

Basic Study on Scale-Free Networks and Targeted Antivirus Prophylaxis Supported by Information Communication Tools

Isao Nakajima, Seisa University, Japan

Kiyoshi Kurokawa, Health and Global Policy Institute, Japan

Seiji Morita, Tokai University School of Medicine, Japan

Yoshihide Nakagawa, Tokai University School of Medicine, Japan

ABSTRACT

With the aim of slowing the spread of infectious disease in the earliest phase of an outbreak, the authors performed visual simulations using scale-free networks focused on circumstances such as “normal” daily life, pandemic outbreaks, and the Fukushima nuclear accident following the Great East Japan Earthquake of 2011. Due to limitations associated with face-to-face contacts and delays in the timing of intake of iodine tablets, iodine preparations for protecting the thyroid gland could be taken effectively by only 5% of the population in the aftermath of the Fukushima nuclear accident. For targeted antivirus prophylaxis (TAP) to be more effective, timing of the distribution of anti-viral medication needs to be planned well in advance and instructions to “take it now!” must be communicated effectively in a timely manner. The results of this study suggest that information communication technology (e.g., pulse oximeters, mobile phones) can play an important role in managing TAP policies.

KEYWORDS

COVID-19, Pulmonary Edema, Pulse Oximeter, Scale-Free Network, Telemedicine

1. BACKGROUND

Under pandemic outbreak conditions, where many patients need to be treated at the same time, it is impossible for doctors to see, treat, and prescribe medication individually for each patient, or for pharmacists to provide medication counseling and explain precautions to each patient face-to-face. Thus, patients may be required take medication themselves without the benefit of treatment by doctor or counseling by a pharmacist. The act of taking medication at one's discretion without a doctor's diagnosis or pharmacist's face-to-face medication counseling is called self-medication. Targeted antivirus prophylaxis (TAP) is a policy that allows suitable antivirus tablets to be distributed to citizens before the outbreak of a pandemic. TAP involving self-medication during a pandemic is considered to be a medical policy that should be enacted in the future (Bolle et al., 2008; Evans, 2021; Malik et al., 2020; Nakajima, 2020; Nasir et al., 2020; Wegbom et al., 2020).

Self-medication has a long history, and it goes without saying that it involves substantial risks. What can be done to reduce these risks? In this manuscript, based on a survey on the distribution of an iodine preparation for self-medication immediately after the Fukushima nuclear power plant accident and a simulation of scale-free networks in a pandemic outbreak environment, we assumed a regular

DOI: 10.4018/IJEHMC.287587

This article published as an Open Access article distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0/>) which permits unrestricted use, distribution, and production in any medium, provided the author of the original work and original publication source are properly credited.

population topology and manipulated various factors involving information and communications technologies (ICTs; e.g., mobile phones, the Internet, broadcasting services) in order to identify problems and thus to reduce risks.

1.1 Definition

Here, TAP is defined as the advance distribution of antiviral drugs to citizens as a public health policy measure against a pandemic outbreak. Self-medication is defined as citizens purchasing medicines from pharmacies over the Internet, selling medicines over the Internet, or storing previously prescribed medicines and taking them at a later time at their own discretion. TAP is a policy for social disasters, and thus it closely resembles the distribution and administration of iodine preparations associated with nuclear power plant accidents, whereas self-medication has increased in recent years because the spread of the Internet has made it relatively easy to purchase drugs. TAP is also an indispensable social system in developing countries for citizens who cannot afford to visit a doctor. Needless to say, face-to-face consultations with doctors and pharmacists do not take place under TAP or under self-medication conditions.

1.2 Self-Medication

Self-medication has a long history. In Egypt, India, and China, it was common practice to decoct medicinal herbs to suit one's physical condition, and in Fijian festivals, *kina* (a kind of herb used to induce mass hypnosis) has historically been used as self-medication. As a rule, however, self-medication usually involves a fairly weak medicine with only mild effects.

Japan has had a unique system of selling medicines beginning 300 years ago in the Edo period. With the permission of the Edo shogunate, the Kaga clan (present-day Kanazawa) had a policy of selling medicines, and merchants in Toyama distributed "deployment medicines" throughout Japan, either on foot or on horseback. In modern times, this system involves visiting each household and distributing sets of household medicines, such as stomach and cold medicines, laxatives, and painkillers.

The concept of this business model, "use-first pay-later", which first appeared in Toyama, was unique in Japan. Each household paid a visiting merchant for the medicines used during the year, after which, the merchant would replenish the medicines, record the details of the visit in a notebook, and visit the home again one year later (2021).

With the implementation of universal health-care in Japan in 1961, the number of people visiting a doctor even for minor illnesses increased, which led to a new financial problem for the government: escalating national health-care costs. Against this background, Toyama's "use-first pay-later" system, which helped promote the idea of self-medication, that is, curing minor illnesses by oneself, can be seen to have contributed to lowering annual medical care costs by over 40 trillion yen.

1.3 Self-Medication for Coronavirus Disease 2019 (Covid-19) In Developing Countries

There is currently no effective treatment for COVID-19 (European Centre for Disease Prevention and Control, 2020; World Health Organization (WHO), 2020a; World Health Organization, 2020b), a disease caused by the novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). In Togo, Africa, four out of five people are reported to be practicing self-medication due to a shortage of physicians as well as for economic reasons (Sadio et al., 2020). Similarly, examples of self-medication practices in the setting of COVID-19 outbreaks have also been reported in Bangladesh. Although these reports have shown some efficacy, chloroquine/hydroxychloroquine, which is used in many cases, caused arrhythmia in some users, and there are also scattered reports that describe the potential dangers involved in the decision to use it (Kapoor et al., 2020; Rattanaumpawan et al., 2020).

