

REVIEW

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# Opportunities and challenges encountered in managing cervical cancer during the coronavirus disease 2019 pandemic

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## Abstract

**Objectives** The COVID-19 pandemic, while putting pressure on the global healthcare system, has had a significant impact on the prevention, diagnosis, and treatment of cervical cancer. The aim of this study is to provide an overview of the challenges and opportunities presented to cervical cancer during the COVID-19 pandemic and to provide lessons for better coping with cervical cancer in future pandemics.

**Methods** The search terms included the following: SARS-CoV-2 and/or COVID-19 with cervical cancer and HPV. The initial literature search began on June 1, 2022 and ended on March 1, 2023.

**Outcome** COVID-19 has hindered the cervical cancer screening, delayed the diagnosis and treatment of cervical cancer, increased the public's anxiety, and negatively affected the management of cervical cancer. However, the occurrence of COVID-19 pandemic has promoted the development of new human papillomavirus (HPV) tests and improved the rates of HPV self-sampling, offering a small window of opportunity to eliminate cervical cancer.

**Conclusions** In the next few years, the COVID-19 pandemic will come to an end, and the eradication of cervical cancer should always be carried out. We should draw lessons and experience from this global pandemic, and make efforts for the subsequent eradication of cervical cancer.

**Keywords** COVID-19, Cervical cancer, HPV, Anxiety

## Introduction

It has been more than 3 years since the coronavirus disease 2019 (COVID-19), a lung disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), was declared as a pandemic. The virulence of the novel coronavirus variant has been greatly reduced, but it

remains a global concern and poses a major challenge to the global healthcare system [1]. In the previous COVID-19 pandemic, caring for and treating COVID-19 patients have been a major goal of most countries; however, this may have affected other priorities of the global healthcare system, such as cancer treatment and screening, and may even have delayed the identification and diagnosis of cancer patients, thus affecting their survival [2–5]. As one of the three major types of gynecological cancers, several aspects of cervical cancer have been greatly affected by the current pandemic: vaccination, screening, diagnosis, and treatment; the pandemic also caused emotional and psychological pressure among this patient group. Although the COVID-19 pandemic has negatively affected the efforts of the World Health Organization (WHO) to eliminate cervical cancer, some new HPV

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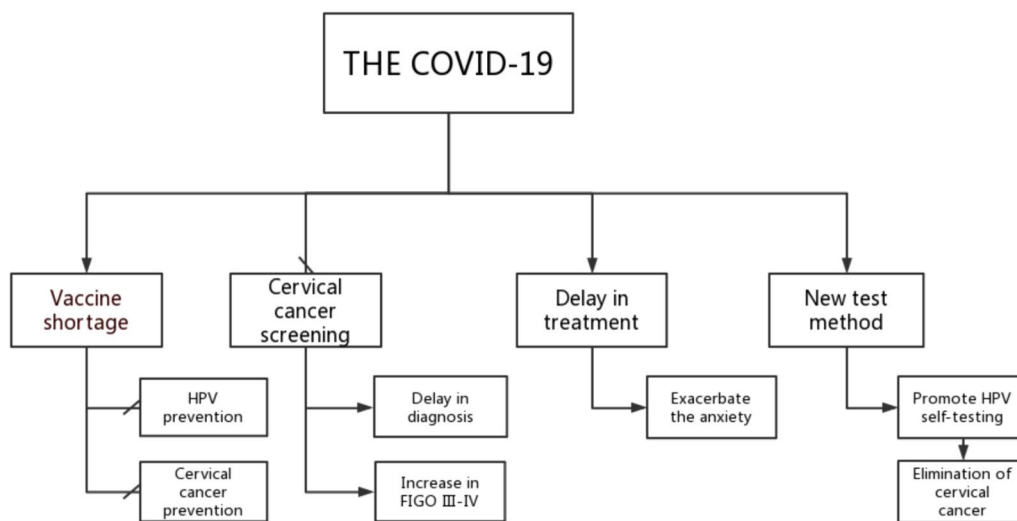
detection strategies have been developed based on the COVID-19 detection method, making it possible for people to detect HPV at home. If this method is promoted, the detection of HPV will be improved further. This is an opportunity that the past COVID-19 pandemic has given to eliminate cervical cancer. This review aimed to address the opportunities and challenges faced by cervical cancer patients during the COVID-19 pandemic, as shown in Fig. 1.

