## ORIGINAL ARTICLE



# A perspective on dental activity during COVID-19: The Italian survey

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#### Abstract

**Objectives:** During the months of March and April 2020, Italy saw an exponential outbreak of COVID-19 epidemic. Dental practitioners were particularly limited in their routine activity, and the sole performance of urgent treatments was strongly encouraged during the peak of the epidemic. A survey among dental professionals was performed between 6th and 13th of April, in order to evaluate the status of dental practice during COVID-19 in Italy.

**Materials and Methods:** An online anonymous questionnaire was administered to retrieve data on the dental procedures performed, the preventive measures adopted, and the predictions on the future changes in dentistry following the pandemic.

**Results:** The survey was completed by 3,254 respondents and, according to the results obtained, dental activity was reduced by the 95% and limited to urgent treatments. The majority of the surveyed dentists employed additional personal protective equipment compared to normal routine, although in a non-negligible number of cases difficulty in retrieving the necessary equipment was reported.

**Conclusions:** The survey provided a snapshot of dental activity during the SARS-CoV-2 outbreak. Overall, following the peak of the epidemic, it is probable that dental activities will undergo some relevant changes prior to fully restart.

#### KEYWORDS

dental education, dental public health, infection control, practice management, prevention, virology

# 1 | INTRODUCTION

COVID-19 has seen in the last few months a worldwide diffusion, with more than 9 million cases confirmed (https://gisanddata.maps. arcgis.com/apps/opsdashboard/index.html#/bda7594740fd402 99423467b48e9ecf6). Italy was the country with the earliest diffusion in Europe. Lockdown was disposed at the end of February in some northern regions, Lombardy and Veneto, to limit the

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exponential increase in the number of infected subjects, and was followed on the 9<sup>th</sup> of March by the rest of the country due to the rapid escalation in the numbers of contagion. The highest number of active cases (108,237) was registered on the 20<sup>th</sup> of April and was followed by a slow, progressive decrease, which led to the complete end of the lockdown on the 3<sup>rd</sup> June 2020.

During the peak of the epidemic, dental care was considered an essential service. However, Italian regulations imposed to limit as much as possible routine activity during the lockdown, as only urgent procedures which could not be postponed could be performed. As a matter of fact, the straightforward transmission route of SARS-CoV-2, the relatively close contact with the patient and aerosol generation during the majority of dental procedures concur to exposing dental practitioners to a higher risk of contagion, (Izzetti, Nisi, Gabriele, & Graziani, 2020; Meng, Hua, & Bian, 2020; Peng et al., 2020). Indeed, Sars-CoV-2 is transmitted through aerosol and droplets and has a relatively long resistance in aerosol for up to 3 hours (van Doremalen et al., 2020).

Numerous guidelines and recommendations on resuming dental activities are released these days (Cochrane Oral Health, 2020). Standard procedures appear insufficient in protecting from SARS-CoV-2, and thus specific measures to prevent virus transmission should be adopted to safeguard the health of both patients and oral care providers (Izzetti et al., 2020; Meng et al., 2020; Peng et al., 2020). In particular, several steps have been added for the correct management of dental patients in order to identify subjects at higher risk of being infected. Phone and in-office triage, along with temperature recording, have become routine procedures to investigate the presence of symptoms suggestive for COVID-19 and behaviours which may have caused contagion (Izzetti et al., 2020; Meng et al., 2020). Moreover, COVID-19 has led to a re-design of the dental office, from the waiting room to the clinical setting, and has made necessary the adoption of Personal Protective Equipment (PPE) also for non-clinical staff (Izzetti et al., 2020; Meng et al., 2020).

During the lockdown, a survey on the current status of dental profession was performed, with the aim to give insight into how dentistry was changing and what were the expectations for the future. In the present work, the acute impact of the COVID-19 pandemic on the dental profession in Italy and the predictions on the impact on dentistry are reported.

