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Review Article

Progress of public health policy regarding global infectious diseases over the past decade in Japan

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ABSTRACT

This article aims to examine progress of public health policy regarding global infectious diseases over the past decade in Japan.

A narrative review was conducted, overviewing items of the Infectious Disease Committee and the Tuberculosis Committee of the Ministry of Health, Labour and Welfare between 2010 and 2019.

The mean value of items discussed in each meeting were 9.7 items. Among these items, these committees have discussed about countermeasures in terms of reduced burden of indigenous infectious diseases such as measles, rubella and pertussis, and increased risk of imported infectious diseases such as Ebola virus disease, Middle East Respiratory Syndrome, plague, avian influenza, pandemic influenza and tuberculosis.

These changes regarding infectious diseases lead to loss of target population, difficulty of early detection, and market failure in old and new antibiotics and others, which requires challenge to scattered at-risk targets, effort to training and awareness, and creation of novel public health policy for research and development as well as production and supply. Over the past decade, public health policy regarding global infectious diseases have been one of the key targets under the triangle of global infectious disease, and recent experience of Coronavirus disease 2019 will further prioritize it in Japan. However, the principles of public health policy are globally vulnerable in the Post-Corona era, which can lead to the collapse of democratic way. To combat global infectious diseases without going off the road, we need to learn about the past history of public health policy.

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1. Introduction

Coronavirus disease 2019 (COVID-19) has changed public health policy and its principles, globally. In the Post-Corona era, travel restriction is easily adopted against rule of the 2005 International Health Regulations (IHR), and lockdown is also being implemented in some countries. Digital contact tracing applications using personal data such as Global Positioning System (GPS) have been introduced for systematic contact tracing beyond concern about individual privacy, which democratic societies would normally consider to be unacceptably high. These countermeasures against COVID-19 have damaged the principles as well as the economy in each country, and thus global leaders are currently facing difficulties in implementing countermeasures against COVID-19 in the context of global infectious disease, public health policy and the economy.

From Pre-Corona era, global infectious diseases have been one of the key targets in public health policy in the Government of Japan. The Ministry of Health, Labour and Welfare (MHLW) has established a new organization, named Global Infectious Disease Control Office on October 1st, 2017, to focus on prevention and control of global infectious diseases by centralizing relevant responsibilities. Cabinet secretariat has also established Coordination Office of Measures on Emerging Infectious Disease on September 11th, 2017, to coordinate relevant policies regarding global infectious diseases in the Government of Japan under the Prime Minister. Through the coordination mechanism of cabinet, relevant ministers have adopted the Basic Guidelines for Strengthening Measures on Emerging Infectious Diseases, to promote relevant countermeasures against global infectious diseases that threaten the global security in collaboration with relevant ministries.

In a historical perspective, the burden of indigenous infectious diseases has dramatically decreased in Japan over the past century. For example, the number of deaths due to tuberculosis decreased from 171 thousands in 1943 to 2 thousands in 2018. Indigenous malaria was eradicated in 1961 and we have no cases of diphtheria after 1999 in Japan. The national vaccination program has reduced the number of measles cases, leading to verification of measles elimination in Japan.

On the other hands, the risk of imported infectious diseases is increasing due to the increase in foreign visitors to Japan and Japanese tourists going abroad. In line with the Tourism Nation Promotion Basic Plan, the number of foreign visitors to Japan increased from 8 million in 2008 to 31 million in 2018. In 2014, we have outbreak of dengue in Tokyo, which was the first outbreak after 1940s. There are no cases of Ebola virus disease in Japan, yet, but there are some suspicious but denied cases, which received a great deal of attention from mass media.

Outbreaks of imported infectious disease tend to be political issues primarily through fear to the infectious diseases. The outbreak of dengue in Tokyo has received a great deal of attention from the Japanese, because it was an infectious disease unfamiliar to the Japanese. In South Korea, the outbreak of Middle East Respiratory Syndrome (MERS) has caused political and financial cost beyond the health crisis. These experiences have helped the Government of Japan strengthen its public health policy regarding global infectious diseases under a multi-sectoral framework.