**Results**

**Effect of COVID-19 in cervical cancer screening**

After the COVID-19 pandemic, many countries and regions have reduced or even discontinued cancer screening, including cervical cancer screening [6–8]. The COVID-19 pandemic has exposed the lack of pharmaceutical products, personal protective equipment, and diagnostic supplies worldwide [9]. This has undoubtedly impacted the implementation of cervical cancer screening programs, with up to 74% of the 57 HPV DNA testing laboratories from 30 countries reporting the lack of supplies and staffing shortages (54%) [10]. According to the study conducted by Shen et al. [11], during the COVID-19 pandemic in the United States, the cervical cancer screening rate decreased by 80–90%; in Taiwan and China, the cervical cancer screening rate decreased by 15–40%. Although the American Cancer Society has stated that cancer screening during the COVID-19 pandemic is still important, the decline in cervical cancer screening rates is inevitable. Similar results have been observed worldwide, with Poland reporting a cervical cancer screening rate of 17% among women in 2020 as

a result of the COVID-19 pandemic [12]. The number of samples accepted by the United Kingdom laboratories responsible for HPV screening also decreased significantly from April to June 2020, and approximately 70% of women were forced to delay cervical cancer screening [13]. Castanon et al. [13] estimated that of the 146,391 women whose next scheduled screening was postponed due to the COVID-19 pandemic, an additional 60 cases of cancer were expected to occur. Compared with developed countries, the cervical cancer screening rate in low-income countries is adversely affected [14]. In low-income countries, the medical resources are relatively scarce, and the COVID pandemic has increased the tension on medical resources. Cervical cancer screening and other non-essential health services have been temporarily suspended to prioritize the care of symptomatic COVID-19 patients. According to the COVID-19 and the Cancer Global Modeling Alliance, interruptions in cervical cancer screening associated with the COVID-19 pandemic will increase the cancer burden in women aged below 50 years by 5% and 6% [15]. Due to low income, ethnicity, remoteness of residence, and gender, these unserved people have experienced differences in cancer screening and management in the current pandemic, and social and healthcare-related inequalities caused by COVID are further exacerbating [16]. In addition to the obvious reduction in screening rates due to the strain on health resources in the current pandemic, the impact of a decline in patient’s interest in undergoing preventive screening cannot be ignored. A 2020 study that examined the number of Google searches for the term “pap smear” showed a 54.1%



**Fig. 1** The summary of the effects of COVID-19 on cervical cancer

decrease in the use of these search terms compared with that in the same period prior to the pandemic [17]. Although the COVID-19 pandemic has caused difficulties in the implementation of cervical cancer prevention measures, the corresponding response measures are constantly being promoted. Of course, the impact of COVID-19 on cervical cancer screening will also be short-lived, as these screening services resume soon after the pandemic.

#### **COVID-19 pandemic causing great difficulties to the vaccination of HPV**

HPV is the most important cause of cervical cancer; therefore, the primary preventive measure against cervical cancer is HPV vaccination [18, 19]. Prior to the COVID-19 pandemic, countries worldwide have been promoting cervical cancer vaccination to prevent cervical cancer. The WHO also has a strategy to accelerate the elimination of cervical cancer, and 200 million doses of HPV vaccine were administered worldwide by 2020 [20, 21]. In the COVID-19 pandemic era, the realization of this strategy has become a major challenge. Compared with that in 2019, the global annual dose of the HPV vaccine was reduced by 24% in 2020 [12]. A gap in global vaccination rates is not expected to occur until 2031 [22, 23]. However, an analysis of Google searches shows that since the beginning of the pandemic, the level of interest in HPV vaccination has remained unchanged compared with that prior to the COVID-19 pandemic [24]. Although the COVID-19 pandemic reduced the people's enthusiasm to undergo cervical screening, it did not dampen their enthusiasm for HPV vaccination. However, due to the shortage of health resources caused by the pandemic, interruption of the vaccine supply chain, and deterioration of the country's financial health status, cervical cancer vaccination has been affected to a certain extent [25–28]. The coverage rate of HPV vaccine in rural areas is 10% lower than that in urban areas, which is caused by a number of factors, including low public awareness, reduced interest of medical staff in carrying out prevention activities, and limited number of outlets providing medical services [29]. In many countries worldwide, a large proportion of the population lives in rural areas; therefore, essential methods to promote HPV vaccination in these areas should be developed. The COVID-19 pandemic has caused great difficulties in implementing cervical cancer vaccination. To overcome this difficult period and complete the WHO strategic plan to eliminate cervical cancer, funded by governments of various countries, the implementation of national free HPV vaccination is an effective method.