Oseltamivir (trade name: Tamiflu), an antiviral oral drug with relatively few side effects, is extremely effective against the influenza virus. However, the fact that there are currently no highly

effective oral pharmaceuticals to treat COVID-19 is also a basis for objection to self-medication. The oral drug favipiravir (6-fluoro-3-hydroxy-2-pyrazinecarboxamide, trade name: Avigan) (Agrawal et al., 2020; Fujifilm, 2020; Joshi et al., 2021; Logical India, 2020; Shinoda et al., 2019), approved as an antiviral drug in Japan, is being considered by a government agency to combat COVID-19. Furthermore, China has manufactured a similar drug and distributed it free of charge to Chinese citizens and African countries. Favipiravir has not been distributed worldwide and its use as a self-medication is considered to be limited.

1.4 Stable Iodine Products for Use After Nuclear Power Plant Accidents

In the Chernobyl nuclear power plant accident, a low-power experiment was conducted using a containment vessel, which failed, causing an explosion that released large amounts of the radioactive isotope iodine-131 (^{131}I) into the atmosphere. When ^{131}I enters the human body, it accumulates in the thyroid gland and can cause thyroid cancer. To reduce this accumulation, it is necessary to saturate the thyroid gland with stable iodine immediately before exposure to ^{131}I . In Chernobyl, this iodine preparation was not distributed sufficiently, and many children developed thyroid cancer as a result.

During the Fukushima nuclear accident, the containment vessels were not cooled sufficiently, which led to substantial damage and the release of ^{131}I into the atmosphere in the form of aerosols. The amount of ^{131}I released was the second largest in history, after Chernobyl. Unnecessary exposure to radiation could have been avoided in both the Chernobyl and Fukushima accidents if the public had been briefed in advance on the risks of exposure and had adequate knowledge regarding its prevention, and if iodine tablets had been distributed to each household in the potential evacuation zone in advance of any accident.

The deployment of hand-delivered iodine preparations at the Fukushima nuclear power plant is still being investigated and will be discussed in the next section. In the Fukushima nuclear accident, stable iodine preparations were distributed to prevent thyroid exposure, but less than 5% of the residents (age 40 years and younger) took them at an effective time (Nakajima & Kurokawa, 2020).

2. METHODS

This paper does not discuss the advantages and disadvantages of self-medication for COVID-19, but rather how a disaster medical policy (e.g., TAP) should be carried out in the environment of a pandemic outbreak in the future to provide appropriate guidance for the intake of antiviral medications and to reduce associated risks using information and communications technology (ICT). Similar to iodine tablets which must be taken with suitable timing to prevent thyroid damage after a nuclear disaster, antiviral medication must be taken at the appropriate time in order to limit the spread of infectious disease during the earliest stage of pandemic. With this objective, we attempted to grasp conceptually the relationship between the period immediately after a pandemic outbreak and the Fukushima nuclear accident using a scale-free network method based on power-law distribution.

2.1 Power-Law Distribution

Power-law distribution is a statistical model. The most common power law satisfies a constant and is represented by:

$$f(x) = ax^k - O(ax^k) \quad (1)$$

where a is the constant, O is the Landau symbol, and k is the scaling exponent. This relationship means that if the scale of the independent variable of the function changes along with the scale function, the proportionality constant also changes, but the form of the function itself is preserved.

This relationship becomes more apparent when the logarithms of both variables are taken, and is linear if drawn on a log-log graph.

Scientific interest in power-law relations stems partly from the ease with which they are generated by certain general classes of mechanisms. The demonstration of a power-law relation in some data can point to specific kinds of mechanisms that might underlie the natural phenomenon in question and can indicate a deep connection with other seemingly unrelated systems. The ubiquity of power-law relations in physics is partly due to dimensional constraints, whereas in complex systems, power laws are often thought to be signatures of hierarchy or specific stochastic processes.

The power law in the region where x is 1 or more is called a Pareto distribution; its probability density function is expressed by Equation 2, the expected value is expressed by Equation 3, and the variance is expressed by Equation 4.

$$(a/b)/(x/b)^{a+1} \quad (2)$$

$$\frac{ab}{a-1} \text{ for } a > 1 \quad (3)$$

$$\frac{ab^2}{(a-2)(a-1)^2} \text{ for } a > 2 \quad (4)$$

2.2 Scale-Free Network Method

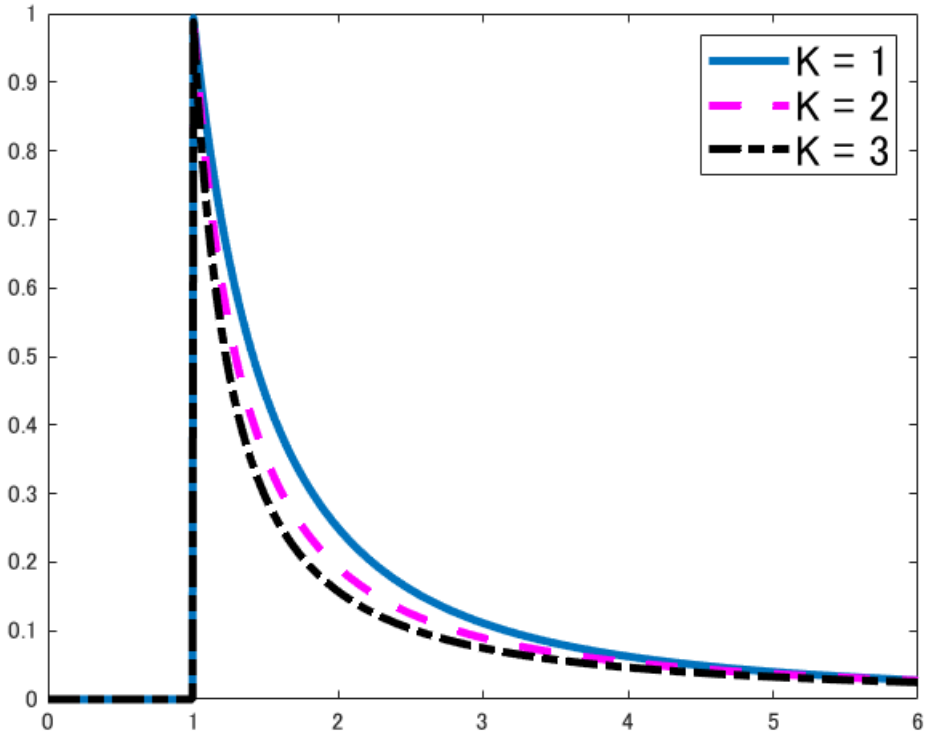
In 1999, Albert, Jeong, and Barabasi showed that the number of webpages increase in accordance with the number of hyperlinks based on a power law (Albert et al., 1999). When each web page is regarded as a node, the distribution of its bond order satisfies this relationship as follows:

$$P(k) \sim k^{-\nu} \quad (5)$$

where $P(k)$ is the distribution of the bond. Events in the natural world and their probability distributions are often based on the Gaussian distribution, but in social life, many events can be approximated by this power law. For example, the following social activities and phenomena have been reported: the Internet, citation relationships in academic papers (Redner, 1998), co-authorship relationships (Newman, 2001a; Newman, 2001b; Newman, 2001c), metabolic networks (Jeong et al., 2000), protein networks (Jeong et al., 2001), e-mail exchanges (Ebel et al., 2002), sexual contacts (Liljeros et al., 2001), and infectious disease models. Although there are some cutoffs at the base of the power distribution due to physical restrictions, it is known that the exponent γ is in the range of $2 < \nu < 3$ in most cases (Albert & Barab'asi, 2002; Amaral et al., 2000; Barab'asi & Albert, 1999; Dorogovtsev & Mendes, 2010; Newman, 2003; Strogatz, 2001).

Barabasi and Albert proposed a simple model that reproduces scale-free networks [20,29]. In their model, nodes are added one by one. Each added node selects m nodes from the existing nodes, which are combined with the master of the order distribution of each node, but at this time, the total order distribution can be obtained by solving the equation with a probability proportional to the bond order to derive.

Figure 1. Power-law distribution



$$P(k) = 2m(m+1) / k(k+1)(k+2) \quad (6)$$

When k is large,

$$P(k) \sim k^{-3} \quad (7)$$

can be approximated. In other words, the scale is considered to be extremely effective a network analysis of social life in which the network topology and spatial shape cannot be grasped.

This property is called scale-free because it does not include physical distance as a parameter.

In the field of network theory, a network is indicated in which links (branches) are concentrated on some nodes (points). Specifically, the number of links can be thought of as the number of people who can convey information or exchange things, and the node can be thought of as an individual who is involved in this human network. For example, a doctor in a town where the patients gather or a teacher in a school visited by parents and students can be regarded as a network with a large number of links. This is referred to as scale-free because no “scale” can express the distribution of links. Nodes with concentrated links are called hubs. This is the idea of a correspondent and how to handle information transmission. It is one of the means to aim at and understand the state conceptually. In other words, it is not a rigorous simulation; rather, it is intended for understanding the concept. The first treatise regarding this was published in *Nature*, and the mathematical basis has been proven.

2.3 Modeling

We shall consider the following condition: face-to-face delivery of a drug to a patient, with the setting that it is effective only within a limited time frame. The person decides whether to take the medication (e.g., an iodine preparation for thyroid saturation, an antiviral drug that suppresses initial infections, etc.) as follows:

$$\text{Medicinal effect } \epsilon(c) = E * C(t) / (C(t) + a^h) \quad (8)$$

where a^h is the dose to achieve the maximum efficacy of 50%. However, $C(t)$ in the blood will be decreased when the administration time deviates from the time frame. In other words, if the timing of the administration is not appropriate, the effect will be lost, even if the medication is taken. Even if the patient is fortunate enough to have received the medication face-to-face, using this model, it will have no effect unless he/she is given information about when to take it. If the patient takes it at the wrong time, he/she will return to the initial state, just as if no medicine had been taken. In terms of infectious diseases, it is the same model as the susceptible–infected–susceptible (SIS) model. The fact that the SIS model is a scale-free network is explained in the literature (Crokidakis & Argollo, 2012). It has also been reported that the susceptible–infected–recovered model is similar to the power law (Blasiusa, 2020).

2.4 Graphical Algorithms And Functions In MATLAB

We used the BA model algorithm (scale-free network graph) in MATLAB. Its algorithm (Tapan, 2021) is as follows:

Step 1: (Initial state): $n >$ Place a complete graph consisting of one vertex

Step 2: Add a new vertex (growth)

Step 3: Extend an edge from the vertex added in Step 1 to n existing vertices.

At this time, do you put an edge on each vertex?

At that time, it is proportional to the order of each vertex (dominant selection)

Step 4: Repeat Step 1 and Step 2 for the number of vertices added

An example of the use of this function is as follows:

$A = \text{BAgraph_dir}(N, m0, m)$,

where N is the number of nodes in the network, $m0$ is the size of the seed network, and m is the average degree of the seed network; use $m0=m$ or $m < m0$. For example,

$A = \text{BAgraph_dir}(200, 10, 10)$.

The resulting adjacency matrix contains a 1 in row i , column j if i connects to j . A has a power-law in-degree distribution. The algorithm may take about 2–3 minutes to generate an adjacency matrix for $N=200$.