The MHLW is responsible for due process of the Act on the Prevention of Infectious Diseases and Medical Care for Patients with Infectious Diseases, namely the Infectious Diseases Control Act, which is at the core of the legal framework for prevention and control of infectious disease in Japan. From the perspective of prevention and control of global infectious diseases, the MHLW remains a major player in the Government of Japan, and the Infectious Disease Committee and the Tuberculosis Committee under the Health and Science Council of the MHLW advise on the relevant public health policy from an academic perspective. Therefore, it is important to review discussions in these committees in order to analyze public health policy regarding global infectious diseases.

I conducted a narrative review of public health policy regarding global infectious diseases over the past decade in Japan, examining progress of public health policy in terms of reduced burden of indigenous infectious diseases and increased risk of imported infectious diseases.

2. A narrative review of public health policy

A narrative review of public health policy regarding global infectious diseases over the past decade in Japan was conducted, overviewing items of the Infectious Disease Committee and the Tuberculosis Committee of the MHLW between 2010 and 2019. Although the framework of the Health and Science Council regarding infectious diseases was reconstructed on April 1st, 2013, items in both of former and current committees were included in this analysis. A total of 562 items was identified in 58 meetings, including 414 items for 39 meetings of the Infectious Disease Committee and 148 items for 19 meetings of the Tuberculosis Committee between 2010 and 2019.

Informed consent is not needed in this study, because I used publicly available data from website of the MHLW.

The t-test was used to examine differences in mean values of items in each meeting by the Infectious Disease Committee and the Tuberculosis Committee.

All statistical tests were 2-sided and conducted using SAS, version 9.4 (SAS Institute, Cary, NC, USA). P values below 0.05 were considered significant.

Between 2010 and 2019, the mean value and 95% confidence intervals (95%CIs) of items discussed in each meeting were 9.7 items (8.1–11.3). The Infectious Disease Committee have discussed 10.6 items (8.3–12.9) in each meeting, whereas the Tuberculosis Committee have discussed 7.8 items (6.6–9.0) (P for difference was 0.04). Among these items, these committees have discussed about countermeasures against reduced burden of indigenous infectious diseases such as measles, rubella and pertussis and increased risk of imported infectious diseases such as Ebola virus disease, MERS, plague, avian influenza, pandemic influenza and tuberculosis.

In the 11th meeting of the former Infectious Disease Committee on October 15th, 2012, the amendment of Preventive guideline of Specific infectious diseases of measles was discussed, which led to...
requesting medical doctors to file a notification with the prefectural governor via the chief of the nearest public health center within 24 h from April 1st, 2013. This amendment aimed to immediate containment of measles outbreaks as well as verification of elimination, after the additional national vaccination program for persons aged 13 years old and persons aged 18 years old between 2008 fiscal year and 2012 fiscal year. This request of immediate notification was not regulated by the Infectious Diseases Control Act, in which medical doctors had to file a notification within seven days in this time, and therefore, after discussion between the 2nd meeting (January 30th, 2014) and the 5th meeting (June 20th, 2014) of the current Infectious Disease Committee, a ministerial ordinance was revised to make measles the infectious disease that medical doctors who has diagnosed must file a notification ... immediately in notifiable disease surveillance under the Infectious Diseases Control Act from May 21st, 2015. In the 9th meeting of the Infectious Disease Committee on April 2nd, 2015, the secretariat reported the measles elimination verification by Western Pacific Regional Office of World Health Organization on March 27th, 2015, but outbreaks are still occurring such as in Kansai international airport (reported in the 19th meeting on October 17th, 2016) and Okinawa prefecture (reported in the 24th meeting on April 26th, 2016). These outbreaks are thought to be triggered by an imported case of measles.

Similar to measles control, we also had some of discussions about challenges for rubella control. After discussion in the 21st meeting of the Infectious Disease Committee on June 19th, 2017, rubella also became the infectious disease that medical doctors must file a notification ... immediately from January 1st, 2018, aiming to immediate containment and verification of elimination. In Japan, a national vaccination program of rubella for Junior high school girls was started in August 1977, and then in April 1995, the program for boys and girls in addition to infants was started. Gender difference in the history of the national vaccination program have led to gender difference of herd immunity in middle-aged population. Responding to a large outbreak of rubella from 2018, reported in the 26th meeting of the Infectious Disease Committee on September 27th, 2018, an additional national vaccination program was launched for these middle-aged males from 2019.