#### **COVID-19 pandemic adversely affecting the treatment of cervical cancer patients**

The novel coronavirus pandemic not only has an indelible impact on the prevention of cervical cancer but also affects the choice of surgical method for cervical cancer patients, which has a negative effect on the treatment of cervical cancer patients [30]. However, the impact of COVID-19 on cervical cancer patients is more focused on the longer waiting period for surgery and the delays in treatment than on the change in surgical methods.

Physical isolation, travel restrictions, and reduced public transport facilities (including roads, railways, and airports) owing to the COVID-19 pandemic have made it difficult for patients to reach hospitals for treatment. Second, during the COVID-19 pandemic, patients are worried about contracting COVID-19 while staying in healthcare facilities, which further discourages them from seeking medical attention [31]. In addition, most hospitals have discontinued performing some non-essential surgical procedures and postponed the provision of some non-essential services during the COVID-19 pandemic [32, 33]. All of these factors have led to a serious delay in the completion of treatment for cervical cancer patients, thus decreasing their survival rate. In the current COVID-19 pandemic, the delayed diagnosis and treatment of cervical cancer have resulted in an increase in the number of patients and deaths. A previous study in Brazil showed that the proportion of women diagnosed with the International Federation of Gynecology and Obstetrics stage III–IV cervical cancer increased from 43.3% before the pandemic to 56.8% during the pandemic [34]. However, Gupta et al. [31] stated that the mortality rate (2.52%) associated with a 9-week delay in cervical cancer treatment was estimated to be 2.52%, which further increased to 3.8% due to a 6-month delay. According to various studies, in patients with cervical cancer, pelvic control decreases by 0.7–1% and the overall survival decreases by 0.6–0.8% each day for each additional day of interruption of standard 56-day radiotherapy treatment, which has a significant impact on the early stage of cervical cancer [35–38]. In the current COVID-19 pandemic, maximizing medical conditions to save and extend the lives of most patients is the highest priority [39, 40]. Gupta et al. [31] found that, compared with patients with advanced-stage cervical cancer, disease progression in patients with early-stage cervical cancer was more likely to be delayed by COVID-19. So when healthcare resources were stretched by the COVID-19 pandemic, many hospitals prioritized patients with diseases that could be cured or that could benefit from treatment. When medical resources are strained by a pandemic, they can be moderately tilted in patients who benefit more to reduce the adverse effects of a pandemic.

### **COVID-19 pandemic intensifying the anxiety and psychological stress of cervical cancer patients**

The COVID-19 pandemic not only affects the treatment and prognosis of cervical cancer but also increases the psychological pressure and anxiety levels of patients with cervical cancer [41, 42]. During the COVID-19 pandemic, various preventive measures and a shortage of medical resources have made it more difficult for patients to seek medical care, causing anxiety among patients with various cancer types, including cervical cancer. Despite the heightened anxiety of patients caused by the pandemic, Ghosh et al. found that the majority of patients (68%) preferred to continue receiving chemotherapy; this finding suggests that patients may be more concerned about treating their cancer than the risk of contracting COVID-19 [43]; those receiving palliative chemotherapy are more concerned about their disease progression status than the risk of contracting COVID-19. This may be because they already know that their prognosis is poor and fear that their disease status will worsen during the COVID-19 pandemic. Hence, the medical staff can provide patients with more psychological comfort and support during treatment to help relieve their anxiety. Compared with the status when the COVID-19 pandemic first emerged in 2019, the people's anxiety has gradually reduced owing to the enhanced understanding of COVID-19, the continuous update on COVID-19 treatment methods, and the development of COVID-19 vaccines. This finding suggests that doctors should focus on assessing anxiety levels and reducing anxiety in order to manage patients' mental health during the pandemic.

