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Article

Biosafety in Dental Care Facing Highly Transmissible SARS-CoV-2 Variants: Introduction of Prospective Setting Protocol in Prevention of COVID-19

Andrej Thurzo [1*], Alexandra Bražinová [2], Neda Markovská [3], Iveta Waczulíková [4], Martin Smatana [5], Wanda Urbanová [7], Veronika Kurilová [9], Peter Sabaka [10], Bela Mriňáková [11], Ivan Varga [12], Ladislav Czakó [6], Helena Kosnáčová [13, 14], Jana Kaiferová [8], Martin Strunga [1], Branislav Gális [6], Georgia Fountoulaki [3] and Bohuslav Novák [1]

[1] Department of Stomatology and Maxillofacial Surgery, Faculty of Medicine, Comenius University in Bratislava, 81250 Bratislava, Slovakia; Thurzo3@uniba.sk, bohuslav.novak@fmed.uniba.sk, martin@3Dent.sk

[2] Institute of Epidemiology, Faculty of Medicine, Comenius University in Bratislava, 81250 Bratislava, Slovakia; alexandra.brazinova@gmail.com

[3] Department of Stomatology, Faculty of Medicine, Slovak Medical University in Bratislava, 83303 Slovakia; neda.markovska@gmail.com, tzina.fountoulaki@gmail.com

[4] Department of Nuclear Physics and Biophysics, Faculty of Mathematics, Physics and Informatics, Comenius University, Mlynska dolina F1, 84248 Bratislava, Slovakia; iveta.waczulikova@fmph.uniba.sk

[5] Ministry of Education, Science, Research and Sports of Slovak Republic, Slovakia; mar.smatana@gmail.com

[6] Department of Oral and Maxillofacial Surgery of Medical Faculty of Comenius University and University Hospital Bratislava, Bratislava, Slovakia; czako@ionline.sk, brano.galis@gmail.com

[7] Department of Orthodontics and Cleft Anomalies, Dental Clinic 3rd Medical Faculty Charles University, Faculty Hospital Kralovske Vinohrady, Prague, Czech Republic; wanda.urbanova@gmail.com

[8] 1st Department of Dentistry, Faculty of Medicine Pavol Jozef Safarik University, Trieda SNP 1, 04011 Kosice, Slovakia; renyurban@gmail.com, kaiferova@gmail.com

[9] Faculty of Electrical Engineering and Information Technology, Slovak University of Technology, Ilkovicova 3, 812 19 Bratislava, Slovakia; veronika.hanuskova@gmail.com

[10] Department of Infectiology and Geographical Medicine, Faculty of Medicine, Comenius University in Bratislava, Slovakia; petersabaka@gmail.com

[11] 1st Department of Oncology, Medical Faculty of Comenius University and St. Elisabeth Cancer Institute, 81250 Bratislava, Slovakia; bela.mrinakova@ousa.sk

[12] Institute of Histology and Embryology, Medical Faculty of Comenius University in Bratislava, 81372 Bratislava, Slovakia; ivan.varga@fmed.uniba.sk

[13] Department of Genetics, Cancer Research Institute, Biomedical Research Center, Slovak Academy of Sciences, Dubravska Cesta 9, 84505 Bratislava, Slovakia; pavol.vitovic@fmed.uniba.sk

[14] Department of Simulation and Virtual Medical Education, Faculty of Medicine, Comenius University in Bratislava, Sasinkova 4, 81272 Slovakia; helena.svobodova@fmed.uniba.sk

* Correspondence: Thurzo3@uniba.sk; Tel.: (+421 903 110 107)

Abstract: With arrival of highly transmissible Omicron variants in global pandemic, dentistry is facing another challenge to preserve biosafety of dental care. With a mission to protect both patients and healthcare workers, adaptability to the changing epidemiologic situation is required from dental professionals. This work presents a prospective sustainable biosafety setting for routine orthodontic care. The protocol is composed from combination of available technologies focused on the air-borne part of a virus pathway. Introduced biosafety protocol has been clinically evaluated after 18 months of application in the real clinical environment. The protocol has three fundamental pillars: (1) UVC air disinfection; (2) air saturation with certified virucidal oils through nebulizing diffusers; (3) complementary solutions. As a method of evaluation pseudonymous online smart form was used. Protocol operates with premise that everybody as a hypothetical asymptomatic carrier. Results from 115 patient feedbacks imply that with this protocol in place, there was no observed or reported translation of virus from patient to another patient or from patient to doctor or nurse and vice versa, albeit nine patients have retrospectively admitted visiting the clinic as probably infectious. Despite promising results, a larger clinical sample and exposition to current mutated strains is necessary for reliable conclusions about protocol virucidal efficiency.

