

Aging Research Institute Newsletter

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Happy 99 Nowruz

According to the statistics declared by the scientometric center of the Ministry of Health and Medical Education, Aging Research Institute (including Neuroscience, Physical Medicine and Rehabilitation, and Psychiatry and Behaviour Sciences Research Centers) has shown a growing trend in publishing scientific papers over the past year. The number of published articles has increased from 133 in 2018 to 188 in 2019, with a growth rate of 41%. The editorial board members congratulate the dean of the research institute and the heads of the relevant research centers on this success.



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* Please note that from April, 2020, we are ceasing newsletters' printings temporarily due to the impact of COVID-19. Please visit our website for more information.

Editorial

Management of critically ill elderly patients

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Over the last 150 years, the rapid aging of the population occurred in developed countries and in those undergoing transition. But unfortunately, to date, health-care is not prepared to meet the burden and challenges of the increased number and complex management of the elderly. The distribution of geriatric medicine is unequal; geriatric medicine is not a mandatory part of undergraduate medical school programs and the specialty of geriatric medicine is still not recognized in many countries(1). Number of critically ill patients admitted to ICU has been increased in the last two decades. Nowadays, the mean age of admitted critically ill patients reaches to 65 years old in many countries which carries a high burden of resources especially in patients with 80 years and over. Characteristics of these old patients beside age itself predispose them to the followings: different comorbidities, organ dysfunctions, malnutrition, cognitive dysfunction and functional decline and frailty. In addition, history of polypharmacy is a special concern in old patients which should be noticed during initial diagnosis and management of them. If there is a potential benefit from ICU admission, it should be considered otherwise the elderly critically ill patients should be admitted to high dependency unit or palliative care wards(2). The most common reasons for ICU admission in elderly patients are acute hypox-

emic failure, sepsis, scheduled surgeries for different reasons and cognitive dysfunction. Functional elderly patients have a favorable long-term outcome following ICU admission and that age alone should not be used in making ICU triage decisions. However, elderly patients who may require prolonged mechanical ventilation appear to do poorly and a time limited trial in the ICU may be appropriate in such patients.

During triage, a multidisciplinary approach considering patients and their relatives' wish and physicians' idea should be performed. When an older patient has been admitted to the ICU, the most appropriate treatment should be given. However, this does not necessarily mean maximal treatment. During decision making for these treatments and interventions (especially invasive), severity of the disease and cost effectiveness regarding the outcome should be considered. If an intervention seems to be inappropriate or refused by the patient or their next of kin, it should be avoided(3). For patients in their terminal phase limitation or withholding treatment are recommended with the aim of achievement of the most comfortable death.

It is recommended that these elderly patients should be discharged from ICU as soon as they recover from initial problem. During discharge, shared decision making with a geriatrician may improve the patient's outcome. The most important risk factors for mortal-

ity after ICU discharge are illness severity, age, comorbidities, time and location of ICU discharge and discharge protocol. Older patients surviving the ICU often suffer from sequels, including increased long-term mortality, poor quality-adjusted survival, cognitive impairment and functional disability. In the some situations the patients are at risk of loss of function, inability to return home, requirement for a nursing home and/or remain bed bound for the rest of their lives(4). The outcome of the very old patients has improved over the past decades but remains poorer than for younger patients. Several factors account for this high mortality which is more related to underlying disease than age itself. For better management of geriatric patients, geriatric principles should be learned by physicians and incorporated into critical care medicine. This change in behavior and culture will require the skill and investment of leaders in critical care and geriatrics on the local, national, and international levels, and training the next generation of leaders.

Keywords: Critically ill; Elderly patients; Geriatric medicine

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Top Article



Congratulations to Dr. Sanam Dolati, Ph.D. in immunology, TUOMS, on having her article entitled: "Prospects for the application of mesenchymal stem cells in Alzheimer's disease treatment", published in *Life Sciences journal*, (IF=3.44) which has been selected as the top article of this issue. Aging Research Institute expresses the warmest greeting to her.