2.5 Scenario

In a small village with 50 residents, we assumed face-to-face interaction. We simulated the following: 1) a village in normal daily life, 2) a village with a SARS-CoV-2 outbreak, and 3) a village immediately after the Fukushima nuclear accident. The parameter conditions and scenarios are as follows.

Scenario 1

Human interaction in ordinary daily life, hub: five people (convenience store clerk, doctor, village chief, postal worker, elementary schoolteacher), links: 280.

Scenario 2

SARS-CoV-2 infection/spread, hub: three people (convenience store clerk, doctor, village mayor), links: 200.

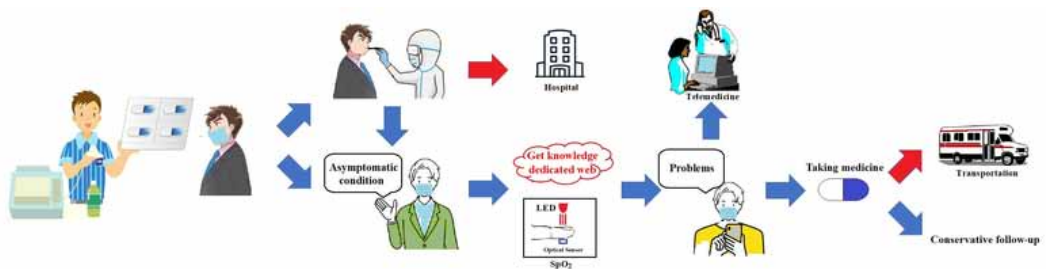
Scenario 3

After the Fukushima nuclear accident, hub: one person (village mayor), links: 80.

2.6 Simulation Results

As shown in Figure 2, in the social network (here, face-to-face exchange), some kind of mutual relationship can be grasped visually. In the society with COVID-19 infection and spread, people in the hub can hand over medicines because of their interaction with other humans (nodes), but in case of the Fukushima nuclear accident, the village mayor is the one who distributes the medicines, and it can be visually understood that the number of people who can be contacted is limited to 25. In the Fukushima nuclear accident, people under the age of 40 years are eligible to take iodine preparations (e.g., Minamiaizu area: 83,635 [34%] of 247,404 people); thus, 18 of 53 people under the age of 40 years would have been able to get a tablet. However, based on the results of a field survey, only three of 18 people (5% of the population under the age of 40 years) got the instruction to “take it now!” in a timely manner (Nakajima & Kurokawa, 2021).

Figure 2. Results of the scale-free network (normal life, COVID-19, Fukushima nuclear power plant accident) simulations



In other words, in addition to the delivery of medicine, the instruction to “take it now!” is also extremely important. It goes without saying that multimedia technology is useful across spaces for this purpose. In this way, to analyze the network of people in the event of a disaster, the scale-free network method, which can grasp the event visually, appears to be useful.

2.7 What Should Tap Be in Response to These Results?

Even in small villages, residents can obtain information as long as mobile phones, hard-wired lines, and Internet connections are maintained, which represents a major difference from the distribution of iodine preparations after the Fukushima nuclear accident, when communication lines were cut off.

When implementing TAP, two points are important: 1) can the drug be distributed second, and 2) is there a specific time when it should be taken, or can the patient take it at a time of his/her own choosing? In the former case, the drug is distributed by a doctor, village chief, or convenience store

clerk, so there is an increased risk of infection, but distribution is possible just before an outbreak. Since the latter case involves telecommunications, only information is sent and received, so there is no risk of infection by medical personnel. However, if the telecommunications carrier technician were to get infected, there could be disruptions, but not to the degree of those after the Fukushima nuclear accident.

Although not shown in Figure 2, this assumption may be advanced in the time-axis direction in developing countries. Specifically, depending on the number of infected people and doctors, or the number of beds available for severely ill patients, and due to the economic background of patients, the number of cases receiving treatment at home is expected to increase in developing countries. Therefore, it is presumed that TAP should be implemented earlier in developing than in developed countries.

3. CONSIDERATIONS

3.1 Candidate Drugs to Be Distributed as Tap

In the 2009 swine flu pandemic, oseltamivir was experimentally selected for TAP as a hand-delivered oral drug; however, with the novel SARS-CoV-2 (Germann et al., 2006; Lee et al., 2010), few drug candidates are currently available. In South America, there is data that the incidence of COVID-19 is low in areas where Ivermectin was distributed free of charge. In contrast, a paper published in JAMA in March 2021 denied the effectiveness of Ivermectin (López et al., 2021). However, an open letter has been issued for JAMA's treatise, and some doctors disagree with this treatise(2021). It goes without saying that if Ivermectin is effective, it is a candidate for TAP because it has no side effects and is extremely inexpensive.

Favipiravir is one of the limited number of oral drugs considered a possible treatment for COVID-19 because it has been shown to suppress the onset of early pneumonia. Although it is considered to be a candidate for TAP, only asymptomatic patients are targeted. Multimedia support would be a necessary condition.

Initially, favipiravir was developed as an anti-influenza drug by Toyama Chemical (currently Fujifilm) with a research and development subsidy from the US military. Since it is an RNA polymerase inhibitor, it is also effective against RNA coronaviruses, and has been used in China and Africa after obtaining additional approval for COVID-19. Since it is effective, it is administered worldwide. The US Food and Drug Administration may also approve its use in the near future. For adults, 1600 mg should be orally administered twice on the first day, and 600 mg once on the second to fifth days. The total administration period is 5 days.