### **Increased risk of developing COVID-19 and serious events in patients with cervical cancer**

Both malignancy and tumor treatment may lead to decreased physical capacity (performance status) and impaired immune status. Furthermore, patients have an increased need for medical care and hospitalization [44]. In the current pandemic, patients with cancer appear to be more likely to be diagnosed with COVID-19 and at a higher risk of experiencing severe events [45]. A previous study conducted by Chinese scholars showed that receiving tumor therapy in the last 14 days prior to infection was identified as a risk factor for developing serious events (hazard ratio: 4.07, 95% confidence interval: 1.08–15.3) [46]. The coronavirus receptor angiotensin-converting enzyme 2 (ACE2) and transmembrane serine protease 2 (TMPRSS2) play key roles in SARS-CoV-2-infected cells [47]. The expression levels of ACE2 and TMPRSS2 in different tumor cells may indicate the susceptibility of different tumors to COVID-19. ACE2 and TMPRSS2 are overexpressed in many cancers, including cervical squamous cell carcinoma and cervical adenocarcinoma

[48, 49]. All of these factors may increase the risk of developing COVID-19 and serious events in patients with cervical cancer. With this in mind, determining the method of managing patients with cervical cancer during the COVID-19 pandemic is particularly important. Cervical cancer poses a considerable threat to the lives of patients, and delayed treatment may affect the effectiveness of cancer treatment. In this particular period of the COVID-19 pandemic, the recommendations for the management of cervical cancer should consider several aspects, including the staging of cervical cancer, choice of tumor treatment, local incidence of COVID-19, and local medical conditions.

### **Recommendations and lessons for the management of cervical cancer patients in developing countries during the pandemic**

The incidence of cervical cancer is high in developing countries, which will face more challenges during the COVID-19 pandemic owing to the scarcity of healthcare resources in these countries [50]. Approximately 85% of cervical cancer cases occur in developing countries [51]. In these countries, the scarcity of medical resources were even more pronounced during the COVID-19 pandemic. In view of the management of cervical cancer in developing countries, with the maximum protection of the rights and interests of patients, Estevez-Diz et al. [50] provided some suggestions in Table 1.

Although cancer patients may have an increased risk of developing serious events related to COVID-19, tumor treatment in cancer patients cannot be substantially delayed to avoid endangering the tumor prognosis. Therefore, the doctors need to carefully consider the treatment management of different patients, and the management of each patient should be decided on a case-by-case basis; the doctors should determine the risks and benefits of each strategy.

### **Effect of the COVID-19 pandemic in the development of some HPV detection methods and the promotion of self-detection of HPV**

The COVID-19 pandemic has affected the screening of HPV to a certain extent; however, in the current COVID-19 pandemic, some new virus detection methods have been used, such as bamboo shoots after a spring rain, which also greatly promoted the performance of HPV screening. These new detection methods, such as the TruScreen (TS01) test [52] (a portable instrument that uses optical and electrical signals to analyze cervical tissues with a built-in algorithm in real time), TR512-peptide-based virus detection [53] (which enables the TR512-peptide-based biorthogonal capture and enrichment of commercially available

**Table 1** The summary of the recommendations for cervical cancer management during the COVID-19 pandemic

Situation	Suggestion
Unnecessary hospitalization	Avoid
The visits to hospitalized patients	Restrict
Screening for COVID-19	Take and divert according to the result
Advanced incurable cancer	Suspend
early-stage cervical cancer	Consider the local health systems
Locally advanced cervical cancer	Uninterrupted radiotherapy and chemotherapy
Surgical staging of locally advanced cervical cancer	Avoid
The delay in surgery has a negative impact on the patient's health	Avoid such delays

Texas red fluorophore-labeled nucleic acids on functionalized paper), and CRISPR-assisted DNA detection [54] (a novel dCas9-based DNA detection technique), can be used for the detection of HPV, has a low cost, high detection speed, and good specificity and sensitivity. The update and emergence of these testing methods will undoubtedly provide a great opportunity to eliminate cervical cancer. Therefore, an appropriate HPV testing method should be selected, and the goal of eliminating cervical cancer should be achieved.