The pertussis was designated as the infectious disease that medical doctors who has diagnosed must file a notification ... within seven days in notifiable disease surveillance under the Infectious Disease Control Act from January 1st, 2018 after the discussion in the 21st meeting of the Infectious Disease Committee on June 19th, 2017, to detect all of pertussis cases in Japan. Before this amendment, pertussis cases were reported from hospitals participating in sentinel surveillance. From reported cases by the sentinel surveillance, it was estimated to have approximately 10–56 thousands cases annually in Japan after the successful national vaccination program for infants. However, the reported cases may be biased mainly in adults, because the hospitals participating in the sentinel surveillance were mainly from pediatric sentinel sites. Aiming to completely evaluate the effect of national vaccination program for pertussis, pertussis was designated as the infectious disease in notifiable disease surveillance.

In the 23rd meeting on December 15th, 2017, the Infectious Disease Committee discussed designation of acute flaccid paralysis (AFP) in the Infectious Disease Control Act. Although AFP is well known as caused by acute poliomyelitis, ongoing to be eradication in the world, we have an outbreak of AFP in 2015 in Japan, which is thought to be caused by enterovirus D68. Aiming to complete eradication of acute poliomyelitis as a primary reason, AFP was designated as the infectious disease that medical doctors who has diagnosed must file a notification ... within seven days for persons under 15 years old in notifiable disease surveillance from May 1st, 2018.

In the 33rd meeting on July 17th, 2019 and the 34th meeting on November 28th, 2019, the Infectious Disease Committee have discussed countermeasures against shortage of Cefazolin. Relative reduction in economic burden of infectious diseases brought withdraw from domestic production of antibiotics by pharmaceutical companies inside Japan, and the shortage of Cefazolin in March 2019 led to postponement of surgery in some of hospitals.

Some of countermeasures against antimicrobial resistance (AMR) was also discussed especially in area of those for appropriate use of antibiotics such as publication of Manual of Antimicrobial Stewardship, which was discussed in the 20th meeting on March 27th, 2017 and the 34th meeting on November 28th, 2019 of the Infectious Disease Committee. In the 21st meeting on June 19th, 2017, the Infectious Disease Committee decided to amend Guidelines on Prevention of Specified Infectious Diseases for Sexually transmitted diseases, including indication of importance of facilitating the development of antibiotics, which aimed at facilitating the development of injections of Benzylpenicillin benzathine hydrate for treatment of syphilis.

The Infectious Disease Committee also has discussed about risk of global infectious diseases, responding to outbreaks of infectious diseases such as Ebola virus disease, Marburg virus disease, MERS, plague, Zika virus disease and avian influenza. In the 13th Infectious Disease Committee, the secretariat reported release of director’s notification to medical doctors and quarantine office for Ebola virus disease from the MHLW (reported in the 6th, 17th, 23rd, 25th, 26th, 27th, and 33rd meeting between October 8th, 2014 and November 28th, 2019), MERS (reported in the 4th,11th, 12th, 21st and 26th meeting between May 29th, 2014 and September 27th, 2018) and plague (reported in the 23rd meeting on July 17th, 2019).

Regarding diagnosis, the National Institute of Infectious Diseases (NIID) started operation of Biosafety level 4 (BSL4) facility for highly pathogenic virus such as Ebola virus disease by import of these virus on September 27th, 2019, reported in the 34th meeting on November 28th, 2019. In the 10th meeting of the Infectious Disease Committee on May 29th, 2015, secretariat has reported the start of the Infectious Disease Emergency Specialist (IDES) training program for human resource development, following the largest outbreak of Ebola virus disease in West Africa.

Regarding treatment of these global infectious diseases, Designated Medical Institution for Class I Infectious Diseases based on the Infectious Diseases Control Act was equipped in all prefectures after the designation by Miyagi prefecture on May 1st, 2018, which allow us to treat patients of Ebola virus disease in all prefectures in the perspectives of facility. On the other hand, it was pointed out that human resource development was also necessary in these hospitals by recommendation from Minister of Internal Affairs and Communications, reported in the 24th meeting of the Infectious Disease Committee on April 26th, 2018. Joint External Evaluation (JEE) under IHR also pointed out the importance of improvement in capacity of risk assessment, reported in the 31st meeting of the Infectious Disease Committee on January 28th, 2019.