Special Section

COVID-19; What we know so far

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While the emergence of the 2019 new coronavirus (SARS-CoV-2) infection in Wuhan, China, in December 2019, it has rapidly disseminated across China and many other countries [1–8]. Up to this point, SARS-CoV-2 has affected more than 2,400,000 patients all around the world and has become a main health concern around the world. The World Health Organization (WHO) stated a new name for the epidemic disease caused by SARS-CoV-2 on 11 February 2020: coronavirus disease (COVID-19). The International Committee on Taxonomy of Viruses has renamed the previously temporarily named 2019-nCoV as severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) [3].

Primary studies suggested an association among a single local fish, wild animal market, and most cases of infection, demonstrating possible animal-to-human transmission. However, studies have increasingly indicated human-to-human transmission of SARS-CoV-2 through droplets or direct contact [2, 8–10]. Based on the evidence of a growing incidence of infections and the risk of transmission by asymptomatic carriers, SARS-CoV-2 is transmitting effectively among humans [5, 10–13]. Additionally, the accessible global travel could further increase its worldwide spread

[12]. On 30 January 2020, the WHO declared the COVID-19 outbreak as the sixth public health emergency of international concern, following H1N1 (2009), polio (2014), Ebola in West Africa (2014), Zika (2016) and Ebola in the Democratic Republic of Congo (2019). Finally, on 12 March 2020, SARS-CoV-2 outbreak became a pandemic. Therefore, health workers, governments and the public need to get together globally to prevent its expansion [14].

Clinical manifestations

Clinical presentation of COVID-19 highly have signs of viral pneumonia such as SARS and MERS. Most cases are mild cases (81%) with self-limiting symptoms and two-week recovery. Severe patients deteriorate rapidly with acute respiratory distress syndrome (ARDS) and septic shock, eventually causing multiple organ failure [15].

The SARS-CoV-2 was more likely to infect elderly men with underlying conditions (mainly hypertension, cardio-cerebrovascular diseases, and diabetes). Males were more vulnerable to SARS-CoV-2 infection, because of their X chromosome and sex hormones' effect on innate and adaptive immunity. Smoking may be a negative prognostic indicator for COVID-19 [16–18].

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Symptoms have usually mild and nonspecific onset, presenting by fever, dry cough, and shortness of breath. Very few COVID-19 patients have gastrointestinal (e.g. diarrhea) and prominent upper respiratory tract symptoms [17, 19]. However, fever presents in only 43.8% of COVID-19 patients as an initial presentation, and after hospitalization it develops to 87.9% [17]. Those patients without fever or even asymptomatic may be left un-quarantined as silent infection source, if the control methods concentrate on fever detection. Furthermore, the onset of symptoms may help physicians determining patients with poor prognosis. Pharyngeal pain, dyspnea, dizziness, abdominal pain and anorexia are more likely to occur in patients admitted to the ICU [20].

In regards to laboratory findings, a significant decrease in the total number of lymphocytes indicating a consumption of immune cells and an impairment to cellular immune function can be used as an index in the diagnosis of SARS-CoV-2 infection [18]. Also in ICU patients' plasma levels of IL2, IL7, IL10, GSCF, IP10, MCP1, MIP1A, and TNF α are higher compared to non-ICU patients [19]. There are many differences in laboratory findings between ICU patients and the others, including higher white blood cell and neutrophil counts, higher levels of D-dimer, creatine kinase, and creatinine in ICU patients [20]. Typical chest CT scan of COVID-19 pneumonia manifests small subpleural ground glass opacities that grew larger. After two weeks, the lesions are gradually absorbed and extensive opacities with subpleural parenchymal bands are left in recovery patients. However, it is found that patients with normal radiologic findings on primary presentation consisted of 23.9% and 5.2% of severe and non-severe cases respectively, which makes this disease more complicated.

Treatment

There are no vaccine or specific cure for COVID-19 in general and new therapeutic drugs are emerging one after another. Therefore, there is an urgent need for global inspection of COVID-19 patients. Besides, more studies are needed to specify the safety and efficacy of these new drugs and guide clinical decision.

