

## FOCUS ON HEALTH PROFESSIONALS DURING THE SARS-COV-2 PANDEMIC - LITERATURE REVIEW

# PROFISSIONAIS DE SAÚDE EM FOCO DURANTE A PANDEMIA DE SARS-COV-2 - REVISÃO DE LITERATURA

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#### **ABSTRACT**

Introduction: The epidemics claim changes in behavior and often completely change the lives of health professionals. In addition to instituting the need to evaluate old methods of disease prevention. This study aimed to analyze the aspects related to biosafety and the health conditions of health professionals in the context of the SARS-CoV-2 pandemic. Methods: In this narrative review, articles were searched in various databases, organizations, and health entities using keywords compatible with MeSH, including COVID-19, Pandemia, Health professionals, Coronavirus 2019, SARS-CoV-2, personal protective equipment (PPE), Biosafety. Results and Discussion: The review of articles and manuals published in this area revealed that health professionals are being infected with SARS-CoV-2 and effective prevention measures and the correct use of PPE are needed, in addition to health assessment and monitoring, including mental health, of these professionals. Conclusion: There is a lack of data on which PPE may have the best protective effect against SARS-CoV-2, as well as how to use, remove, disinfect, store and replace it. It is essential to offer support to health professionals, both the provision of PPE, as well as in training and maintenance of mental health to reduce the adverse effects that this pandemic can generate in this population.

Keywords: COVID-19, Pandemia, Health professionals, SARS-CoV-2, personal protective equipment.

#### **RESUMO**

Introdução: As epidemias requerem mudanças de comportamento e muitas vezes mudam completamente a vida dos profissionais de saúde, além de instituir a necessidade de avaliar métodos antigos de prevenção de doenças. O objetivo desta revisão foi analisar os aspectos relacionados a biossegurança e as condições de saúde dos profissionais de saúde no contexto da pandemia por SARS-CoV-2. Métodos: Nesta revisão narrativa foram pesquisados artigos em várias bases de dados, organizações e entidades de saúde, utilizando palavras-chave compatíveis com MeSH, incluindo COVID-19, Pandemia, Profissionais de saúde, Coronavírus 2019, SARS-CoV-2, Equipamento de proteção individual (EPI) e Biossegurança. Resultados e Discussão: A revisão de artigos e manuais publicados nesta área revelou que os profissionais de saúde estão sendo infectados por SARS-CoV-2 e são necessárias medidas eficazes de prevenção e o uso correto de EPI, além da avaliação e monitoramento da saúde, incluindo a saúde mental, desses profissionais. Conclusão: Mais estudos e investimentos em estrutura e recursos humanos são necessários. Há uma falta de dados sobre quais EPI podem ter o melhor efeito protetor contra o SARS-CoV-2, bem como seu modo de uso, remoção, desinfecção, armazenamento e tempo de substituição. É essencial oferecer apoio aos profissionais de saúde, tanto no fornecimento de EPIs, quanto no treinamento e manutenção da saúde mental para reduzir os efeitos adversos que essa pandemia pode gerar nessa população.

Palavras-chave: COVID-19, Pandemia, Profissionais de saúde, SARS-CoV-2, Equipamento de proteção individual.

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### INTRODUCTION

At the end of 2019, pneumonia cases of unknown etiology were reported by Wuhan Municipal Health Commission, Hubei, China (ZHU; ZHANG; WANG; LI et al., 2020). The causative agent was identified on January 7, 2020, as the 2019-nCoV virus (LI; FAN; LAI; HAN et al., 2020) and later named by the International Virus Taxonomy Committee as SARS-CoV-2 (COSSARIZZA; DE BIASI; GUARALDI; GIRARDIS et al., 2020; LI; FAN; LAI; HAN et al., 2020). The cases have spread across China and the world, prompting World Health Organization (WHO) to issue a worldwide public health alert regarding the emergence of a new epidemic viral disease and subsequently to declare COVID-19 pandemic (COSSARIZZA; DE BIASI; GUARALDI; GIRARDIS et al., 2020; LI; FAN; LAI; HAN et al., 2020; WHO, 2020). Just as COVID-19 spread around the world, fear and uncertainty about the course of disease were also widespread and opinions were divided since only consensus, so far, is about its causative agent (COSSARIZZA; DE BIASI; GUARALDI; GIRARDIS et al., 2020; WHO, 2020).