In 2009, we faced pandemic influenza, which request us to revise the countermeasures. In perspectives of legal framework, the Act on Special Measures for Pandemic Influenza and New Infectious Diseases Preparedness and Response was newly promulgated in May 11th, 2012, and the Infectious Disease Committee discussed some of countermeasures such as national vaccination programs for pandemic influenza (the 11th, 14th, 19th, 21st, 25th, 31st and 33rd meeting between July 8th, 2015 and July 17th, 2019), stockpile of anti-influenza agents (the 12th, 14th, 20th, 21st, 24th, and 33rd meeting between September 18th, 2015 and July 17th, 2019), and amendment of the National Action Plan for Pandemic Influenza and New Infectious Diseases and the National Guideline for Pandemic Influenza and New Infectious Diseases (the 10th meeting of the
former Infectious Disease Committee and the 1st, 14th and 34th meeting of the current Infectious Disease Committee between October 17th 2011 and November 28th, 2019) as well as monitoring avian influenza cases as the potential pandemic influenza.

For preparedness to the Olympic and Paralympic Games Tokyo 2020, the Sentinel Surveillance of Suspected Diseases under the Infectious Diseases Control Act was amended for early detection of unknown emerging infectious diseases after discussion in the 26th and 27th meeting of the Infectious Disease Committee on September 27th, 2018 and November 29th, 2018. The Sentinel Surveillance of Suspected Diseases was established on April 1st, 2008, aiming to early detection of bioterrorism by widely reporting patients with fever and respiratory symptom or rash from hospitals participating in this sentinel surveillance. However, this sentinel surveillance required a great deal of effort by medical doctors to report suspected cases of infectious disease, making it difficult to detect unusual cases of infectious disease. In the amended sentinel surveillance, medical doctors could report the probable cases of infectious disease with fever and respiratory symptom or rash or blister that medical doctors could not diagnose as specific infectious disease, to receive the support of diagnosis by detailed examination of NIID and prefecture’s Public Health Institute.

In the 6th meeting of the Infectious Disease Committee on October 8th, 2014, NIID reported a large outbreak of dengue in Yoyogi park and other places. The imported dengue cases have been reported before the 2014’s outbreak, but it was the first outbreak in Japan since the 1940s. From the 6th meeting to the 10th meeting, the Infectious Disease Committee discussed about countermeasures against mosquito-borne infectious diseases such as dengue, leading to publication of Guidelines on Prevention of Specified Infectious Diseases for Mosquito-borne infection on April 28th, 2015.

Countermeasures against Zika virus diseases were also discussed against threat to the outbreak, in response to the declaration of Public Health Emergency of International Concern (PHEIC) by World Health Organization (WHO) on February 1st, 2016. Zika virus diseases became a global agenda before the Olympic and Paralympic Games Rio 2016. Against Zika virus disease, the Infectious Disease Committee discussed about an amendment of cabinet order of the Infectious diseases Control Act in the 15th meeting on February 4th, 2016. Based on this discussion, Zika virus disease was designated as the 4 class infectious disease under the Infectious Diseases Control Act and the quarantine infectious disease under the Quarantine Act on February 15th, 2016, to conduct vector control and quarantine measures.

In the 9th meeting of the Tuberculosis Committee on February 26th, 2018, new screening measure of tuberculosis was discussed to detect persons with tuberculosis coming from foreign countries before entrance into Japan from six countries with high tuberculosis burden, because the persons with tuberculosis are mainly born abroad among young population. For example, approximately 60% of newly diagnosed tuberculosis was occupied by persons born abroad for aged 20—29 years old. Although persons without Japanese nationality having tuberculosis were not permitted to enter the board under the Immigration Control and Refugee Recognition Act, we have no systematic measure for identification of persons with tuberculosis in the immigration.

For treatment of tuberculosis, the amendment of guideline for tuberculosis treatment was discussed in the meeting of the Tuberculosis Committee. In Japan, patients with tuberculosis are able to receive the treatment by only 5% of co-payment for outpatients under the Infectious Diseases Control Act. We introduced Delamanid (discussed in the 4th meeting of the tuberculosis committee on July 23rd, 2014), Levofloxacin (discussed in the 6th meeting of the tuberculosis committee on September 25th, 2015), and Bedaquiline (discussed in the 9th meeting on February 28th, 2018) as antibiotic of tuberculosis in the list of medicine for tuberculosis treatment under the Infectious Diseases Control Act after the discussion in the Tuberculosis Committee.