Medical interventions can be divided into four major categories: general treatment, coronavirus specific treatments, antiviral treatments and others. General treatments includes nutritional interventions and immuno boosters. Intravenous gamma-globulin, interferon, and thymosin are believed to enhance our immune system to fight with SARS-CoV-2. Chloroquine is a medicine used for treatment of malaria and autoimmune disease, had shown remarkable inhibition in the spread of SARS-CoV-2 at both entry and post-entry stages of the infection. Also, it was shown to reduce

Elderly Harassment



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“Do not worry; COVID-19 only kills the elderly and the sick!”

“A 103-year-old woman has survived the novel coronavirus disease!”

I do not know what it feels like to hear the above sentences. Does it make you happy that you are out of harm's way? Or does it make you devastated as the face of your elderly loved ones constantly passes by your eyes; can you stop thinking of them even for a moment?

I do not remember any lines in the Hippocratic Oath, pertaining to any ignorance about the death of the elderly. The truth is that we are facing Coronavirus-Related elderly abuse nowadays. Isn't it true that the elderly are the precious treasures of experience of every family? How dare those expressions devalue their lives? Sharing such statements unhesitatingly in the media causes devastating anxiety in the elderly, even deadlier than the coronavirus. These days the elderly are already anxious, hopeless, and frustrated and feel that they have reached the end of the line; yet, they want nothing but the health and well-being of their beloved ones.

How can we battle the virus while we ourselves, have let our dear ones down?

Shhhhh! Watch out your words! Let's not be deadlier than the coronavirus.

exacerbation of pneumonia, promote a virus-negative conversion, improve radiological findings, and shorten the disease course [21,22]. However, there are some recent controversies regarding its use, mainly considering its complications.

Due to the crucial role of the S-protein in coronavirus, therapies and vaccine exploration targeting S-protein-ACE2 interaction may be very promising. Appropriate modification of the human monoclonal antibody may be effective for treatment of COVID-19 [23]. What's more, potential therapies targeting the renin-angiotensin system to increase ACE2 expression and inhibit ACE may be developed to treat COVID-19 in the future.

There are no effective antiviral treatment for coronavirus infection, even the strong candidates as lopinavir/ritonavir and abidol exhibited no remarkable effect on clinical improvement [24]. Expectation and attention were shifted to “remdesivir” which may

be the most potential wide-spectrum drug for antiviral treatment of SARS-CoV-2. Studies revealed that remdesivir is highly effective and safe in the control of SARS-CoV-2 infection [25]. However, more studies are needed to confirm its effectiveness.

It seems that we should still wait and keep our fingers crossed to be able to overcome this disease by finding its vaccine or definite cure.

Keywords: COVID-19; Clinical manifestations; Treatment
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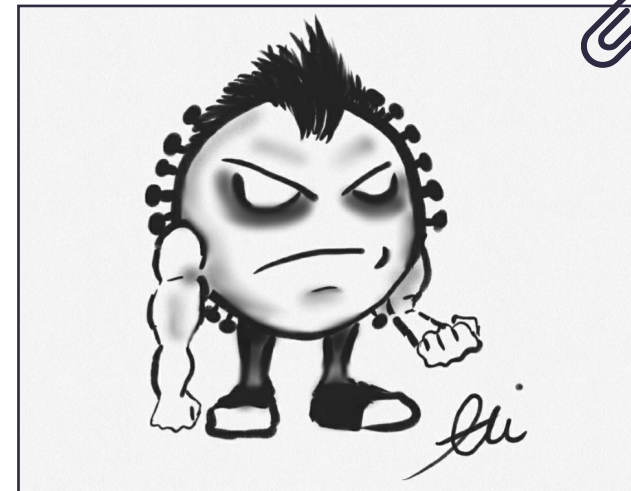
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Be Ready for Coronavirus

WHO is giving advice on how to protect ourselves and others



Be Safe from coronavirus infection

If you are 60+ or if you have underlying condition like:

- Cardiovascular disease
- Respiratory condition
- Diabetes

by avoiding crowded areas or places where you might interact with people who are sick.

Be Smart and Inform Yourself about coronavirus

- Follow accurate public health advice from WHO and your local health authority.
- Follow the news on latest coronavirus updates
- To avoid spreading rumors, always check the source you are getting information from
- Don't spread rumors
- Call your doctor
- Seek care immediately!