#### **MATERIALS & METHODS** 2

After a protocol preparation and approval from the Committee on Bioethics of the University of Pisa (Review No. 11/2020), a questionnaire for dental practitioners, aimed at investigating various aspects of dental activity during the early stages of the COVID-19 pandemic, was specifically developed for the study. Initially, the preliminary questionnaire was pretested on 20 subjects prior to administration on a national scale. For all the items of the questionnaire, an intraclass correlation coefficient (ICC) >0.80 was considered satisfactory. In cases of items with ICC values <0.80, the questionnaire was edited in order to increase ICC. An online platform was directly emailed by the National Federation of Medical Doctors and Dentists (Federazione Nazionale Ordine dei Medici Chirurghi e Odontoiatri, Commissione Albo Odontoiatri-FNOMCeO) to all the provincial coordinators with the request for distribution among colleagues. An open invitation was posted on social media and promoted via professional networks. The survey was administered between the 6<sup>th</sup> April and the 13<sup>th</sup> April 2020.

The questionnaire (Appendix S1) addressed the following dimensions:

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- Demographic and professional status
- Professional activity during the epidemic
- Adherence to preventive measures
- Questions on the future perspectives of dental practice.

The demographic and professional status section aimed at collecting data on age, gender, practice location, professional background and practice organization (number of dental chairs, collaborators, dental assistants). The status of dental activity was investigated in terms of types of treatments performed and number of procedures per week.

The adherence to the preventive measures suggested by the Italian dental institutions and associations was investigated according to four domains previously identified (Izzetti et al., 2020). In particular, these domains were as follows:

- Phone Triage (Phase I)
- In-office triage and dental office preparation (Phase II)
- Dental treatment (Phase III)
- Postdental treatment management of the dental office (Phase IV).

A focus on highly epidemic areas, registering the higher number of cases, was also performed in order to evaluate the potential presence of differences between the regions in Northern Italy and the rest of the country.

Finally, the subjective predictions on the potential changes occurring in dental practice following the pandemic were investigated, in order to give an overview of the professionals' point of view.

Sample size estimation for representativeness was set at 1,491 responses, considering a CI of 95%, an error of 2% and maximum heterogeneity in a population of 50,000 subjects. Overall, the total number of dental professionals in Italy is reported to be around 62,000, although unofficially it would appear that the active dentists are approximately 45,000 (according to the National Federation of Medical Doctors and Dentists-FNOMCeO; https://portale.fnomceo.it/).

Data analysis was conducted using SPSS version 26 (IBM). Descriptive and inferential statistics were provided. Chi-square and Fisher-Yates tests were used to compare categorical parameters and frequencies. Non-parametric correlation analyses were performed with Spearman rank analyses. Data were graphically tested for normality, and logarithmic or square root transformations were made as needed before applying the adequate non-parametric tests. Statistical significance was set with a *p*-value of .05.

# 3 | RESULTS

## 3.1 | Demographic and professional status

A total of 3,254 respondents completed the survey, representing about the 5.25% of Italian dental professionals. The study sample's geographic distribution reflected the distribution of general dental population. The sample was representative of the general dental population in Italy per gender and age. The characteristics of the respondents are illustrated in Table 1. In the results, only significant data are presented.

# 3.2 | Professional activity during the epidemic

At the time of the survey (6<sup>th</sup>-13<sup>th</sup> April 2020), 99.7% of participants reduced the activity to urgent treatments or totally stopped working. As per the procedures performed, the treatment of pulpitis, prosthesis de-cementation and abscess were the most common urgent procedures provided (Table 1). The mean number of procedures performed per week was 5.27/dentist. Overall, it is estimated that the surveyed

TABLE 1	Summary	of sample	characteristics
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professionals have guaranteed 11,778 urgent dental treatments from the start of the lockdown (9<sup>th</sup> March 2020) to the date of the survey.

#### 3.3 | Adherence to preventive measures

# 3.3.1 | Phone triage

Phone triage was performed by the 95% of the sample, and 98.8% assessed the presence of symptoms suggestive for COVID-19. Moreover, the potential risk of contact with infected subjects was also investigated by the majority of surveyed dentists (Table 2).