Especially in China, favipiravir is considered an effective therapeutic agent against COVID-19. When used in a model of deadly influenza-infected animals, favipiravir resulted in the survival of all animals, whereas oseltamivir did not. Favipiravir is an antiviral agent that can effectively treat lethal RNA virus infections with an extremely high viral load. It has also been used effectively to treat Ebola, which was prevalent in West Africa in 2014. Since that time, the effectiveness of combination therapy with favipiravir and oseltamivir for severe influenza pneumonia has been reported. In addition, favipiravir has been used to treat severe febrile thrombocytopenia syndrome in Japan.

As a general rule, favipiravir is not a drug that can be given to all patients; it is intended for asymptomatic cases and limited to the purpose of suppressing the onset of early pneumonia and preventing its aggravation. Many medical institutions administer it relatively routinely to middle-aged patients (with no possibility of pregnancy) who develop pneumonia, but its use is premised on close observation by a nurse.

In other parts of the world, for example, the Republic of Togo in Africa, only extremely wealthy individuals have access to medical professionals. As of February–April 2020, less than 20% of the patients in Togo will be seen by a doctor (World Health Organization, 2020b). It can therefore be

Table 1. Examples of information to be posted online (Joshi et al., 2020)

<p>Dose: For adults, 1600 mg should be orally administered twice daily on the first day, and 600 mg once daily on the second to fifth days. The total administration period is 5 days.</p> <p>Administration: <u>Administer with caution in patients with gout or a history of gout and patients with hyperuricemia</u></p> <p>Contraindications: The most common side effect of this drug is teratogenicity. Do not administer to young boys or pregnant or potentially pregnant women; if administered to lactating women, breastfeeding should be discontinued.</p> <p>In animal studies, early embryo lethality (rats) and teratogenicity (monkeys, mice, rats, and rabbits) have been observed at doses similar to or below clinical exposure. In animal experiments, histopathological changes in the testes were observed in rats [12 weeks old] and young dogs [7–8 months old], and sperm abnormalities were observed in mice [11 weeks old]. In all cases, recovery or recovery tendency due to drug suspension was observed.</p> <p>Metabolic pathway This drug is not metabolized by cytochrome P-450 (CYP), but mainly by aldehyde oxidase (AO) and partly by xanthine oxidase (XO). It also inhibits AO and CYP2C8 (paclitaxel), but has been reported to have no CYP-inducing effect.</p> <p>There are reports that AO contributes to toxicity by AO metabolites and to chemical substances and metabolism, and many believe that its relationship with the onset of toxicity should be considered. Since it is known that there are individual differences in AO metabolic activity, as well as species differences, it is becoming more important to consider the contribution of AO drug metabolism in humans.</p> <p>Clinical data will therefore need to be fed back to drug development.</p>

said that self-medication is being carried out in Togo because favipiravir is sold in the market with assistance from China.

3.2 Tap Operating Conditions

At the peak of the COVID-19 outbreak, few or no beds have been available for mildly ill patients, and thus the medical establishment needs to provide a solution for individuals who prefer a calm and restful home environment as opposed to a crowded hospital. Death from mild cases is common with COVID-19; therefore, a reliable and effective device to detect infection is necessary. One such device is a pulse oximeter (Figure 3), which can be purchased online for about USD\$40.

The pulse oximeter was invented by Dr. Takuo Aoyagi of Nihon Kohden in 1974 to determine optically the ratio of hemoglobin in blood bound to oxygen (oxygen saturation). Hemoglobin absorbs red light when not bound to oxygen, and does not absorb red light when bound to oxygen. Using this property, it is possible to measure how much oxygen is contained in hemoglobin in the blood, and this ratio is called oxygen saturation (SpO_2).

Commercially available pulse oximeters have the advantage of being able to measure SpO_2 easily by inserting a finger into a spring-loaded clip containing an optical sensor. Light from an LED is applied to the base of the fingernail and this light passes through the finger to a sensor embedded in the device under the pad of the finger. If the finger is too shallow or too deep, SpO_2 cannot be measured accurately, and if the finger is inserted incorrectly, e.g. the direction light is reversed, the measured value will be low. In the event of shock, measurement is not possible.

SpO_2 levels between 96% and 98% are normal, 100% suggests hyperventilation syndrome, and 90% or less suggests respiratory distress. However, the average range of normal values decreases with aging, and at 90 years, even 90% SpO_2 is considered normal. Therefore, it is important to measure arterial oxygen saturation (SaO_2) on a daily basis. In addition, since the LED light is used as a percutaneous substitute for measurement, it is accurately called SpO_2 (p = percutaneous: percutaneous). To be precise, there is a slight divergence between SpO_2 and SaO_2 .

Figure 3. Example of the actual operation of TAP with multimedia technology. Every patient should learn about the side effects of favipiravir beforehand from the dedicated web (shown in Table 1)