In emergency health situations, health professionals, including nursing, are the most exposed, as they are present in the so-called "front line" and, consequently, end up being infected and to die (COFEN, 2020b). Health professionals died during a series of epidemics, such as plague, smallpox, measles, cholera, influenza, Ebola, SARS, and MERS. And, with COVID-19, the scenario has been shown to be even worse. Although this mortality reflects the willingness of health professionals to risk-taking care of other people, it can also be inducing by governments that ask these people to face outbreaks without the structure, materials, and often qualifications necessary to be successful and safe (COFEN, 2020b; FARMER, 2014). Thus, this narrative review aimed to analyze aspects related to biosafety and the health conditions of health professionals in the context of the SARS-CoV-2 pandemic.

## **METHOD**

It is a narrative review that aimed to know and analyze publications related to infection by SARS-CoV-2, health professionals, personal protective equipment (PPE), biosafety, and its consequences. This review searched for articles published in PubMed, Scopus, Embase, MedRxiv, Science Direct, and Web of Science databases, as well as in national and international health organizations and entities. The following descriptors were

used: COVID-19, Pandemia, Health professionals, Coronavirus 2019, SARS-CoV-2, PPE, Biosafety.

## **RESULTS AND DISCUSSION**

## Risk of contagion among health professional

According to Brazilian Federal Council of Nursing (COFEN), nursing category totals more than 2.2 million professionals working at the most diverse levels of healthcare in Brazil (COFEN, 2020b).

Other health professionals are also part of patient care process, including physiotherapists, who are responsible for monitoring and operating respirators, devices that replace lung functions in the event of diseases that compromise this organ, as in the severe cases of COVID-19 (MARTINEZ; MACIEL; MARTINS; MATTE *et al.*, 2020).

All categories of health professionals are in fight against SARS-CoV-2 and, due to their frequent exposure to patients, need to use Personal Protective Equipment (PPE) and mental support to face this pandemic and to achieve lowest absenteeism rates and/or negative repercussions of this essential population at that time (ADAMS; WALLS, 2020).

New outbreaks of coronavirus can be particularly dangerous for healthcare professionals. In Whuan, 15 health workers were infected at a hospital, demonstrating the potential for direct infection between people (PAULES; MARSTON; FAUCI, 2020).

In a study aiming to describe the epidemiological and clinical characteristics of SARS-CoV-2 infection, 138 confirmed cases of COVID-19 was retrospectively analyzed at Zhongnan Hospital in Wuhan, China. Of the 138 patients, 57 (41.3%) were presumed to have been infected in hospital, including 17 patients (12.3%) who were already hospitalized for other reasons and 40 health professionals (29%). In this series of unique cases, 26% of patients received care in intensive care unit (ICU), and mortality was 4.3% (WANG; HU; HU; ZHU *et al.*, 2020).

In China, 3300 health workers were infected with SARS-CoV-2, beginning of March and at the end of February at least 22 professionals died in China. In Italy, 20% of health professionals who were working to **COVID-19** combat became infected with SARS -CoV-2 and some died (LANCET, 2020).

In Brazil, there is no official survey of how many health professionals were infected or died from SARS-CoV-2 infection. However, according to Brazilian Federal Nursing Council, more than **28** thousand nursing professionals were infected and **295** died as a result of COVID-19, in Brazil, until **July 21**, 2020. The majority of cases are between 31 and 40 years old, and **57**% of deaths were registered between 41 and 60 years (COFEN, 2020b).

#### **Professional exhaustion**

During disease outbreaks, as in the case of this pandemic, health professionals on the front lines, in addition to being exposed to the risk of contagion by pathogens, are also subjected to unfavorable service conditions such as unfavorable working hours, psychological stress, violence, fatigue, Burnout syndrome, stigma and physical/psychological factors. Healthcare teams describe physical and mental exhaustion, the torment caused by difficult screening decisions, and the pain of losing patients and colleagues, all in addition to the risk of infection (LANCET, 2020).

Knowing the risks of infection by SARS-CoV-2, by itself, is already complex. When it is necessary to care for affected colleagues, it can become unforgettable. Another situation that can lead to increased stress in health professionals is the distance/isolation that occurs due to the fear that they may transmit the infection to family members and the general population (WONG; LEO; TAN, 2020).