Sample characteristics         3,254 (62.5% M, 37.5% F)           Global sample         3,254 (62.5% M, 37.5% F)           Mean age         46.36 ± 12.20           Year of activity start         2,000 ± 11	
-	
Year of activity start 2,000 ± 11	
Dental office owners 2,116 (65%)	
Dental professionals practicing in Lombardy & Veneto 898 (27.6%)	
Dental professionals currently working 118 (3.6%)	
Dental professionals currently not working 958 (29.4%)	
Dental professionals working only at University/national health service 62 (1.9%)	
Dental professionals working near to national health service dental center 1,362 (41.9%)	
Dental professionals informed on COVID-19 preventive measures 1,940 (90%)	
Characteristics of the dental office owners	
Mean number of co-workers (dental professionals) 2.45 ± 2.083	
Mean number of dental assistants $2.24 \pm 1.73$	
Mean number of dental chairs 2.83 ± 1.64	
Dental offices with more than 3 dental chairs 477 (22.5%)	
Mean number of appointments/day before COVID-19 $16.83 \pm 13.03$	
Activity status	
Currently not working 24.4%	
Only emergency treatment 75.5%	
Working as usual 0.3%	

#### Dental treatment performed

		Mean frequency/week of emergency treatments					
	0	2	5	≥10	Recurrence of the treatment	Total number of treatments performed in the sample	
Pulpitis	27.2%	44.2%	7.4%	0.1%	17.5%	2,066	
Abscess	52.2%	42.2%	5.1%	0.0%	15.9%	1,876	
Dental impaction	81.6%	16.8%	1.5%	0.0%	6.1%	722	
Haemorrhage	91.1%	7.8%	1.0%	0.1%	2.9%	347	
Trauma	76.4%	22.0%	1.6%	0.0%	7.9%	935	
Broken orthodontic devices	65.0%	30.2%	4.7%	0.1%	11.6%	1,376	
Prosthesis de-cementation	48.7%	44.6%	6.7%	0.1%	17.2%	2,029	
Broken removable prosthesis	65.5%	30.8%	3.7%	0.0%	11.5%	1,359	
Paediatric dentistry emergencies	73.1%	24.3%	2.6%	0.1%	1.1%	1,063	
Total						11,778	

### TABLE 2 Adherence to preventive measures

TABLE 2         Adherence to preventive measures						
Phase I – Phone triage						
Dentists performing phone triage	95% (2,010)					
Symptoms investigation	98.8%					
Fever	98.9% (1,988)					
Ocular conjunctivitis	57.5% (1,155)					
Cough	95.7 % (1,923)					
Breathing difficulties	91.2% (1,834)					
Diarrhoea	43.7% (879)					
Muscular pain	50.6% (1,017)					
Anosmia/ageusia	67.8% (1,362)					
Questions on patient contacts						
Contacts with subjects coming from highly epidemic areas (Lombardy & Veneto)	86.0% (1,728)					
Contacts with infected or potentially infected subjects	96% (1,930)					
Phase II – In office triage and dental office preparat	tion					
Patient arriving at the dental office						
In-office triage	49.5%					
Body temperature check	25.2%					
Contactless device	82.2%					
Ear device	10.8%					
Standard device	7.5%					
Waiting room organization						
Hydro-alcoholic solution for hand disinfection	92.2%					
Removal of unnecessary objects from the waiting room	94.2%					
Agenda organization	96.7%					
30 min per appointment	6.6%					
1 hr per appointment	46.6%					
>1 hr per appointment	46.6%					
Discouraging the presence of accompanying people	97.5%					
Phase III – Dental treatment						
Clinical area						
Environment disinfection	99.1%					
0.1% Sodium hypochlorite	34.9%					
70% Isopropyl Alcohol	70.1%					
Other disinfectants	44.4%					
Clinical staff preparation						
Clinical staff hand washing before treatment	99.1%					
20 s	40.6%					
40 s	40.5%					
60 s	18.8%					
Hand disinfection with hydro-alcoholic	55.7%					

solution

Personal protective equipment

(Continues)

