The issues in annual health checkups (human dock system) in Japan to prevent non-communicable diseases

Tatsuo Shimosawa[1], Chiari Kojima[2]

[1]Department of Clinical Laboratory, Graduate School of Medicine, International University of Health and Welfare, Chiba, Japan; [2]Department of Clinical Laboratory, Mita Hospital, International University of Health and Welfare, Tokyo, Japan

Contributions: (I) Conception and design: T Shimosawa; (II) Administrative support: T Shimosawa; (III) Provision of study materials or patients: None; (IV) Collection and assembly of data: C Kojima; (V) Data analysis and interpretation: Both authors; (VI) Manuscript writing: Both authors; (VII) Final approval of manuscript: Both authors.

Correspondence to: Tatsuo Shimosawa, MD, PhD. Department of Clinical Laboratory, Graduate School of Medicine, International University of Health and Welfare, 850 Hatakeda, Narita, Chiba 286-8520, Japan. Email: tshimo-tky@umin.ac.jp.

Abstract: The modern health checkup system started in the 1970s in Japan and contributed largely to reducing mortality in non-communicable diseases, especially cerebrovascular diseases. However, there remain issues in our health checkup system. Quality management is not necessarily well performed and preanalytical and analytical errors are often found in laboratory exams in health checkup systems. Moreover, among non-communicable diseases, cancer screening does not achieve an acceptable impact on early detection of cancer. This is partly due to the low number of participants in cancer screening because it is not free for charge and is an optional examination. In order to increase this number, not only a populational approach but also an individualized and more precision approach is necessary. By analyzing accumulated data, we are now able to pick up genetical and epigenetic risk factors. Epigenetic markers such as DNA methylation, histone modification or microRNAs could be a solution for the future to develop more accurate and individualized health checkups and contribute to our welfare. High-impact interventions for non-communicable disease can be delivered through a regular health checkup and risk stratification to strengthen early detection of reversable risks and curable disease and timely and effective treatment.

Keywords: Cancer; epigenetic markers; quality control (QC); screening test

Received: 20 December 2023; Accepted: 07 April 2024; Published online: 22 April 2024.

doi: 10.21037/jlpm-23-97

View this article at: https://dx.doi.org/10.21037/jlpm-23-97

Introduction

Background

Even during the coronavirus disease 2019 (COVID-19) pandemic, the leading causes of death were ischemic heart disease, stroke, and chronic obstructive pulmonary disease (1), so-called non-communicable diseases (NCDs) all over the world. The major risks for the burden of NCD are classified into three categories, modifiable behavioral, metabolic, and environmental risk factors. Among them, metabolic risks such as hypertension, hypercholesterolemia, and diabetes (1) which are without symptoms in the early stage and not diagnosed without measuring blood pressure, blood cholesterol level, and glucose level. These days, home blood pressure monitoring or urinary glucose or blood glucose levels can be measured in some countries at home but it is not widely accepted. So that, only by regular health checkups participants can know their risks.

Rationale and knowledge gap

A recent study aimed at the optimal target blood pressure showed the intensive treatment of blood pressure (systolic blood pressure lower than 120 mmHg) is superior to reducing cardiovascular events and mortality than standard treatment (systolic blood pressure lower than 140 mmHg) (2). In this

study, when we calculate the number needed to treat (NNT), it is about 50 patients/3 years. Hypertensive patients are followed for longer than 3 years and if we follow the patients for 30 years, NNT is 5 patients/30 years and it is an acceptable number. However, in this trial, when we calculate NNT in patients with chronic kidney disease (CKD) it is about 1,300 patients/3 years and 130 patients/30 years which is not readily acceptable. This data implies the importance of early detection of risk factors, prevention of development of risk factors, and intensive treatment or risks when the patients have comorbidities. So that health checkups are a good way to screen risks and prevention by educating the participants.

Objective

In this review, we summarized Japanese system for public health checkups and issues to be improved to obtain maximal effect in preventing NCDs.

Historical background

The idea of health checkups was first reported in 1861 by Dr. Horace Dobell (3) and in 1926 G. Scott Willamson and Innes Hope Pearse launched a membership health check service for workers and their families (Pioneer Health Centre). It ensures the members to have access to a doctor (4). In Japan, free regular health checkups started in 1911 to prevent tuberculosis, dysentery, and other communicable disease among factory workers (5). Later on, blood pressure measurements, and urinalysis [1972], electrocardiogram (ECGs), hemoglobin (Hb), aspartate aminotransferase (AST), alanine aminotransferase (ALT), cholesterol [1989], and other exams are included, and finally in 1998 blood glucose is added to this system. By adding these examinations, these checkup systems can be used to screen for risks of cardiovascular diseases and cancers. Besides these free checkups, we developed the "human dock" in the 1950s, which is not covered by insurance but can be checked for multiple risks, and in some occasions, gastric fiber, computed tomography (CT) scan, magnetic resonance imaging (MRI), and ultrasound exam can be done upon the participants' request.

