Patijn ON, Pijl H, Witkamp RF, de Visser M, et al. Nutrition and lifestyle intervention in type 2 diabetes: pilot study in the Netherlands showing improved glucose control and reduction in glucose lowering medication. BMJ Nutrition, Prevention & Health. 2019;2:43-50.

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