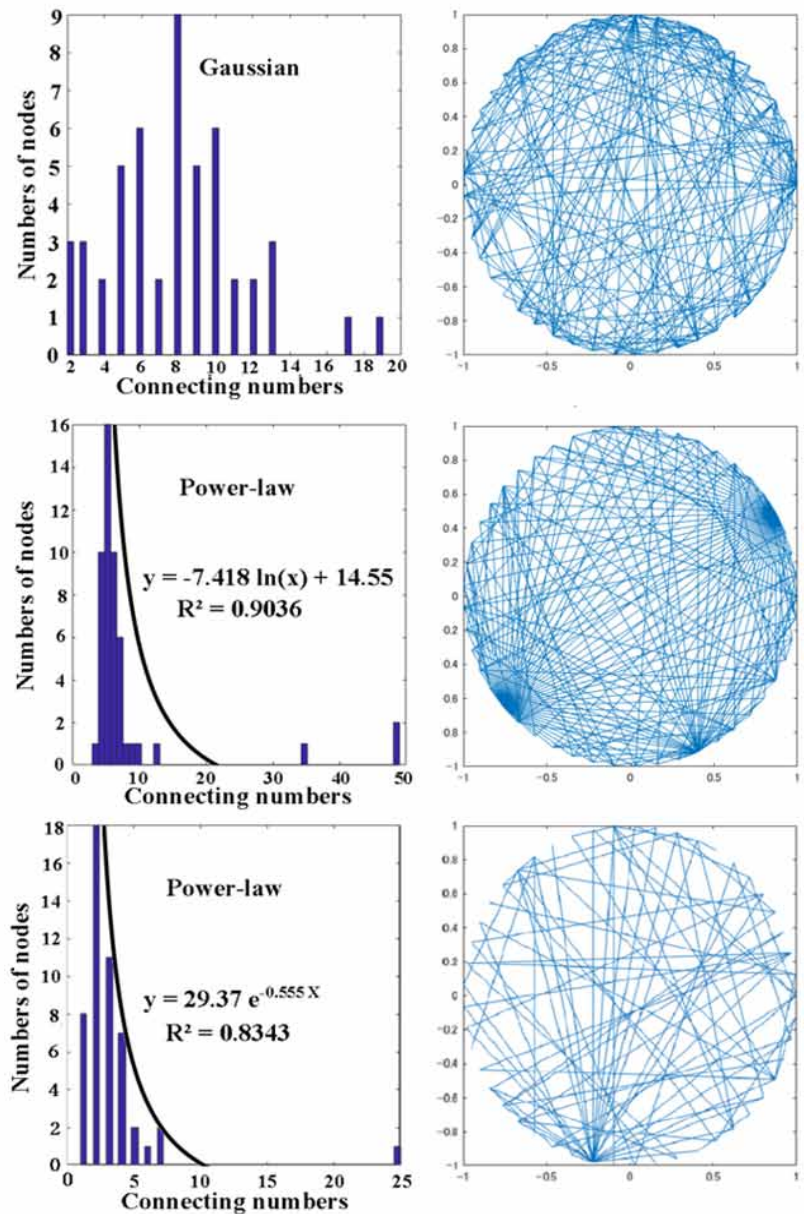
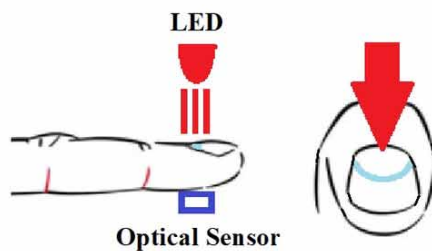


Figure 4. Pulse oximeter with optical sensor



Furthermore, if peripheral circulatory insufficiency or the pulse wave associated with shock cannot be properly detected, accurate evaluation with SaO_2 is required; however, in the situation where there is no dissociation between SaO_2 and SpO_2 , oxygen supply is basically evaluated as SaO_2 with SpO_2 .

3.3. Operation Example with Multimedia

Most cases of SARS-CoV-2 infection are asymptomatic or extremely mild. Younger people tend to experience milder cases, whereas older cases tend to be more severe. The problem is that there are many asymptomatic cases that can lead to death from pulmonary edema while the patient's progress is being monitored at home, and this system can be used to detect such cases. The aim of using multimedia is to save as many lives as possible during the COVID-19 pandemic. TAP is a policy that allows people to purchase medicine at convenience stores before disease onset; however, this does involve additional risks, so a pulse oximeter and prior drug knowledge obtained via the Internet are essential. In addition, consultation (e.g., via telemedicine) with a medical institution is a prerequisite.

In early-stage pulmonary edema, the ventilation volume is maintained, so the concentration of CO_2 in the blood does not rise. Difficulty breathing reflects the partial pressure of CO_2 in the blood; therefore, the patient does not have any complaints. However, pulse oximeters can be used to detect early-stage pulmonary edema. If the pulse oximeter reading is more than 4% lower than average, this may indicate pneumonia. In other words, even if there are no symptoms, if there is a dissociation of

4% or more, self-treatment is impossible, so it is recommended to engaged in telemedicine with a medical institution; this is the time to take medicine at home.

If the pulse oximeter values do not improve, the patient should immediately call an ambulance and be admitted to a medical institution. Even if the pulse oximeter values do improve, the patient should take the prescribed amount of favipiravir for 5 days and remain at home. The biggest advantage of this system is that the medical side has no risk of infection.

During the Fukushima nuclear accident, stable iodine preparations were distributed to prevent thyroid exposure, but less than 5% of the residents (aged 40 years or younger) took them at an effective time.

In early-stage pneumonia, favipiravir is effective in 73% of adults. Unfortunately, the remaining 25% will need to be transported by ambulance. Unlike oseltamivir for influenza, no effective oral tablets are currently available to treat COVID-19. Distribution of medicines by local governments in the turmoil of a global pandemic is not possible, so the Ministry of Health needs to develop TAP policies in advance.

4. CONCLUSIONS

Self-medication has a long history, but it involves increased risks. This paper discusses TAP, a policy in which antiviral drugs are distributed to residents immediately prior to a pandemic outbreak, information such as drug side effects is collected in advance via the Internet, and early-onset pneumonia is detected using a pulse oximeter. However, this system involves taking antiviral drugs distributed in advance at the patient's own discretion in reference to instructions from medical institutions through telemedicine. Based on a report of trial cases in Japan, we expect favipiravir to be a good candidate for TAP, as it appears to be effective for about 73% of patients, even those treated at home (GemMed, 2020).

ACKNOWLEDGMENT

The concept of TAP with favipiravir as a candidate for oral medication was announced in July 2020 at the International Telecommunications Union's coronavirus control webinar, entitled "Public Webinar on New eHealth Solutions to Combat Pandemics with ICT". This study was supported by KDDI Foundation Japan and performed in compliance with all relevant ethical standards.