Until 1964 when automated multiphasic health testing and services were available in California, all the tests were done manually and thereafter automated analysis on blood samples, urine samples, and imaging were available, and checkup could be done in one or two days. These rapid checkups accelerated the number of participants and a lot of companies support the fee for "human dock" of not only their employees but also family members. According to the National Living Infrastructure Survey 2022, about 73% of males and 66% of females above 20 years old undergo annual health checkups in Japan (6).

After the development of the health checkup system (*Table 1*) and human dock system, in Japan dramatic decline in the mortality rate of stroke, that is mainly hemorrhagic stroke, is observed (*Figure 1*) (7). It is not solely due to the detection of hypertension, diabetes, or hypercholesterolemia but the development of effective treatment, changes in dietary habits (reduction of salt intake) and other factors. In contrast, cancers, congestive heart failure, and ischemic heart disease are still increasing. The high mortality rate for cancer is partly due to the small number of participants in cancer health checkups in Japan which is not for free and optional examination. In 2022 (8), the highest number of participants was lung cancer screening by chest X-ray (male 53% and female 46%) and the lowest one was colon cancer by fecal occult blood (male 44% and female 38%).

Accuracy control in laboratory exams in health checkups

Accuracy control in laboratory examination is a critical aspect of ensuring the reliability and validity of laboratory test results. Accurate and precise laboratory test results are essential for making informed clinical decisions, diagnosing medical conditions, monitoring patient health, and conducting medical research. Accredited laboratories either commercial or in hospital follow quality assurance (QA) programs including both internal quality control (IQC) or external quality assessment (EQA), calibrations, standardization, validation, and verification. In addition, documentation that enables tracking the record, training of staff, root cause analysis to implement corrective and preventive action, and continuous improvement are required. Most of the facilities of health checkups or human-dock in Japan follow this QA but some do not. We should inform the status of the laboratory in the facility to participants.

Preanalytical errors

Preanalytical error is mistakes or issues that occur in the laboratory testing process before the actual analysis of a patient's specimen takes place. These errors can

Table 1 Japanese health basic checkup system

Age	Contents
18 months old and 3 years old (mandatory)	Physical measurement, nutritional status, oral health, physical and mental developmental problems, vaccination history
	At age of 3 years, vision, ear, nose and throat examination
6–22 years old (mandatory, if they go to school)	Height and weight
	Nutritional status
	General physical exam including oral check by dentist
	Urinalysis
<39 years old (mandatory for employees)	Height, weight, abdominal circumference, vision, hearing
	Chest X-ray, sputum test
	Blood pressure
	Complete blood count
	AST, ALT, γ-GTP
	Lipid profile (HDL cholesterol, LDL cholesterol, triglyceride)
	Glucose
	Urinalysis
	ECG
40–74 years old (mandatory)	In addition to <39 years old, optional exam of creatinine, HbA1c and fundoscopy
≥75 years old (voluntary)	In addition to <39 years old, uric acid, creatinine, HbA1c and fundoscopy
At any age optional test for cancer screening	Fecal occult blood
	Chest X-ray
	Gastric fiber

AST, aspartate aminotransferase; ALT, alanine aminotransferase; γ-GTP, gamma-glutamyl transpeptidase; HDL, high-density lipoprotein; LDL, low-density lipoprotein; ECG, electrocardiography; HbA1c, hemoglobin A1c.

significantly impact the accuracy and reliability of test results. Preanalytical errors can occur at various stages. Among them, specimen collection includes several factors such as mislabeling, inadequate sample volume, hemolysis, contamination, incorrect anticoagulant and patient preparation. In health checkup facilities, when they do not have their own laboratory they transport samples to commercial laboratories and the condition of transportation (temperature, prevention of degradation and contamination) is also an issue. We sometimes experience preanalytical errors in urine examination by mislabeling. A bar-code and patient name labeled sampling cup is handed to each participant and when a participant visit our facility together with his/her partner, they sometimes mix up sampling cups. By examining urinary sediment, we can detect the mix-ups, i.e., the "male" labeled urine shows epithelial cells from the vagina and we know the sample is from his wife.