#### **Protective measures**

With pandemic becoming larger, access to Personal Protective Equipment (PPE) for healthcare professionals is a growing and important concern, because shortage of PPE was described in most affected facilities and there is prediction that health care systems around the world can operate at capacity above maximum capacity for many months. But professionals need to be valued and understood as human, and their safety must be prioritized, since health professionals are **the** most valuable resources in all countries. Machines can be replaced, supplied urgently, not professionals (FARMER, 2014).

Preparing for growing number of cases of SARS-CoV-2 infection is essential. To this end, the essential equipment needed to care for patients must be guaranteed and keep the health workforce safe and effective. But to achieve this goal, a concerted approach is

required from all sectors, from municipal, state, and federal governments, to the private sector and to health service providers. Failure to act in a coordinated manner would make it impossible for many patients to obtain the care they need. In addition, it would lead to situation experienced in other countries such as Italy, with an overburdened and outdated health system, in which frontline health professionals must make a difficult decision about who receives and who does not receive care. Furthermore, without adequate PPE, health professionals tend to fall ill, compromising the functioning of entire health system. The human and economic costs of this scenario should not be underestimated (RANNEY; GRIFFETH; JHA, 2020).

Infection data from health professionals released recently has aroused widespread concern about **the** infection prevention and control in health institutions and general population (COFEN, 2020a). Increasing awareness of personal protection, sufficient PPE, and adequate preparation and response would play an important role in reducing the risk of infection for healthcare professionals (LANCET, 2020). It is important to note that the risk of exposure to infection caused by inappropriate behavior may be greater than risk caused by deficient PPE.

Health professionals who care for patients with COVID-19 are under enormous stress. The performance of PPE work activities is complicated and uncomfortable, especially if long-term procedures are required (COSSARIZZA; DE BIASI; GUARALDI; GIRARDIS *et al.*, 2020; LANCET, 2020; WHO, 2020).

According to WHO when healthcare professionals need to perform aerosol-generating procedures, they should pay attention to precautions that include the following PPE kit: gloves, apron/cloak, model N95 respirators and eye protection (glasses/face shields). However, it is worth noting that the WHO has a list of detailed precautions for health professionals, by activity and procedure for the use of PPE to care for individuals with suspected or confirmed COVID-19. Health professionals who must use PPE must be properly trained to wear and safely remove PPE, always emphasizing that their hands are clean before any contact with the face (BRASIL, 2020).

The widespread use of recommended barrier precautions (such as masks, gloves, aprons, and glasses) in the care of all patients with respiratory symptoms should be of the highest priority. There will be undiagnosed but infected patients everywhere, many of them with clinically mild cases or atypical presentations. Evidence related to transmissibility and mortality informs health professionals about the importance of

surveillance, preparation, active management, and protection from cross-infection in management of patients (ADAMS; WALLS, 2020; BRASIL, 2020; LANCET, 2020).

Controlling exposure to occupational hazards is a fundamental way to protect personnel. Exposures to respiratory pathogens transmissible in health facilities can generally be reduced or possibly avoided through administrative controls, correct and effective use of PPE. Immediate detection, effective screening, and isolation of potentially infectious patients are essential to avoid unnecessary exposures among patients, health professionals, and visitors to the unit (CDC, 2020).

Adherence to evidence-based guidelines for masks of Centers for Disease Control and Prevention (CDC), hand hygiene, and environmental hygiene increases the safety of health professionals (ADAMS; WALLS, 2020). The CDC reports that N95 respirators are the most frequently used PPE to control exposures to airborne infections, although their effectiveness is highly dependent on proper adjustment and use. However, the ideal way to prevent airborne transmission is to use articulation of interventions across the hierarchy of controls, not just the PPE (CDC, 2020).

On the other hand, a recent study states that protection is possible even without N95 or PFF2 masks. Health professionals were evaluated in various hospital outpatient practices. Surgical masks, when applied to patient and caregiver, provided protection effectively similar to that of N95 masks in incidence of laboratory-confirmed influenza among caregivers who were routinely exposed to patients with respiratory viruses. In a randomized study aimed at comparing effect of N95 respirators versus medical masks on prevention of influenza and other viral respiratory infections among healthcare professionals, the authors concluded that N95 respirators did not result in significant differences in laboratory-confirmed influenza (RADONOVICH; SIMBERKOFF; BESSESEN; BROWN et al., 2019).