Be Kind and Support Loved Ones during coronavirus

- Check in regularly especially with those affected
- Encourage them to keep doing what they enjoy
- Share WHO information to manage anxieties
- Provide calm and correct advice for your children
- Show empathy with those affected
- Learn about the disease to assess the risk
- Adopt practical measures to stay safe



World Health Organization



Protect Others from getting sick



1. Avoid close contact when you are experiencing cough and fever
2. Avoid spitting in public
3. If you have fever, cough, and difficulty breathing seek medical care early and share previous travel history with your health care provider.
4. When coughing and sneezing cover mouth and nose with flexed elbow or tissue.
5. Throw tissue into closed bin immediately after use.
6. Clean hands with alcohol-based hand rub or soap and water after coughing or sneezing and when caring for the sick.

Protect Yourself and Others from getting sick



Wash your hands:

1. after coughing or sneezing
2. when caring for the sick
3. before, during, and after you prepare food
4. before eating
5. after toilet use
6. when hands are visibly dirty
7. after handling animals or animal waste



Is wearing rubber gloves while out in public effective in preventing the new coronavirus infection?

No. Regularly washing your bare hands offer more protection against catching COVID-19 than wearing rubber gloves. You can still pick up COVID-19 contamination on rubber gloves. If you then touch your face, the contamination goes from your gloves to your face and can infect you.

When to use a mask

Wear a mask if you are **coughing** or **sneezing**. For **healthy people**, wear a mask only if you are taking care of a person with suspected SARS-CoV-2 infection.



When and how to wear medical masks to protect against coronavirus

If you wear a mask, then you must know how to use it and dispose of it properly.

Before putting on a mask, **clean hands** with alcohol-based hand rub or soap and water.

Cover mouth and nose with mask and make sure there are no gaps between your face and the mask.

Avoid touching the mask while using it; if you do, clean your hands with alcohol-based hand rub or soap and water.

Replace the mask with a new one **as soon as it is damp** and **do not re-use** single-use masks.

To remove the mask: remove it from **behind** (do not touch the front of mask); discard immediately in a **closed bin**; clean hands with alcohol-based hand rub or soap and water.



“Masks are effective **only** when used in combination with **frequent hand-cleaning** with **alcohol-based hand rub** or **soap and water**.”

Does the new coronavirus affect older people, or are younger people also susceptible?

People of **all ages** can be infected by the new coronavirus (SARS-CoV-2). Older people, and people with pre-existing medical conditions (such as asthma, diabetes, heart disease) appear to be more vulnerable to becoming severely ill with the virus. WHO advise people of all age to take steps to protect themselves from the virus, for example by following good hand hygiene and good respiratory hygiene.



Coping with Stress during SARS-CoV-2 outbreak



It is normal to **feel sad, stressed, confused, scared** or **angry** during a crisis. Talking to people you trust can help. **Contact your friends and family.**

If you must stay at home, maintain a healthy lifestyle including **proper diet, sleep, exercise** and **social contacts with loved ones** at home and by email and phone with other family and friends.



Don't use **smoking, alcohol** or **other drugs** to deal with your emotions.

If you feel overwhelmed, talk to a health worker or counsellor. **Have a plan**, where to go to and how to seek help for physical and mental health needs if required.

Get the facts. Gather information that will help you accurately determine your risk so that you can take reasonable precautions. Find a **credible source** you can trust such as **WHO website** or, a local or state public health agency.



Limit worry and **agitation** by lessening the time you and your family spend watching or listening to media coverage that you perceive as upsetting.

Draw on skills you have used in the past that have helped you to **manage previous life's adversities** and use those skills to help you **manage your emotions** during the challenging time of this outbreak.



“This is a time for **facts**, not **fear**. This is a time for **science**, not **rumors**. This is a time for **solidarity**, not **stigma**. We are all in this together.”



Remember

1. Exposing yourself to the sun or to temperatures higher than 25C degrees **DOES NOT** prevent the coronavirus disease (COVID-19).



2. You can recover from the coronavirus disease (COVID-19). Catching the new coronavirus **DOES NOT** mean you will have it for life.



3. Being able to hold your breath for 10 seconds or more without coughing or feeling discomfort **DOES NOT** mean you are free from the coronavirus disease (COVID-19) or any other lung disease.