Analytical errors

Analytical errors refer to mistakes or issues that occur during the actual analysis or testing of a participant's specimen in a laboratory. These errors also can lead to incorrect or imprecise test results. Analytical errors can arise from various sources and instrumentation and equipment are the most common cause those include malfunctioning, calibration errors, contamination of instruments, inaccurate preparation or handling of reagents and chemicals, and quality control (QC) or QA errors. In addition, interferences by substances in the sample or condition of

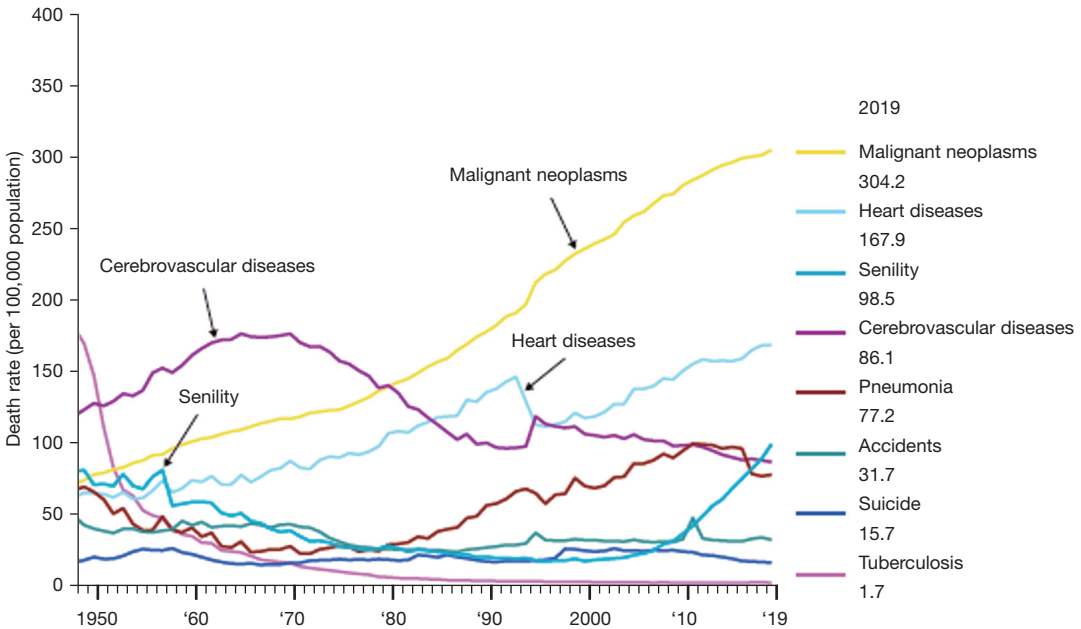

Figure 1 Trends in death rates from leading causes of death, 1950–2019. Modified from the study (7). Mortality due to cerebrovascular diseases declined from 1970s. It is partly due to blood pressure is routinely measured in health checkups since 1972 and blood pressure control rate increased in Japan. In Japan thiazide diuretics (hydrochlorothiazide) is first launched in 1959 but the screening of hypertension was not widely done until 1972.

samples such as pH, sample volume, and others can interfere with the accuracy of the assay. Most of the analytical methods are designed to minimize interference, however, it can still be observed. Urinary protein and albumin are good biomarkers for detecting early stages of CKD and are incorporated with CKD grading by guideline (9). The study shows the urinary albumin level differs from testing kit to kit when comparing liquid chromatography/mass spectrometry (LC/MS) data (10). Although all the kits are accredited, these serious problems remain. We surveyed the urinary protein level and compared the results by dipstick and quantitative evaluation (11). Around 41,000 samples from negative to 4+ in urinary protein by dipstick. It is well known that alkaline urine is a major cause of false positive proteinuria, and in this study, we clarified that a lower specific gravity (SG) sample causes false negative result. In addition, there were sexual differences in SG of urine and females was lower in SG and the sensitivity in trace positive for proteinuria cases was lower in females.

Low-density lipoprotein cholesterol (LDL-C) is a well-acknowledged risk factor for atherosclerosis and it is pivotal to measure LDL-C accurately. These days we use calculation methods and automated direct measurement in health checkups. When triglyceride levels is lower than 400 mg/dL, the Friedwald equation is applicable but higher than 400 mg/dL, there are several methods such as the extended Martin/Hopkins equation or Sampson equation up to 800 mg/dL of triglyceride (12). It is reported that the Martin/Hopkins equation is superior to the Sampson equation (13). It is still required to establish widely and accurately applicable calculation methods. To measure LDL-C directly we have to consider the interference by Lp(a)-C which is composed of apolipoprotein (a) covalently bound to the apolipoprotein B-100 moiety of LDL. The elimination method of Lp(a)-C varies from reagent to reagent and indeed direct measurement kit does not meet the standardization in Japan (14).

What is our next step to reduce cancer and cardiac mortality by utilizing a health checkup and human dock system?