Keywords: SARS-CoV-2; Omicron; biosafety protocol; dentistry; orthodontics; sustainability

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1. Introduction

More than two years have passed since the first stage of SARS-CoV-2 pandemics. From the beginning several experts expressed their doubts that this new virus has a potential to cause a global pandemic with significant socio-economic impacts. Today we already know it has caused unprecedented damage in many fields, as well as the domain of dental community including healthcare and education [1–7].

Currently, we are facing a surge of highly transmissible variants (Omicron strains BA.1 overtaken by more transmissible BA.2) of SARS-CoV-2 causing disease COVID-19, albeit fortunately less virulent than previous strains. Dentistry is now facing these highly transmissible SARS-CoV-2 variants with currently highly protected, albeit waning, immunity in population after massive vaccinations. There is a demand for a bio-safe workflow in dental care. Despite Covid being currently less lethal than it has ever been, the overall risk of infection, post-viral syndrome (long-Covid) remains higher than it was in the beginning of the pandemics. So far, dental professionals have been able to anticipate the risks of the incoming waves and their seasonability. The biosafety measures at the dental offices have been revised repeatedly in effort to protect the patients and healthcare workers [2,8–16]. Dentists have changed their behavior and adapted their workflows[1,2,17].

Dental care is characteristic by its close person-to-person contacts and treatment procedures that produce aerosols. Dental healthcare professionals - including dentists, dental assistants, dental hygienists, and nurses were aware of high risk of exposure in the early stages of COVID-19 pandemic [18,19]. It is fact that dentists have a high risk of contracting COVID-19 from their patients because of its transmission by respiratory droplets and the use of dental handpieces that can generate aerosols [20,21] as well as the physical proximity to their patients [19,22,23]. Understanding the significance of aerosol transmission and its implications in dentistry can facilitate the identification and possible correction of negligence in daily dental practice [24]. Mitigation of particles that can carry the virus and thus mitigation of the risk of pathogen transmission in dental offices often confirm high effectiveness of personal protective equipment in protecting patients and dentists from aerosols [25].

In March 2020, nearly 200,000 dentists in the United States closed their offices to patients in fear fueled by concerns that aerosols generated during dental procedures are potential vehicles for transmission of respiratory pathogens through saliva [26]. The findings published by Meethil et al. 2021 in the Journal of Dental Research [27] suggest lower risks for transmission of the SARS-CoV-2 virus during dental procedures than anticipated. Click or tap here to enter text.With this understanding, an asymptomatic carrier coughing in the dental office should be considered a much higher risk, than having an orthodontic attachment removed with a dental bur producing aerosol.

Preprocedural rinsing is one of the introduced biosafety precautions later in this work. Authors have learned from their clinical experience, this can occasionally lead to patient`s coughing, thus providing the very opposite of the intended effect. While preprocedural rinsing has been encouraged since the beginning of the pandemic, guidance about which antiviral to use has been unclear. The American Dental Association (ADA) initially recommended 1.5% hydrogen peroxide and 0.2% povidone iodine for use as an antiviral prerinse [29,30]. When actual antiviral testing of these commercial rinses on SARS-CoV-2 finally did become available, a different picture began to emerge. At the same time when the ADA was recommending 1.5% hydrogen peroxide as an antiviral prerinse, the Centers for Disease Control and Prevention (CDC) was advising that 1.5% hydrogen peroxide needs 18 to 20 minutes to inactivate rhinovirus, the virus that causes the common cold [31]. An extensive review inspecting the antiviral efficacy of hydrogen peroxide mouthwash was published in the Journal of Hospital Infection in October 2020 [32]. Authors concluded that: “there is no scientific evidence supporting the indication of hydrogen peroxide mouthwash for control of the viral load regarding SARS-CoV-2 or any other viruses in saliva.” [32]. As a result of this knowledge, and additional