REFERENCES

- Agrawal, U., Raju, R., & Udwardiac, Z. (2020). Favipiravir: A new and emerging antiviral option in COVID-19. *Medical Journal, Armed Forces India*, 76(4), 370–376. doi:10.1016/j.mjafi.2020.08.004 PMID:32895599
- Albert, R., & Barabási, A.-L. (2002). Statistical mechanics of complex networks. *Reviews of Modern Physics*, 74(1), 47–97. doi:10.1103/RevModPhys.74.47
- Albert, R., Jeong, H., & Barabási, A.-L. (1999). Diameter of the world-wide web. *Nature*, 401(6749), 130–131. doi:10.1038/43601
- Amaral, L. A. N., Scala, A., M. Barthélemy, M., & Stanley, H. E. (2000). Classes of small-world networks. *Proc. Nat. Acad. Sc. USA*, 97, 11149–52. .10.1073/pnas.200327197
- Barabási, A.-L., & Albert, R. (1999). Emergence of scaling in random networks. *Science*, 286(5439), 509–512. doi:10.1126/science.286.5439.509 PMID:10521342
- Blasiusa, B. (2020). Power-law distribution in the number of confirmed COVID-19 cases featured. *Interdisciplinary Journal of Nonlinear Science*, 30(9), 093123. Advance online publication. doi:10.1063/5.0013031
- Bolle, L. D., Mehuys, E., & Adriaens, E. (2008). Home Medication Cabinets and Self-Medication: A Source of Potential Health Threats? *The Annals of Pharmacotherapy*, 42(4), 572–579. doi:10.1345/aph.1K533 PMID:18364405
- Crokidakis, N., & Argollo, M. (2012). Critical behavior of the SIS epidemic model with time-dependent infection rate. *Journal of Statistical Mechanics*, 05(05), P05012. Advance online publication. doi:10.1088/1742-5468/2012/05/P05012
- Doctors, U. S. (2021). *Open Letter by U.S. Doctors: JAMA Ivermectin Study Is Fatally Flawed*. <https://jamaletter.com/>
- Dorogovtsev, S. N., & Mendes, J. F. F. (2010). Evolution of networks. *Advances in Physics*, 51(4), 1079–1187. doi:10.1080/00018730110112519
- Ebel, K., Mielsch, L. I., & Bornholdt, S. (2002). Scale-free topology of e-mail networks. *Physical Review E: Statistical, Nonlinear, and Soft Matter Physics*, 66(3), 035103. doi:10.1103/PhysRevE.66.035103 PMID:12366171
- European Centre for Disease Prevention and Control. (2020). <https://www.ecdc.europa.eu/en/geographical-distribution-2019-ncov-cases>
- Evans, M. (2021). *COVID-19: how to treat coronavirus at home*. Patient. <https://patient.info/news-and-features/covid-19-how-to-treat-coronavirus-at-home>
- Fujifilm. (2020). *Avigan shown to be effective in Japanese Phase-3 trial for COVID-19*. Reuters. <https://jp.reuters.com/article/fujifilm-avigan/fujifilms-avigan-shown-to-be-effective-in-japanese-phase-3-trial-for-covid-19-idUSKCN26E0F9>
- GemMed. (2020). *Severely ill patients with new corona, 77% were treated with Avigan and 73% were relieved, 16% were treated with ECMO and 64% were relieved — Medical Directors' Meeting (2) on September 11, 2020*. <https://gemmed.ghc-j.com/?=36000>
- Germann, T. C., Kadau, K., Longini, I. M., & Macken, C. A. (2006). Mitigation strategies for pandemic influenza in the United States. *Proceedings of the National Academy of Sciences of the United States of America*, 103(15), 5935–5940. doi:10.1073/pnas.0601266103 PMID:16585506
- Jeong, H., Mason, S. P., Barabási, A.-L., & Oltvai, Z. N. (2001). Lethality and centrality in protein networks. *Nature*, 411(6833), 41–42. doi:10.1038/35075138 PMID:11333967
- Jeong, H., Tombor, B., Albert, R., Oltvai, Z. N., & Barabási, A. L. (2000). The large-scale organization of metabolic networks. *Nature*, 407(6804), 651–654. doi:10.1038/35036627 PMID:11034217
- Joshi, S., Parkar, J., Ansari, A., & Tiwaskar, M. (2021). Role of favipiravir in the treatment of COVID-19. *International J of Infectious Diseases*, 102, 501–508.

Joshi, S., Parkar, J., Ansari, A., Vora, A., Talwar, D., Tiwaskar, M., Patil, S., & Barkate, H. (2020). Role of favipiravir in the treatment of COVID-19. *International Journal of Infectious Diseases*, 102, 501–508. doi:10.1016/j.ijid.2020.10.069 PMID:33130203

Kapoor, A., Pandurangi, U., Arora, V., Gupta, A., Jaswal, A., Nabar, A., Naik, A., Naik, N., Namboodiri, N., Vora, A., Yadav, R., & Saxena, A. (2020). Cardiovascular risks of hydroxychloroquine in treatment and prophylaxis of COVID-19 patients: A scientific statement from the Indian Heart Rhythm Society. *Indian Pacing and Electrophysiology Journal*, 20(3), 117–120. Advance online publication. doi:10.1016/j.ipej.2020.04.003 PMID:32278018

Lee, V. J., Yap, J., Cook, A. R., Chen, M. I., Tay, J. K., Tan, B. H., Loh, J. P., Chew, S. W., Koh, W. H., Lin, R., Cui, L., Lee, C. W. H., Sung, W.-K., Wong, C. W., Hibberd, M. L., Kang, W. L., Seet, B., & Tambyah, P. A. (2010). Oseltamivir ring prophylaxis for containment of 2009 H1N1 influenza outbreaks. *The New England Journal of Medicine*, 362(23), 2166–2174. doi:10.1056/NEJMoa0908482 PMID:20558367