Reducing cancer and cardiac mortality through health checkups and human dock systems involves a multi-faceted approach that integrates early detection, risk assessment, and preventive measures. As I mentioned above, the

number of participants is still low for cancer checkups and population and personalized approaches to increase it. We already have accumulated data and they should be analyzed to assess an individual's risk and provide personalized health recommendations and interventions based upon the individual's risk profile. To promote a personalized approach, genetic testing both in DNA mutation and epigenetic modification can be applied, however, in health checkups, the tests should be minimally invasive, and somatic mutations cannot be detected unless we biopsy certain organs which is highly invasive. Epigenetic changes also require biopsy, however, kidney diseases can be detected by evaluating DNA methylation in urine sediment cell (15), and also circulating microRNA can be a future candidate for biomarkers to detect disease conditions.

Conclusions

NCD is a big burden on our society especially in low-income societies. Income and NCD relations could be due to the cost of health care, exposure to environmental risks such as smoking, high consumption of alcohol. Management of NCDs includes detecting, screening, and treating these diseases, reducing modifiable risk factors. High-impact essential NCD interventions can be delivered through a regular health checkup to strengthen early detection and timely treatment.

Acknowledgments

Funding: None.

Footnote

Peer Review File: Available at https://jlpm.amegroups.org/article/view/10.21037/jlpm-23-97/prf

Conflicts of Interest: Both authors have completed the ICMJE uniform disclosure form (available at https://jlpm.amegroups.org/article/view/10.21037/jlpm-23-97/coif). T.S. serves as the unpaid Associate Editor-in-Chief of *Journal of Laboratory and Precision Medicine* from September 2023 to August 2025. The other author has no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

References

1. World Health Organization. Noncommunicable diseases [cited 2024 3/26]. Available online: https://www.who.int/news-room/fact-sheets/detail/noncommunicable-diseases
2. SPRINT Research Group, Lewis CE, Fine LJ, et al. Final Report of a Trial of Intensive versus Standard Blood-Pressure Control. N Engl J Med 2021;384:1921-30.
3. Dobell H. Lectures on the Germs and Vestiges of Disease : and on the Prevention of the Invasion and Fatality of Disease by Periodical Examinations. London: J. Churchill; 1861.
4. Pearse IH, Crocker LM. The Peckham Experiment: A Study in The Living Structure of Society. London: George Allen and Unwin Ltd.; 1943.
5. Tatara K. Development of public health system since the incunabula age until today. Nihon Koshu Eisei Zasshi 2018;65:255-65.
6. Annual Changes in Death Rate for Leading Causes of Death. Figure 6 [cited 2024 Apr 12]. Available online: https://www.mhlw.go.jp/toukei/saikin/hw/jinkou/geppo/nengai19/xls/R1zu.xlsx
7. Director-General for Statistics, Information Policy and Industrial Relations, Ministry of Health, Labour and Welfare. Vital Statistics of Japan 2019. Japan: Japanese Government; 2020.
8. 2022 Edition Annual Health, Labour and Welfare Report: Ministry of Health, Labour and Welfare, Japan; 2022 [cited 2024 Mar 26]. Available online: https://www.mhlw.go.jp/toukei/saikin/hw/jinkou/geppo/nengai19/index.html
9. Stevens PE, Levin A; Kidney Disease: Improving Global Outcomes Chronic Kidney Disease Guideline Development Work Group Members. Evaluation and management of chronic kidney disease: synopsis of the

kidney disease: improving global outcomes 2012 clinical practice guideline. Ann Intern Med 2013;158:825-30.
10. Bachmann LM, Nilsson G, Bruns DE, et al. State of the art for measurement of urine albumin: comparison of routine measurement procedures to isotope dilution tandem mass spectrometry. Clin Chem 2014;60:471-80.
11. Kojima C, Umemura H, Shimosawa T, et al. Sex differences in the evaluation of proteinuria using the urine dipstick test. Front Med (Lausanne) 2023;10:1148698.
12. Islam SMT, Osa-Andrews B, Jones PM, et al. Methods of Low-Density Lipoprotein-Cholesterol Measurement: Analytical and Clinical Applications. EJIFCC 2022;33:282-94.
13. Sajja A, Park J, Sathiyakumar V, et al. Comparison of Methods to Estimate Low-Density Lipoprotein Cholesterol in Patients With High Triglyceride Levels. JAMA Netw Open 2021;4:e2128817.
14. Nakamura M, Koyama I, Iso H, et al. Measurement performance of reagent manufacturers by Centers for Disease Control and Prevention/Cholesterol Reference Method Laboratory Network lipid standardization specified for metabolic syndrome-focused health checkups program in Japan. J Atheroscler Thromb 2009;16:756-63.
15. Marumo T, Hoshino J, Kawarazaki W, et al. Methylation pattern of urinary DNA as a marker of kidney function decline in diabetes. BMJ Open Diabetes Res Care 2020;8:e001501.

doi: 10.21037/jlpm-23-97
Cite this article as: Shimosawa T, Kojima C. The issues in annual health checkups (human dock system) in Japan to prevent non-communicable diseases. J Lab Precis Med 2024.