4. Drinking alcohol **DOES NOT** protect you against COVID-19 and can be dangerous.

5. COVID-19 virus can be transmitted in areas with hot and humid climates.



6. Cold weather and snow **CANNOT** kill the new coronavirus.

7. UV lamps **SHOULD NOT** be used to sterilize hands or other areas of skin as UV radiation can cause skin irritation.

8. Spraying alcohol or chlorine all over your body **WILL NOT** kill viruses that have already entered your body.



9. Vaccines against pneumonia **DO NOT** provide protection against the new coronavirus.

10. Antibiotics are **NOT EFFECTIVE** in preventing and treating the new coronavirus.



11. There is no evidence from the current outbreak that eating garlic has protected people from the new coronavirus.



12. There is no evidence that regularly rinsing the nose with saline has protected people from infection with the new coronavirus.

13. Thermal scanners **CANNOT** detect people who are infected but are not yet sick with fever.

14. Hand dryers are **NOT EFFECTIVE** in killing the SARS-CoV-2.

15. Taking a hot bath **DOES NOT** prevent the new coronavirus disease.



Hidden Age Discrimination in Corona Crisis Management; a Threat to the Health of Older Adult and Society

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"Don't worry; Corona Viruses (Covid19) most often among older people or those have tendency to a disease, are fatal". It is a theme these days, especially in the early days of the Covid19 outbreak, that is frequently used in the official media space by legal entities and consequently in the everyday conversations of the general public.

Media and cyberspace are the most important crisis management tools in different societies and governments and play a leading role in conveying people's thoughts, attitudes, and behavior through the transmission of messages and concepts as well as education (1). Naturally, the content of the messages should be such that, while providing the training and induction of the necessary warnings and behaviors to change the behavior, the intimidation is avoided.

At the same time with the prevalence of Covid19 around the world and Iran, the related organizations are conceptualizing and writing health messages to adopt appropriate behaviors to prevent the disease. These messages use the motivation strategy to try to influence messages more effectively. One of these strategy is The Fear Appeal Model. This model, drives

people toward desirable behavior, with emphasizing the negative consequences of doing or leaving some behaviors(2). This attraction is associated with behavioral defense mechanisms. Because messages can generate two motivations in the target audience or groups; motivate avoidance or motivate protection. If the message leads to excessive fear, individuals will come to defense mechanisms to promote fear avoidance behavior(3).

For some time, the media and cyberspace have been using discriminatory messages in the field of Corona Virus Disease, which can also be seen in the conversations of various authorities; "Don't worry; Corona Viruses (Covid19) most often among older people or those have tendency to a disease, are fatal."

This content quotes many of the content circulating in the media space and related to Covid19 disease, in which, to avoid the fear of Covid19, Unintentionally, the high rate of mortality in older adults and vulnerable individuals may have ignored, which is not only an example of elder abuse, and suggests a hidden ageism in societies, but also through the use of a displacement mechanism that is one of the most impor-

tant of neurotic defensive mechanisms to transmit fear and anxiety of being ill, From other age groups, to older age group; Which are more acceptable due to their high vulnerability; And they reproduce these messages in order to invite peace among the people(4).

But this process raises several problems. The use of this mechanism causes the motivation to avoid being activated in the mechanism of fear and people don't pay attention to the severity of the disease and how dangerous it is. As a result, there is no change in undesirable behaviors to health behaviors.

On the other hand, this type of message creates a great deal of fear in the older adults, making it less effective to protect them from the dangers that threaten them, and reducing the willingness of older adults to choose health behaviors. Also, the additional stress can lead to negative psychological consequences among older adults.

It can be concluded that the use of inappropriate and discriminatory content messages, especially in times of crisis, has profoundly harmed community and in fact denies the existence of a crisis by creating another one.

Keywords: Corona; Older adult; Society

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Infection Control and Prevention of COVID-19 in Nursing Homes

(Clinical Practice Guidelines)

* Adopted from CMS/CDC

Restrict visitation of all visitors and nonessential healthcare personnel.

Necessitate individuals who enter in compassionate situations to perform hand hygiene and use personal protective equipment.