 TABLE 2
 (Continued)

Double pair of gloves	50.3%
Gown	79.9%
Hydro-repellent	63.3%
Non-hydro-repellent	28.9%
Both	7.7%
Сар	84.4%
Mask	98.0%
FFP2/FPP3	15.4%
Surgical mask	29.8%
Both	22%
Other devices	33%
Eye protection	98.3%
Glasses	32.4%
Shield	24.4%
Both	29.1%
Other devices	1.5%
Patient preparation	
Disposable shoe covers for the patient	42.5%
Pre-operative mouth rinse	89.9%
Chlorhexidine	34.8%
Povidone-iodine	5.8%
Hydrogen peroxide	40.8%
Cetylpyridinium	2.6%
Dental treatment management	
Minimizing aerosol production	88.5%
Dedicated handpieces	26.5%
Use of manual instruments	49.9%
Use of surgical aspiration systems	57.3%
Use of rubber dam	75.8%
Other strategies	1.4%
Four hands technique	37.8%
Phase IV - After dental treatment	
Ventilation	98.1%
After each treatment	95.7%
At the beginning and end of the working session	9.0%
Other ventilation strategies	34.5%
Hand hygiene (dentist)	98.2%

# 3.3.2 | In-office triage and dental office preparation

Unlike phone triage, the in-office triage questionnaire was performed by 49.5% of dentists. Only the 25.2% performed temperature recording, using in the majority of cases a contactless thermometer.

The set-up of the waiting room (non-clinical area) was adapted to the new situation by almost the totality of the sample, by providing a hydro-alcoholic solution for hand disinfection, removing objects at risk of contamination and reorganizing the schedule in order to guarantee social distancing.

Environment disinfection of the dental setting (clinical area) was mostly provided using isopropyl alcohol and sodium hypochlorite.

TABLE 3	Differences between Lombardy & Veneto versus other
Italian regio	ns

	Veneto & Lombardy	Other Italian Regions	p- value
Definition of urgent dental treatment			
Pulpitis	90.0%	82.2%	.000
Dental impaction	15.8%	11.7%	.014
Paediatric emergency	45.7%	38.7%	.004
Trauma	75.1%	69.7%	.017
Abscess	60.6%	55.2%	.029
Bleeding	34.0%	26.7%	.001
Patient arriving at the dental office			
In-office triage	80.7%	74.1%	.002
Body temperature check	42.4%	37.5%	.046
PPE			
Ability to retrieve PPE	57.2%	66.3%	.000
Dental treatment			
Use of rubber dam	79.7	74.4	.015
Use of surgical aspiration systems	62.4	55.5	.005
Four hands technique	51.2	33.3	.000

In 99.1%, clinical staff performed hand washing for 20–40 s, while the 55.7% also performed hand disinfection with a hydro-alco-holic solution prior to wearing gloves. PPE involved the use of gown, cap, masks and eye protections. In the 50.3% of cases, two pairs of gloves were used (Table 2).

#### 3.3.3 | Dental treatment

In almost 90% of cases, patients were asked to perform a mouth rinse prior to dental treatment, in the majority of cases using hydrogen peroxide. In 88.5% of cases, measures were adopted to limit aerosol production, while the four-hands technique was used only in 37.8% (Table 2).

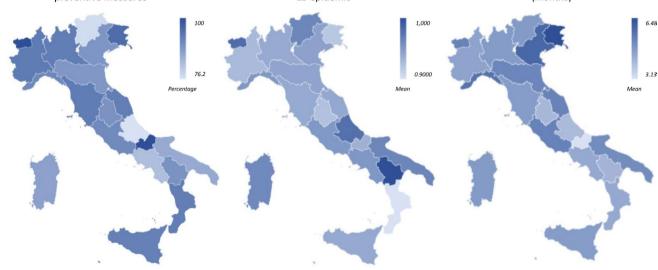
# 3.3.4 | Postdental treatment management of the dental office

Room ventilation was provided after dental treatment in 98.1% of cases. Almost the totality of the sample repeated hand washing and disinfection after removing the gloves at the end of the procedure (Table 2).