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in-vitro and in-vivo testing, the Royal College of Dental Surgeons and the Canadian Dental Hygienists Association have all advised their constituents to discontinue use of hydrogen peroxide as an antiviral prerinse [33]. The Antiviral Research Institute of Utah State University piloted a study in August 2020 of the antiviral efficacy of several oral rinses against SARS-CoV-2 [34]. Of all the tested rinses, 0.12% chlorhexidine gluconate and 1.5% hydrogen peroxide were inadequately effective, even after 60 seconds' exposure. While 0.2% povidone iodine did somewhat better, the only rinse to completely inactivate SARS-CoV-2 was a 100-ppm molecular iodine rinse. It was completely effective within 30 seconds. Neither of the iodine rinses were cytotoxic, but the hydrogen peroxide and chlorhexidine gluconate rinses were. Currently, a molecular iodine rinse is the clear evidence-based winner as a prerinse for SARS-CoV-2. This is particularly important considering that a number of other oral rinses are neutralized in the presence of saliva [35–40]. Oral rinses are a regular part of various dental bio-safety protocols.

Dental care is often provided to oncological or other immunocompromised patients. It is crucial that precautionary measures are implemented so these patients could be treated in a safe environment. A timely adaptation of clinical workflows and implementation of practice modification measures was observed through the world [15,41–44]. These, with the arrival of significantly more infectious Omicron-strains, need to be revised [45]. Moreover, dental care is essential in dealing with toxicity of anti-cancer treatments such as oral mucositis, xerostomia, trismus, osteoradionecrosis, and opportunistic infections [46]. Active cancer has been recognized to have a possible negative impact on COVID-19 clinical course and outcome regardless of pre-existing comorbidities. Two-fold increase in death rate between cancer and non-cancer COVID-19 was observed, estimating that oncological patients represent a particularly vulnerable population [47]. Click or tap here to enter text.Optimal safety protocols must be applied to minimize the risks in this population during dental care.

Current pClick or tap here to enter text.Click or tap here to enter text.reventive biosafety measures often take into consideration possible specific intraoral manifestation of COVID-19. Triad xerostomia, taste and smell dysfunction, and oral mucosal lesions were identified as common manifestations with previous variants; however, with still controversial causality in omicron variants the xerostomia, taste and smell dysfunctions are not common symptoms anymore. The causal relationships between oral lesions and COVID-19 are proven [50–53].Click or tap here to enter text.

Click or tap here to enter text.Pandemics had a significant impact not only on dentists and their colleagues [55], but also on patients` mental well-being. Frequently, the occurrence of depression, anxiety, stress, intrusion, avoidance, and hyperarousal were observed both in patients, as well as in healthcare workers [56–60].

In the beginning of the pandemics the Hospital of Stomatology in Wuhan diagnosed nine dental staff members infected between January to February 2020 [19]. Chinese dental surgeons responded with set of recommendations for the bio-safe management of dental care workflow in the context of the epidemic [22]. Since then, various recommendations and guidelines have been published on professional websites in several countries. For example, in the US (Centers for Disease Control and Prevention (CDC), American Dental Association), in Europe (European Centre for Disease Prevention and Control (ECDC)), in France (Health Ministry, French Dental Association), in the UK (National Health Service, British Dental Association) [61]. One of the first renowned pandemic-dental events in European dentistry was the outbreak in North Italy in Lombardy. All of Lombardy's dentists were evaluated with an online ad hoc questionnaire. 3599 questionnaires were analysed. 502 (14.43%) participants had suffered one or more symptoms referable to COVID-19. Thirty-one subjects were positive to the virus SARS-CoV-2 and 16 subjects developed the disease. Only a small number of dentists (n = 72, 2.00%) were confident of avoiding infection [62].

Several innovative bio-safe approaches of dental diagnostics or treatment were introduced– for example tele-health solutions like Dental Monitoring® (DM) (Dental Monitoring Co., Paris, France) [6,63–68]. Revisions of the then-established protocols in dental healthcare were simple. Dental professionals in their early efforts to adapt their biosafety measures performed typically a web-search conducted in the main databases of the scientific publications, focused mostly on oral rinsing and limitation of in-office aerosol production. This early research often led to possible revisions of biosafety and disinfection protocols at the dental offices [1,2]. Two years of ongoing pandemic has changed the practice of dentistry forever, some of the changes have made dental care more time-consuming, difficult, and costly due to the possible pathways of transmission and mitigation steps needed to prevent the spread of the infection.

Despite the widespread anxiety and fear of the devastating health effects of earlier COVID-19 (2020-2021), only 61% of dentists have implemented a fundamental modification to their treatment protocols. Currently facing the highly transmissible Omicron strains, as an urgent matter of public health, all dentists must identify the additional steps they can take to prevent the spread of air-borne infection [21].