Visitors with symptoms of a respiratory infection should not be allowed entry to the facility at any time.



Suggest visitors to refrain from physical contact with residents and others while in the facility.

If possible, create dedicated visiting areas near the facility entrance where residents can meet with visitors in a sanitized environment; these areas should be disinfected after each resident-visitor meeting.



Cancel communal dining and all group activities.



Remind residents to practice social distancing and perform frequent hand hygiene.

Screen all staff at the beginning of their shift for fever and respiratory symptoms.



Increase the availability and accessibility of alcohol-based hand rubs instructions reinforcing strong hand-hygiene practices, tissues, no-touch disposal receptacles, and face masks throughout the facility.

Properly clean, disinfect, and limit sharing of medical equipment between residents and areas of the facility.



Identify any possible infected individuals and frequently monitor the potential symptoms of respiratory infection as needed throughout the day.

Facilities experiencing an increased number of respiratory illnesses among patients/residents or healthcare personnel should immediately contact their local or state health department.



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How to build friendly cities for older adults

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Aged population is increasing because of enormous developments in health and socio-economic conditions. In the line with this phenomenon, it is imperative to take into account the fundamental or primary needs of older people. Since aging is a natural process, that is defined as an important stage of human life. Therefore, it is not possible to reverse its procedure but we could take control over aging complications through appropriate policymaking. For instance, Policies relating to city construction is one of the most important factors that have been affected older adults' life. Regarding, older people are experiencing phenomena of urbanization and urban development, appropriate and practical policies should be applied for this pivotal issue. Today, the vast majority of older adults live in urban regions. It should be noted that urban areas are not built based on older adults' needs and these inappropriate infrastructures are associated with increased risk of some functional, psychological, and social problems among this group. Then it is necessary that we applied some practical solutions to bring about a comfortable life for them.

Therefore, in this regard, in 2007, World Health Organization (WHO) developed age friendly city project as a respond based on challenges of aging demo-

graphics and increasing urbanization. In this perspective, older adults are equally eligible to benefit from citizenship rights(1). According to a for-mentioned issue, not only the cities and communities should provide accessible services for people aged 60 and over but also community's environments should be adopted based on older adults' need and priorities so that older adults could have access to social facilities in their society. Age-friendly environments foster health and well-being and the participation of people as they age. They are accessible, equitable, inclusive, safe and secure, and supportive. They promote health and prevent or delay the onset of disease and functional decline. They provide people-centered services and support to enable recovery or to compensate for the loss of function so that older people can continue to do the things that are important to them(2).

In 2002, World Health Organization proposed active aging framework, active-aging is "the process of optimizing opportunities for health, participation and security in order to enhance quality of life as people age"(3). This concept has six determinants, including health and social services, behavioral determinants, personal determinants, physical determinants, social determinants and economic determinants. Based on

this framework, World Health Organization turned its attention to the environmental and social factors. In fact, the purpose of age-friendly project is to encourage cities in various countries to change their communities into more age-friendly particularly for aged population.

It should be noted that outside environment and public building could have an effective impact on mobility, independent and quality of life among older adults and it may result in increasing aging in place. According to Age-friendly outdoor spaces and buildings checklist, the authorities should consider 11 items while planning for age-friendly cities: 1) Pleasant and clean environment, older adults usually complain about lack of city's cleanliness and to disturbing noise levels and odors. 2) Importance of green spaces. 3) Somewhere to rest, older people need to take rest when strolling around their local area. 4) Age-friendly pavements, inappropriate pavements could be dangerous for older people especially if they were uneven, narrow and cracked because it may lead to falling. 5) Safe pedestrian crossings, light cross should be amended based on older peoples' needs, for example visual and auditory signals could be applied. 6) Accessibility, older adults believe that cities are not designed based on their needs, therefore they prefer to stay at home due to some barriers (lack of ramp in some areas).7) A secure environment, the vast majority of older adults are afraid of going out because of security issues such as street lighting, violence, crime, drugs and homelessness in public places. 8) Walkways and cycle paths. 9) Age-friendly buildings, features should be considered for building age-friendly cities are: elevators, escalator, ramps, wide doorways and passage, suitable stairs (not too high or steep) with railings, on-slip flooring, and rest areas with comfortable seating, adequate signage, and public toilets with handicap access. 10) Adequate public toilets. 11) Older customers, shopping centers should available for older adults so that they could provide necessity goods independently(1, 4).