#### 3.4 | A focus on northern regions

In Table 3, a comparison between Lombardy and Veneto and the rest of the Italian regions is provided. Overall, in highly epidemic areas, compliance with preventive measures was higher. The 57.2% of dental professionals reported being able to retrieve PPE in northern

(a) Dental professionals informed on COVID-19 (b) Decrease in dental activity during the COVIDpreventive measures 19 epidemic (c) Expected return to normal routine activity (months)



**FIGURE 1** Distribution per region of (a) the number of dental professionals informed regarding the preventive measures for COVID-19 prevention in dental practice, (b) the decrease in dental activity during the COVID-19 epidemic and (c) the expected months to reopening [Colour figure can be viewed at wileyonlinelibrary.com]

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Italy, a slightly lower percentage compared to the 59.9% reported on average in other regions. In northern regions, more than 90% of dental professionals endorsed being informed on the preventive measures to be adopted during COVID-19. Moreover, in highly epidemic areas, a slower restart of routine activity was expected (Figure 1).

# 3.5 | Questions on future perspectives of dental practice

The majority of the sample expected some changes in the dental profession following the epidemic, in particular regarding PPE and dental office set-up in terms of schedule and preparation for treatment. While an increasing use of PPE was reported by the 60% of the surveyed professionals, 90.4% reported difficulty in accessing PPE supply and an increase in PPE costs. The 80.6% feared a reduction in dental activity after the pandemic.

The mean expected time of return to routine dental activity was thought to be around 4.9 months while the majority of the surveyed dentists reported a maximum period of 3 months as the threshold of economical sustainability. A positive correlation (p < .05) was found between the decrease in dental activity and the expected time of return to regular activity. In particular, the higher was the percentage decrease in dental activity, and the longer was the time expected for the return to regular activity (Figure 2).

The mean time estimated for managing treatment suspension without affecting patient's health was thought to be up to 2 months by the 78.3% of the surveyed dentists. In 82.7% of cases, it was believed that standard procedures could be adopted again but increasing protection against aerosol should be needed.

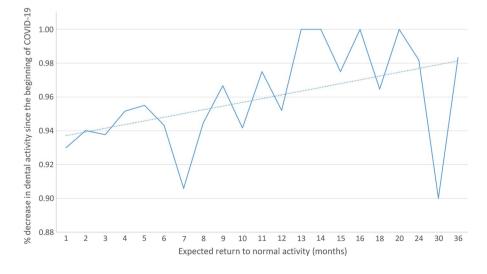
# 4 | DISCUSSION

After the beginning of the lockdown, dental activity was reduced by 95%. In particular, almost the totality of the surveyed sample (99.7%) performed only urgent treatments, consistently with the Italian

government recommendations (Circolare del Ministero della Salute n. 7,422 del 16 marzo 2020). All the dental professionals showed a high level of adherence to the preventive measures suggested (Izzetti et al., 2020).