Liljeros, F., Edling, C. R., Amaral, L. A. N., Stanley, H. E., & Åberg, Y. (2001). The web of human sexual contacts. *Nature*, 411(6840), 907–908. doi:10.1038/35082140 PMID:11418846

Logical India. (2020). *Self-Medicating To Ward Off Or Treat COVID-19 Is A Big No!* <https://thelogicalindian.com/story-feed/awareness/self-medication-coronavirus-covid-19-pandemic-20327>

López, E. L., Isabel, C., & Hurtado, I. C. (2021). Effect of Ivermectin on Time to Resolution of Symptoms Among Adults With Mild COVID-19, A Randomized Clinical Trial. *Journal of the American Medical Association*, 325(14), 1426–1435. doi:10.1001/jama.2021.3071 PMID:33662102

Malik, M., Tahir, M. J., Jabbar, R., Ahmed, A., & Hussain, R. (2020). Self-medication during Covid-19 pandemic: Challenges and opportunities. *J. of Drugs & Therapy Perspectives*, 36(12), 565–567. doi:10.1007/s40267-020-00785-z PMID:33041621

Medicine of Toyama by Toyama Pharmaceutical Association. (2021). *Toyama Prefecture has long been producing and selling pharmaceuticals*. <https://www.toyama-kusuri.jp/en/aboutus/medicine.html>

Nakajima, I., & Kurokawa, K. (2020). Looking Back over a Decade “Final Decision Call after the Accidents of the Fukushima Nuclear Power Plant. *J of Multimedia Information System*, 7(2), 147–156.

Nakajima, I. (2020). *Concept of TAP: drug distributions and remote consultation just before the outbreak*. <https://www.itu.int/en/ITU-D/Study-Groups/2018-2021/Documents/events/2020/Webinar%20Q2-2July6/Isao-Nakajima-Seisa-University-Q2-2-webinar-presentation.pdf>

Nakajima, I., & Kurokawa, K. (2021). Fukushima Nuclear Power Plant accident: Various issues with iodine distribution and medication orders. *American Journal of Disaster Medicine*, 16(2). PMID:34392524

Nasir, M., Chowdhury, A. S. M. S., & Zahan, T. (2020). Self-medication during COVID-19 outbreak: A cross sectional online survey in Dhaka city. *International Journal of Basic and Clinical Pharmacology*, 9(9), 1325. Advance online publication. doi:10.18203/2319-2003.ijbcp20203522

Newman, M. E. J. (2001a). Scientific collaboration networks: I. Network construction and fundamental results. *Physical Review E: Statistical, Nonlinear, and Soft Matter Physics*, 64(1), 016131. doi:10.1103/PhysRevE.64.016131 PMID:11461355

Newman, M. E. J. (2001b). Scientific collaboration networks: II. Shortest paths, weighted networks, and centrality. *Physical Review E: Statistical, Nonlinear, and Soft Matter Physics*, 64(1), 016132. doi:10.1103/PhysRevE.64.016132 PMID:11461356

Newman, M. E. J. (2001c). The structure of scientific collaboration networks. *Proceedings of the National Academy of Sciences of the United States of America*, 98(2), 404–409. doi:10.1073/pnas.98.2.404 PMID:11149952

Newman, M. E. J. (2003). The structure and function of complex networks. *SIAM Review*, 45(2), 167–256. doi:10.1137/S003614450342480

Rattanaumpawan, P. P., Jirajariyavej, S., & Lerdlamyong, K. (2020). Real-world Experience with Favipiravir for Treatment of COVID-19 in Thailand. medRxiv. 10.1101/2020.06.24.20133249

Redner, S. (1998). How popular is your paper? An empirical study of the citation distribution. *The European Physical Journal B*, 4(2), 131–134. doi:10.1007/s100510050359

- Sadio, A. J., Gbeasor-Komlanvi, F. A., & Konu, R. Y. (2020). *Assessment of self-medication practices in the context of Covid-19 outbreak in Togo*. doi:10.21203/rs.3.rs-42598/v1
- Shinoda, M., Hirouchi, H., & Nishimura, K. (2019). *Case Report COVID-19 pneumonia with rapid symptom improvement and conversion to negative result on PCR after administration of favipiravir (Avigan®)*. https://www.kansensho.or.jp/uploads/files/topics/2019ncov/covid19_casereport_en_200512.pdf
- Strogatz, S. H. (2001). Exploring Complex Networks. *Nature*, 410(6825), 268–276. doi:10.1038/35065725 PMID:11258382
- Tapan. (2021). *Scale-free networks using B-A algorithm*. MATLAB Central File Exchange. <https://www.mathworks.com/.../49356-scale-freenetworks>
- Wegbom, A., Edet, C., Raimi, O., & Fagbamigbe, A. F. (2020). Self-medication practices and associated factors in the prevention and/or treatment of COVID-19 virus: A population-based survey in Nigeria, Research Square. DOI: 10.21203/rs.3.rs-91101/v1
- World Health Organization. (2020b). *WHO announces COVID-19 outbreak a Pandemic*. <http://www.euro.who.int/en/health-topics/health-emergencies/coronaviruscovid19/news/news/2020/3/who-announces-covid-19-outbreak-a-pandemic>
- World Health Organization (WHO). (2020a). *Coronavirus disease 2019 (COVID-19) Situation Report-94*. http://www.who.int/docs/default-source/coronaviruse/situation-reports/20200423-sitrep-94-covid19.pdf?sfvrsn=b8304bf0_4