In an investigation of two nurses infected with Ebola virus in Dallas, Texas, the contamination was attributed to the failure or incorrect use of PPE (CHEVALIER; CHUNG; SMITH; WEIL *et al.*, 2014) **as** well as in evaluation studies based on simulations in which the PPE of health professionals were contaminated with pathogens. To assess **the** PPE use and disposal practices, they concluded that inappropriate PPE removal and disposal practices can result in skin contamination and the clothes of health professionals (CASANOVA; ALFANO-SOBSEY; RUTALA; WEBER *et al.*, 2008).

Simulation is an important health training process. *In situ* simulation takes place in care units with scenarios that involve health professionals in their real work environment. And it is very effective for testing team readiness and for improving reliability and safety in work environments. Through *in situ* simulation, the identification and possibilities of solving unexpected problems occur that were not apparent in the initial planning, such as lack of supervision and coordination, environmental limitations, unsatisfactory equipment configuration, communication difficulties, unfamiliarity with protective equipment, loopholes in infection control and inadequate support during the crisis (KURUP; MATEI; RAY, 2017).

Health units can consider measures to extend the existing supply of PPE, especially with regard to N95 disposable respirators, training the staff to use them during serial meetings with patients ("prolonged use", that is, without removing or placing the belt again between meetings) or reuse them ("reuse", that is, removal, storage and replacement between patient meetings). While these practices have the potential benefit of providing respiratory protection with limited supplies of respirators, there is a risk of respirator contamination and contact transmission. The precise balance between the risk of contact transmission and the benefit of prolonged use or reuse associated with this strategy is unknown, although the risk is minimized if health professionals perform hand hygiene every time before and after touching the respirator. However, N95 disposable respirators used during aerosol generation procedures should be discarded after the procedure (CDC, 2009).

In order to prolong useful life of N95 respirators, in addition to correct placement, removal, and storage, it is recommended to use a physical barrier over respirators such as facial protectors (more efficient and reusable) or disposable surgical masks. There is no way to determine the maximum possible number of safe reuses for an N95 respirator as a generic number to be applied in all cases. The safe reuse of N95 is affected by several variables that affect respirator function and contamination over time (REBMANN; ALEXANDER; CAIN; CITARELLA *et al.*, 2009).

Kumar et al. (KUMAR; KASLOFF; LEUNG; CUTTS et al., 2020) tested the ability of 4 different methods decontamination agents for 4 models of N95 masks with experimental contamination with SARS-CoV-2 or vesicular stomatitis virus as a substitute. **The tested methods included** autoclave treatment, gassing with ethylene oxide, ionized nebulization with hydrogen peroxide, and exposure to vaporized hydrogen peroxide. They also proposed determining the tolerance of repeated decontamination cycles for each mask

model, maintaining structural and functional integrity. They concluded that a treatment cycle with all modalities was effective in decontamination and was associated with no structural or functional deterioration. Treatment with vaporized hydrogen peroxide was tolerated for at least 5 cycles per mask. Most notably, standard autoclave treatment was associated with no loss of structural or functional integrity in a minimum of 10 cycles for three pleated mask models. One of the N95 mask model, more rigid and without pleats, however, tolerated only 1 cycle. This finding will be highly relevant for institutions in low-resource areas in the world where autoclaves could reasonably be expected to be available at any health facility. However, it should be noted that this publication has not been peer-reviewed and these findings may or may not apply to other types of N95 masks (KUMAR; KASLOFF; LEUNG; CUTTS et al., 2020).

In another study, the objective was to assess the efficiency of filtration of surgical mask. The data were statistically significant and indicated that surgical masks were associated with very low filtration efficiency. This suggests that surgical masks may be inappropriate against airborne viruses and bacteria (KUMAR; KASLOFF; LEUNG; CUTTS et al., 2020). In a given technical bulletin, it is stated that surgical/procedural masks cannot provide certified respiratory protection; unless they are designed, tested, and certified by government organizations as a respirator (BAE; KIM; KIM; CHA et al., 2020; KUMAR; KASLOFF; LEUNG; CUTTS et al., 2020).