Phone triage was performed by 95% of the sample. Triage, both at the telephone or in-hospital, has been widely employed in several medical fields, in particular emergency care, where it is adopted to assess the need for hospitalization (Boggan et al., 2020). Judson et al. (2020) have applied triage to investigate patients' symptoms to exclude COVID-19. Moreover, Izzetti et al. (2020) reported the application of phone triage to assess patient risk profile. Phone triage aims at evaluating the presence of symptoms suggestive for COVID-19, and the potential contact with infected or at-risk subjects. This measure appears extremely valuable in limiting the contact with potentially infected patients and provides a reliable means for the control of contagion both of dental professionals and other patients. It is important to enquire about potential contacts with high-risk subjects as asymptomatic patients may be infectious (Backer, Klinkenberg, & Wallinga, 2020; Chan et al., 2020; Del Rio & Malani, 2020; Guan et al., 2020; Huang et al., 2020; Rothe et al., 2020). Interestingly, although in the literature triage performance in the preclinical and clinical setting has been previously described (Li & Meng., 2020; Meng et al., 2020; Peng et al., 2020), only 49.5% repeated the triage in office. Temperature recording was performed in 25.2% of cases, whereas one of the symptoms associated to COVID-19 is the development of fever, along with the presence of other clinical manifestations, including dry cough, dyspnoea, and fatigue or myalgia (Chang et al., 2020; Chen et al., 2020; Holshue et al., 2020). We might speculate that such procedures, that is triage repetition and body temperature recording, may have not been part of routine activities, and therefore, compliance might have been affected. Thus, triage repetition and temperature recording appear of utmost importance to assess patient's health status within two different time points to enhance the chance of detection of early symptoms. Moreover, temperature recording should be also used to monitor professional staff on a daily basis (ADA, 2020).

FIGURE 2 Scattered plot of the correlation between the dental activity decrease during the epidemic and the expected time of return to regular activity. The dental professionals who experienced higher decrease in their routine dental activity expected a slower return to normal practice [Colour figure can be viewed at wileyonlinelibrary.com]



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Almost all the sample provided re-organization of the waiting room in order to limit the number of surfaces which could transmit infection (Izzetti et al., 2020). Although thorough disinfection with alcohol-based solutions or chloro-derivatives may inactivate the virus on the surfaces, it is reported that SARS-CoV-2 can persist on surfaces up to 9 days (Kampf, Todt, Pfaender, & Steinmann, 2020) and has an estimated median half-life of approximately 5.6 hours on stainless steel and 6.8 hours on plastic (van Doremalen, 2020). The presence of infectious SARS-CoV-2 was investigated also on surgical masks, where the virus was found to persist for up to 7 days, although being susceptible to standard disinfection methods (Ren et al., 2020). Therefore, removing all the unnecessary objects from the waiting room is an effective measure to limit the risks of infection (ADA, 2020).

Correct hand washing is effective in controlling the diffusion of various diseases (Goldberg, 2017). Performing hand washing for at least 60 s is an effective measure in removing potential infectious microorganisms, especially if associated with the use of hydro-alcoholic solutions which contribute to the inactivation of enveloped viruses, including coronaviruses (Lotfinejad, Peters, Pittet, 2020).

The combination of hand washing and disinfection is, therefore, the best practice in providing virus elimination.

PPE use is crucial to protect healthcare workers from SARS-CoV-2 due to the relatively easy way of transmission. In particular, adequate provision of PPE is the first measure to ensure the safety of healthcare workers (Lancet, 2020). Several protocols have been suggested to correctly protect from COVID-19, providing the protection of eyes, nasal and oral mucosa. In our survey, we found that the majority of dental professionals employed the correct set of PPE, therefore suggesting a high sensitivity towards personal protection. However, it is essential to highlight the reported difficulty in obtaining PPE, which could have limited a wider use.

Considering dental treatment, almost all dentists prescribed a mouth rinse prior to the beginning of the procedure. While the majority employed hydrogen peroxide, a non-negligible number of professionals employed chlorhexidine. Such a result is consistent with the findings of Cagetti and co-workers (2020) in their survey on the dental professionals of Northern Italy, where in the 50% of cases, the use of chlorhexidine-based mouth rinse was reported. In this sense, it would be advisable to evaluate the effects of chlorhexidine on SARS-CoV-2. However, it is not to be forgotten that saliva is a viral reservoir, thus posing the problem of the actual effectiveness of mouth rinsing prior to treatment. Finally, as much as the oral cavity might be virus free, the mere breathing activity of the patient would contribute to the diffusion of the virus in the dental setting.