3. Future aspects

Aiming to examine progress of public health policy regarding global infectious diseases over the past decade in Japan, I reviewed discussions in the relevant committees of the MHLW in terms of reduced burden of indigenous infectious diseases and increased risk of imported infectious diseases.

3.1. Target setting

From the perspective of reduced burden of indigenous infectious diseases, the Infectious Disease Committee have discussed about some of countermeasures after reduction of vaccine-preventable diseases such as measles, rubella and pertussis, which led to an amendment of regulation for enforcement of notification by medical doctors under the Infectious Diseases Control Act [32—34]. After an additional national vaccination program, measles elimination was declared in 2015, and rubella elimination program is still ongoing by revise of reporting system, an additional national vaccination program and others [34—36], although outbreaks of these infectious diseases continue to occur in Japan by imported cases of measles and rubella adding to indigenous cases of rubella [37—41]. Public health policy of infectious diseases aims to reduce these infectious diseases, but reduced burden of indigenous infectious diseases requires further challenge of public health policy including complete vaccination coverage and immediate containment through reporting system for elimination.

Regarding measles outbreaks, we are facing difficulties regarding control of infections in Japanese population, who has high (i.e. >95%) but not perfect (i.e. 100%) herd immunity. Currently, about 95% of the Japanese population have no diagnostic experience in Japan. For early detection of these susceptible individuals as a target population, because they are scattered at-risk targets, who are not in specific mass of populations.

The loss of target population requires challenge to scattered at-risk targets by novel approach to properly identify and to intervene susceptible individuals as scattered at-risk targets despite nationwide measles elimination, due to high but not perfect herd immunity.

3.2. Early detection

Reduced burden of indigenous infectious disease such as measles, rubella and acute poliomyelitis may also lead to difficulty of early detection due to lack of diagnostic experience in clinical setting as well as reduced prior probability. Regarding Ebola virus disease as imported infectious disease, most of medical doctors have no diagnostic experience in Japan. For early detection of these infectious diseases, we need to firstly build core of selected medical doctors by training program. In terms of capacity building, some of programs have been implemented such as study tours to foreign countries where outbreaks occurred, dispatch of infectious diseases control team in the Japan Disaster Relief Team (JDR) and the IDES program [14,42].

To rise the capacity of early detection in overall Japan, timely awareness to medical doctors is also important, because all of
medical doctors have possibility to examine undiagnosed patients with global infectious disease. In terms of awareness, the MHLW released Standard of Disclosure regarding Information of Infectious Diseases for timely and adequate disclosure after detection of patient with an infectious disease such as Ebola virus disease [43], which will help medical doctors to diagnose the patients by increasing prior probability. The revise of reporting system in measles and rubella also lead to awareness for medical doctors in the surrounding area immediately after detection of the patients. We started new reporting system of APP as syndrome around acute poliomyelitis [44,45], which will lead to early detection of acute poliomyelitis cases by medical doctors, whereas few medical doctors currently have diagnostic experience of acute poliomyelitis. JEE pointed out the importance of strengthening the risk communication in Japan [46], which also lead to the early detection by patients themselves.

In the twenty century, travel time around the world had been shortened [47], which makes easy entry into a country by patients with global infectious disease which happens on the other side of the world. This requires early detection of global infectious diseases in clinical setting as well as in entry point of Japan, leading to establishment of Designated Medical Institution for Class I Infectious Diseases in all of prefectures for accumulation of clinical experience and operation of BSL-4 laboratory for construction of laboratory test system of highly pathogenic virus [14,48]. An amendment of the Sentinel Surveillance of Suspected Diseases would also help us to detect global infectious diseases by detailed examination. Regarding COVID-19, the first patient in Japan was detected by the amended sentinel surveillance [49].

For early detection, we need further effort to training and awareness in clinical setting in addition to construction of laboratory test system.