In order to evaluate the filtration performance of common tissue materials against nano-sized particles, including viruses, another study was performed. Five fabric categories were tested for polydispersed and monodispersed aerosols, including sweatshirts, t-shirts, towels, scarves, and prefabricated fabric masks. It is worth mentioning that cloth masks not considered PPE, being recommended only for the general population. The results obtained in the study show that common tissue materials can provide marginal protection against nanoparticles, including those in the particle size ranges containing viruses in exhaled breath. Other studies have evaluated the effectiveness of surgical and cotton masks in filtering SARS-CoV-2 and concluded that none of the masks tested effectively filtered out SARS-CoV-2 during coughing by infected patients (BAE; KIM; KIM; CHA et al., 2020).

Derrick et al. (DERRICK; GOMERSALL, 2005) evaluated **the** use of multiple surgical/procedural masks to provide greater filtration. They concluded that there is an approximate doubling in factor filtration when five masks were used compared to a single mask, however, the absolute filtration factor remained low. Therefore, the use of several

masks was not considered an adequate alternative to replace N95 masks (DERRICK; GOMERSALL, 2005).

In addition to PPE use, other protective measures must also be adopted. Public health measures aimed at reducing viral spread, such as social distance, cough etiquette, and hand hygiene, can make scarcity of resources such as PPE less severe, bridging the gap between medical needs and availability of treatments (ADAMS; WALLS, 2020; KURUP; MATEI; RAY, 2017; LANCET, 2020).

## CONCLUSION

All health professional categories are engaged in the fight against COVID-19 and, due to their close contact with patients, are at greater risk of contagion. For your protection, the use of appropriate Personal Protective Equipment (PPE) and in a correct way is necessary, but there is still no consensus on which are the most effective, with variable use according to health institution. In addition to direct risk of contagion, these professionals are also subjected to conditions of high stress, such as hours of exhausting work and the fear of contaminating their family members, which can worsen their perception of risk and care. Thus, especially during the pandemic period, these professionals who originally care for patients, need to be cared for and recognized as the true protagonists in the fight against COVID-19.

Therefore, further studies are needed on defining the effectiveness of PPE against SARS-CoV-2 and adopting measures aimed at improving the working conditions of these professionals, as well as taking care of their mental health. More investment in structural and human resources is needed to effectively combat the COVID-19 pandemic.

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### REFERENCES

ADAMS, J. G.; WALLS, R. M. Supporting the Health Care Workforce During the COVID-19 Global Epidemic. JAMA, Mar 12 2020.

BAE, S.; KIM, M. C.; KIM, J. Y.; CHA, H. H. et al. Effectiveness of Surgical and Cotton Masks in Blocking SARS-CoV-2: A Controlled Comparison in 4 Patients. Ann Intern Med, Apr 6 2020.

BRASIL. COVID-19 Guidance: Occupational Health and Safety and Infection Prevention & Control. Ministry of Health of Brazil: 9-10 p. 2020.

CASANOVA, L.; ALFANO-SOBSEY, E.; RUTALA, W. A.; WEBER, D. J. et al. Virus transfer from personal protective equipment to healthcare employees' skin and clothing. **Emerg Infect Dis**, 14, n. 8, p. 1291-1293, Aug 2008.

CDC. Regarding Respiratory Protection for Infection Control Measures for 2009 H1N1 Influenza among Healthcare Personnel 14 October 2009. Disponível em: https://www.cdc.gov/h1n1flu/guidance/ill-hcp\_qa.htm. Acesso em: 21 April 2020.

CDC. Strategies for Optimizing the Supply of N95 Respirators: COVID-19 | CDC. Disponível em: https://www.cdc.gov/coronavirus/2019-ncov/hcp/respirators-strategy/index.html. Acesso em: 20 April 2020.

CHEVALIER, M. S.; CHUNG, W.; SMITH, J.; WEIL, L. M. et al. Ebola Virus Disease Cluster in the United States — Dallas County, Texas, 2014. Morbidity and Mortality Weekly Report (MMWR), 63, n. 46, p. 1087-1088, 2014.

COFEN. Profissionais infectados com COVID-19 informado pelos Enfermeiros Responsáveis Técnicos/Coordenadores. Conselho Federal de Enfermagem 2020a.