The awareness of the risks related to aerosol generation was demonstrated by the large number of dentists that reported minimization of aerosol-generating procedures, and the adoption of dedicated strategies. The risks related to dental aerosols were previously highlighted during the spread of the Severe Acute Respiratory Syndrome (SARS) between 2002 and 2004, when the control of aerosols was claimed as a necessary part of dental infection control procedures (Harrel, 2004; Harrel & Molinari, 2004). Moreover, the tropism of SARS-CoV-2 for ACE2 cell receptors and the viral presence in saliva represent a non-negligible risk factor (To et al., 2020; Xu et al., 2020).

Limiting aerosol by working manually is important. However, this is not always possible; thus, several measures may be useful to limit aerosol production (Izzetti et al., 2020; Meng et al., 2020; Peng et al., 2020), with the use of surgical aspiration, the limitation in the use of handpieces, and four-hands technique appearing the most effective. However, in our survey, the four-hands technique was not widely employed.

Finally, post-treatment management was correctly carried out in most cases, providing room ventilation and surface disinfection, due to the reported viral persistence both in aerosol and on surfaces (van Doremalen et al., 2020).

The most critical aspect of this survey is the fact that data are self-reported, particularly for items such as those asking respondents to recall granular behaviours carried out by themselves and their staff. Moreover, given their profession, respondents may have been likely to be uniquely focused on their patients' oral health (and possibly focused on maintaining their practice from a financial standpoint), which may have influenced their opinions about the speed at which regular dental practice should be allowed to resume. Finally, respondents were not explicitly asked to weigh all the aspects against noteworthy risks that characterize this unprecedented situation. Following the peak of the epidemic, numerous doubts arose as per the dental activities to be fully restarted, mostly regarding the use of adequate PPE and the management of aerosols produced by the use of handpieces. Moreover, it was overall observed an attitude towards a modification of dental practice, a relatively slow return to regular activity, and a concern towards treatment management after suspension. Italian dental professionals massively embraced novel and numerous precautions to minimize the professional contagion risk as indicated by the adoption in more than 90% of cases of the majority of the key suggestions provided. It is also likely that these changes might be perpetual as the 70.9% of the sample reports uncertainty on the virus eradication in influencing medium-long term disinfection and clinical protocols. However, the adoption of PPE was strongly influenced by its accessibility (40.3% reported complicated retrieval). Thus, the availability of PPE impacts the overall scenario. Accordingly, the vast majority (97.3%) showed uncertainties in the professional sentiment about the future.

Lastly, it is important to highlight that the abrupt stop of dental activity during the epidemic has left uncompleted an extremely high number of treatments. This is worrying and of concern, as it is believed by the 78.3% that even 2 months more without completing actual treatments would be prejudicial to the oral health of patients.

In conclusion, with the present survey, we aimed to take a photograph of the situation of Italian dentistry during the pandemic. It is remarkable that, despite numerous uncertainties and difficulties, dental healthcare professionals kept ensuring urgent treatments to the population in these dire times, providing the best standard of

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care possible while adhering to the preventive measures suggested by national institutions and associations.

#### CONFLICTS OF INTEREST

There are no known conflicts of interest to disclose. No funding was received to perform the present study.

#### AUTHOR CONTRIBUTIONS

Rossana Izzetti: Conceptualization; Investigation; Methodology; Resources; Writing-original draft; Writing-review & editing. Stefano Gennai: Data curation; Investigation; Software; Visualization. Marco Nisi: Conceptualization; Data curation; Investigation; Methodology; Resources; Writing-original draft. Antonio Barone: Formal analysis; Project administration; Supervision; Validation; Visualization. Maria Rita Giuca: Resources; Supervision; Validation; Visualization. Mario Gabriele: Resources; Supervision; Validation; Visualization. Filippo Graziani: Conceptualization; Data curation; Formal analysis; Investigation; Supervision; Validation.

# PEER REVIEW

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#### SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

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