On the other hand, age-friendly cities could have an important role in reducing ageism, which is related to systematic stereotyping or discrimination against older people(5). In practice, when standards related to World Health Organization's model are taken into consideration, the broad range of barriers that have been already ignored by architects, designers, and urban planners will be completely disappeared. Therefore, older adults are able to have social contribution and obtain their citizen rights.

In Iran, age-friendly city project has been conducting in some cities. For instance, Isfahan is considered as age-friendly city because it can provide age-friendly facilities for older people. Furthermore, in Tehran,

"MANZELAT CARD" is developed cooperation with Culture and Art Organization of Tehran Municipality and Tehran Municipality for older people aged 65 and over. Holders of this card could have access to cultural, artistic, and sports services in their vicinities. World health organization has declared that Tehran province have potential to become an age-friendly city in near future.

Nevertheless, implementation of age-friendly city project needs to be accepted by stakeholders and its benefits must outweigh its costs from policymakers' perspectives. Furthermore, Government should involve related organizations, including secretariat of the national council of the older people ,municipality, department of physical education, and housing and urban development to make cities more tuned to the needs of older people. Unfortunately, to the contrary, efforts have been made in this issue, still there is a long way to achieve this goal.

Keywords: Aged population; Health; Friendly environments

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Student Letter

Metformin; New Applications for An Old Drug

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Metformin is the first-line therapy for Diabetes Mellitus type 2 and the only FDA approved agent for diabetes prevention(1, 2). Metformin is not licensed for use in type 1 and gestational diabetes but it can be safely used for weight loss, which is a major target in diabetic patients(3, 4). This can make metformin a good medicine for cardiovascular diseases prevention. The drug is also effective in the prevention and treatment of antipsychotic-induced obesity in patients with schizophrenia(5). Metformin significantly reduces the frequency of preeclampsia(6) and also, it is used in the treatment of the symptoms associated with polycystic ovary syndrome.

One of the common off-label uses of metformin is in non-alcoholic fatty liver disease (NAFLD). At this time it is not recommended by any guidelines to treat NAFLD(7). According to recent researches, it not only shows no significant improvement in liver histologic condition, but also worsens inflammation(8). Clinicians reported efficacy of metformin in NAFLD can be related to other advantages of medicine like lowering body mass index and blood pressure.

Antiaging and anticancer effects of metformin seem to be promising. A systematic review finds metformin effective adjuvant agent in some cancers. The under-

lying mechanism of antitumor activity is still unknown, but it shows a significant improvement in patients' survival in colorectal, prostate and breast cancers. Effectiveness of metformin for treating endometrial hyperplasia and urothelial cancers is not definite yet(9-11). Also, the medicine's efficacy in the treatment of blood cancer is approved, but it may be related to anti-obesity effects of the drug(12).

Metformin also showed neuroprotective effects in animal models. drug administration inhibits inflammation to improve brain function following traumatic brain injury(13). It provides a potential therapeutic benefit against mild cognitive impairment and Alzheimer's disease. The medicine reduces the risk of dementia in diabetic patients but the usage of metformin for the prevention of dementia in healthy older adults is not recommended by the available evidence(14). In addition, with function in brain tissue, metformin has shown to reduce Duchenne muscular dystrophy progression(15). It can be related to the drug's function in the stimulation of AMP-activated protein kinase.

Tuberculosis (TB) can be another potential indication for metformin prescription. A 2019 systematic review, found metformin an effective medicine in reducing the risk of TB in patients with diabetes. Treatment out-

comes of TB have shown a significant improvement in medicine users(16). Metformin may have a potential therapeutic role against multiple infections, which should be more considered by researchers.

Except for patients with renal insufficiency, metformin can be used safely in almost everyone. Widely use, makes metformin the aspirin of the 21st century(17). Despite more than 60 years of usage, our knowledge of its effect on human health is still increasing and potential clinical applications continue to expand(18).

Keywords: Metformin; Diabetes; Drug

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