COFEN. Saúde de profissionais de enfermagem é foco em tempos de Covid-19. 20 April 2020. Disponível em <a href="http://www.cofen.gov.br/saude-de-profissionais-de-enfermagem-e-foco-em-tempos-de-covid-19\_78321.html">http://www.cofen.gov.br/saude-de-profissionais-de-enfermagem-e-foco-em-tempos-de-covid-19\_78321.html</a>. Acesso em 22 July 2020.

COSSARIZZA, A.; DE BIASI, S.; GUARALDI, G.; GIRARDIS, M. et al. SARS-CoV-2, the Virus that Causes COVID-19: Cytometry and the New Challenge for Global Health. Cytometry A, 97, n. 4, p. 340-343, Apr 2020.

DERRICK, J. L.; GOMERSALL, C. D. Protecting healthcare staff from severe acute respiratory syndrome: filtration capacity of multiple surgical masks. J Hosp Infect, 59, n. 4, p. 365-368, Apr 2005.

FARMER, P. Diary: Ebola. 2014. Disponível em: https://www.lrb.co.uk/the-paper/v36/n20/paul-farmer/diary. Acesso em: 27 May 2020.

KUMAR, A.; KASLOFF, S. B.; LEUNG, A.; CUTTS, T. et al. N95 Mask Decontamination using Standard Hospital Sterilization Technologies. medRxiv. 2020.

KURUP, V.; MATEI, V.; RAY, J. Role of in-situ simulation for training in healthcare: opportunities and challenges. **Curr Opin Anaesthesiol**, 30, n. 6, p. 755-760, Dec 2017.

LANCET, T. COVID-19: protecting health-care worker. The Lancet, 395, n. 10228, p. 922, 2020.

LI, G.; FAN, Y.; LAI, Y.; HAN, T. et al. Coronavirus infections and immune responses. J Med Virol, 92, n. 4, p. 424-432, Apr 2020.

MARTINEZ, B. P.; MACIEL, F.; MARTINS, J. A.; MATTE, D. L. *et al.* COVID-19: Papel do Fisioterapeuta em diferentes cenários de atuação. Disponível em: https://www.coffito.gov.br/nsite/?p=15901. Acesso em: 20 April 2020.

PAULES, C. I.; MARSTON, H. D.; FAUCI, A. S. Coronavirus Infections-More Than Just the Common Cold. JAMA, Jan 23 2020.

RADONOVICH, L. J., JR.; SIMBERKOFF, M. S.; BESSESEN, M. T.; BROWN, A. C. *et al.* N95 Respirators vs Medical Masks for Preventing Influenza Among Health Care Personnel: A Randomized Clinical Trial. **JAMA**, 322, n. 9, p. 824-833, Sep 3 2019.

RANNEY, M. L.; GRIFFETH, V.; JHA, A. K. Critical Supply Shortages - The Need for Ventilators and Personal Protective Equipment during the Covid-19 Pandemic. **N Engl J Med**, 382, n. 18, p. e41, Apr 30 2020.

REBMANN, T.; ALEXANDER, S.; CAIN, T.; CITARELLA, B. et al. APIC Position Paper: Extending the Use and/or Reusing Respiratory Protection in Healthcare Settings During Disasters. 2009.

WANG, D.; HU, B.; HU, C.; ZHU, F. et al. Clinical Characteristics of 138 Hospitalized Patients With 2019 Novel Coronavirus-Infected Pneumonia in Wuhan, China. JAMA, Feb 7 2020.

WHO. WHO Director-General's opening remarks at the media briefing on COVID-19 - 11 March 2020. v. , 11 Mar 2020. Disponível em: https://www.who.int/dg/speeches/detail/who-director-general-s-opening-remarks-at-the-media-briefing-on-covid-19---11-march-2020.

WONG, J. E. L.; LEO, Y. S.; TAN, C. C. COVID-19 in Singapore-Current Experience: Critical Global Issues That Require Attention and Action. JAMA, Feb 20 2020.

ZHU, N.; ZHANG, D.; WANG, W.; LI, X. et al. A Novel Coronavirus from Patients with Pneumonia in China, 2019. **N Engl J Med**, 382, n. 8, p. 727-733, Feb 20 2020.