3.3. Market failure

Reduced burden of infectious diseases leads to shortage of old antibiotics, through reduced sales of antibiotics and overseas dependence of supply chain of production capacity [50–52]. In Japan as well as other developed countries, the market is no longer viable for research and development as well as production and supply of antibiotics regarding infectious diseases, and the G20 summit as well as the G7 summit led by the Government of Japan call for promoting the introduction of pull incentives [53]. However, due to relative reduction in the economic burden of infectious diseases, pharmaceutical companies have withdrawn from domestic production of old antibiotics in the first place [50], despite their significant historical contribution to research and development of antibiotics in Japan. Some of countermeasures against AMR have been implemented, especially in the area of those for appropriate use of antibiotics such as the Manual of Antimicrobial Stewardship [53–56], to prevent future crises of antimicrobial shortages. However, this time, the crisis in clinical practice due to shortage of cefazolin clarified that fragile production and supply of antibiotics due to market failure is not a future crisis but a current crisis.

Discussions mentioned above showed countermeasures against health crisis, but research and development of new medicine and new devices were not mentioned well, which leads to supply of high quality of diagnosis and treatment of infectious diseases. We have few discussions about research and development in the Infectious Disease Committee and the Tuberculosis Committee, because these committee discuss mainly about topics related to due process regarding to the Infectious Diseases Control Act. In Japan, some of researches have been conducted for prevention, diagnosis and treatment of Ebola virus disease such as vaccine [57], rapid diagnosis test using immunochromatography or reverse transcription-loop-mediated isothermal amplification (RT-LAMP) assay coupled with a portable device [58,59] and Faviapiravir [60]. Although these researches were partially supported by research grant from Japan Agency for Medical Research and Development (AMED) funded by the MHLW and the other relevant ministries, we have had few discussions about these topics except in the Public-Private Partnership Conference for Infectious Disease Control in Developing Countries under Cabinet Secretariat.

To promote public health policy regarding global infectious diseases beyond the market failure, we need to create novel public health policy for research and development as well as production and supply of antimicrobials, vaccine and rapid diagnosis test.

3.4. Triangle of global infectious disease

We are implementing a public health policy with the aim of controlling the infectious disease. Because some of global infectious diseases have a significant impact on the economy through direct and indirect damage to social function due to death or hospitalization of essential workers and psychosocial state due to fear to the infectious disease, public health policy regarding global infectious diseases is sometimes prioritized as a political agenda. On the other hand, while increasing contact by accelerating the economy also increases infections, the public health policy easily damage the economy by curbing international traffic and domestic activity (i.e. adverse effects) as we experienced in countermeasures against Ebola virus disease [61] and COVID-19 [11]. Therefore, the triangle of global infectious disease, public health policy and the economy (figure) makes public health policy regarding global infectious diseases a political agenda that goes beyond health issues.

From a historical point of view, the harmonization between public health and international traffic have been a major agenda since International Sanitary Conference [62]. After a long history of one century and more, we have reached harmonization through the spontaneous information exchange and international confidence. In the Pre-Corona era, lockdown was unprecedented in current public health policy regarding infectious disease especially for developed countries, and thus we were surprised in the Wuhan lockdown. Some of countries have introduced digital contact tracing applications using personal data for systematic contact tracing, but we have concern about individual privacy, which democratic societies would normally consider to be unacceptably high [6–10]. Freedom of movement as well as right to privacy is the essential principles of human rights, and they will be also the principles of public health policy. We are currently facing a collapse of these principles in Post-Corona era.

4. Conclusion

In conclusion, this article reviewed discussions in the relevant committees in terms of reduced burden of indigenous infectious diseases and increased risk of imported infectious diseases, in order to examine progress of public health policy regarding global infectious diseases. The daily effects were lessened, but the relative impact of one case became greater. These changes regarding infectious diseases lead to loss of target population, difficulty of early detection, and market failure in old and new antibiotics and others, which requires challenge to scattered at-risk targets, effort to training and awareness, and creation of novel public health policy for research and development as well as production and supply. Over the past decade, public health policy regarding global infectious diseases have been of the key targets under the triangle of global infectious disease, and recent experience of COVID-19 will further prioritize it in Japan. However, principles of public health policy are globally vulnerable in the Post-Corona era, which can
lead to the collapse of democratic way. To combat global infectious diseases without going off the road, we need to learn about the past history of public health policy.

ICMJE statement

All authors meet the ICMJE authorship criteria.

Disclosures

I declare no competing interest.

An author contributed to the conception and design of the study, drafting the article or revising it critically for important intellectual content, and final approval of the version to be submitted.

Declaration of competing interest

The author has no conflicts of interest to declare.

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