Simultaneously, the COVID-19 pandemic has promoted the progress of HPV self-sampling. HPV self-sampling is similar to colon cancer screening at home via fecal tests. Self-sampling is a promising strategy; although it has not been approved for cervical cancer screening worldwide, self-collection of vaginal samples may contribute to better screening. The COVID-19 pandemic also promoted the application of this strategy [55]. A previous Nigerian study [56] has shown that delivering sealed, clean self-samplers to patients and self-collection greatly avoids exposure to COVID-19. Even after the termination of the current pandemic, a convenient method of sample self-collection would certainly promote HPV screening. Self-sampling can also be increasingly performed in countries with low cervical cancer screening rates or in areas with limited local medical resources (such as rural areas) [12]. Self-sampling for HPV testing can be demonstrated with simple graphics or animated videos to achieve the same accuracy as that of clinicians [57]. A study of 180,000 women in the Netherlands showed no difference in the sensitivity and specificity between self-sampling and physician-performed testing [58]. The promotion of self-sampling will also greatly promote cervical cancer screening, especially in areas where HPV screening cannot be completed due to economic backwardness and religious beliefs, and lay the groundwork for further achieving the WHO's goal of eliminating cervical cancer.

### Limitations of the study

This study summarizes the challenges and opportunities for cervical cancer during the COVID-19 pandemic, but is not a systematic study.

### Conclusion

The COVID-19 pandemic has severely affected the screening, diagnosis, treatment and prevention of cervical cancer. The impact of cervical cancer will be especially significant in developing countries, where the majority of health resources are being allocated to combatting COVID-19 and are already limited. During the COVID-19 pandemic, the surgical treatment and chemotherapy of cervical cancer patients have been affected to varying degrees, and the radiotherapy and chemotherapy of many patients have been delayed, resulting in adverse outcomes such as disease progression, poor prognosis and increased mortality.

During the pandemic, patients with cervical cancer have also developed varying degrees of anxiety due to the delays in the treatment of their disease. Although much attention has been paid to managing the patient's condition, providing care and understanding to the patient and improving their mental health should also be taken into consideration. Although some form of flow control strategy may be necessary to stop the spread of COVID-19, the healthcare systems should not only focus on curbing its spread but should also be reorganized to continue providing healthcare and necessary treatments [31]. In developing countries, the management of cervical cancer patients during the pandemic remains a challenge. Better management of patients with cervical cancer in this environment is an urgent matter that should be addressed. The management of cervical cancer varies from person to person, the clinical status of patients should be taken into account, and the pros and cons of the program should be weighed to maximize the protection of patients' rights and interests. However, the COVID-19 environment

brings not only challenges but also opportunities for cervical cancer management. Based on the detection methods used for COVID-19, some convenient and low-cost HPV detection strategies have been developed, and self-testing for HPV at home is promoted. The widespread application of this self-testing method will inevitably accelerate cervical cancer screening and contribute to the elimination of cervical cancer in the post-epidemic era.

## Executive Summary

1. Several aspects of cervical cancer were greatly affected by the current pandemic.
2. The COVID pandemic has increased the tension on medical resources.
3. Healthcare-related inequalities have been further exacerbated by the pandemic.

## Abbreviations

ACE2	Angiotensin-converting enzyme 2
COVID-19	Coronavirus disease 2019
HPV	Human papillomavirus
SARS-CoV-2	Severe acute respiratory syndrome coronavirus 2
TMPRSS2	Transmembrane serine protease 2
WHO	World Health Organization

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## Author contributions

SD: Writing—Original Draft, YW: Supervision, YD: Supervision and Funding Acquisition. All authors read and approved the final manuscript.

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## Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

## Declarations

### Ethical approval and Consent to participate

Not applicable.

### Consent for publication

Not applicable.

### Competing interests

There is no competing interest to declare.

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