The clinical practice bio-safety guidelines developed during the first year of the pandemic offer recommendations which guide dental staff in providing safe dental care in the clinical environment. Such recommendations must be updated as new evidence of virus properties arises [69,70] There is a high level of agreement between different dental specializations about the necessary preventive measures of the routes of transmission. Published data regarding the survivability of the virus on innate objects vary substantially [71]. Nevertheless, due to the wearing of personal protective equipment (respirators, gloves, masks, eye shields, and gowns) and use of disinfection procedures, this risk can be significantly mitigated. Research published by Estrich et al., 2020 found in June 2020 that during the first wave of pandemic only 0.3% of surveyed dentists had a probable COVID-19 diagnosis, from these 82.2% were asymptomatic. The most reported health problems among dentists during pandemics were anxiety and depression [21,72].

The primary aim of most biosafety protocols is to prevent any cross-contamination while allowing the provision of urgent and emergency dental care. Aerosol-producing and other elective procedures should be avoided in the periods of outbreaks of unknown variants [17,73–76]. Various biosafety protocols detail the safety and operational measures to be taken, while providing the dental care in the COVID-era. Falahchai et al. 2020 published a comprehensive protocol regarding dental care during the COVID-19 outbreak. The point in the outbreaks caused by new, not well researched variants, is that these might bring dangerous long-term health hazards enabled by new mutations [77].

With currently globally waning post-vaccination immunity together with less cautious behavior of the masses, there is a high probability of surge of infections providing more opportunities for further virus mutations. Omicron variant BA.2 will be substituted only with even more transmissible strain. Hopes for guaranteed declining virulence of future mutated strains are rather a “wishful thinking” than evidence-based theory. As evidence mounts that the Omicron variant is less lethal than prior strains, one frequently cited explanation is that viruses always evolve to become less virulent over time. This theory has already been soundly debunked. During surges of unexplored mutated variants, the dental treatment might be limited to patients with urgent or emergency situations. Separate waiting and operating rooms should be assigned to patients in order to minimize the risk of infection transmission and the treatment should be provided with the same protective measures with regard to Personal Protective Equipment (PPE) for the dental clinicians and staff [77].

Last two years of pandemic in dental care showed changes of attitude from initial negligence of possible serious impacts of the virus spread, up to panic precautions. After a year, the variables of the pandemic situation have changed with the implementation of mass-vaccination. This represented an important milestone [78,79] suggesting a possible end-game scenario for the COVID-19 pandemic. These expectations were facing disappointment with the arrival of the Omicron variant. Imaginable race between SARS-CoV-2 mutations and vaccine rollouts was slowed down with negative perception of people

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afraid of possible vaccination side effects. Recent study from Czech Republic proved the distribution of side effects among Czech healthcare workers as highly consistent with the manufacturer's data. The overall prevalence of local and systemic side effects was higher than the manufacturer's report [79]. Current data suggest that Omicron capabilities to evade natural human immunity, protective effects of distributed vaccines [80,81] and its resistance to current monoclonal medication [82,83] make the Omicron variant a true dilemma. According to a recent study by Dr Michael Chan Chi-wai, from December 2021, it can infect faster and better than Delta in human bronchus, but with less severe infection in lung [84]. Its newly gained strong ability to infect ACE2 in mice predicts this variant is here to stay until pushed out with more transmissible strain [85].

Recent study of American dental association and research published by Araujo et al., 2021suggests, that US dentists show a high level of adherence to enhanced infection control measures in response to the ongoing pandemic, resulting in low rates of cumulative prevalence of COVID-19 [23]. With the spread of "Omicron-like" mutant strains the likelihood of recurrent infection raises some doubts on whether vaccination alone will provide long-term immunity against COVID-19 and its future variants. Furthermore, several mutations in the receptor binding domain and S2 are predicted to impact transmissibility and affinity for ACE-2 that might be relevant for adaptation of biosafety protocols [86].

From this perspective, the aim to provide biosafe dental workflow in orthodontic or any other dental practices must consider higher transmissibility of the virus and higher number of asymptomatic carriers. Anticipation when the virus spread naturally diminishes or becomes less virulent is not possible nor is certainty that further mutations will be harmless. Therefore, the effective biosafety protocol must be sustainable. Based on these facts, various simulations and modelling data, dental practices may never return to "normal", former routine operation even after global vaccination would be somehow successful as there would still be a significant risk of outbreaks of infection with new mutant strains. Variable, multi-level measures will still be required, depending on the local COVID-19 cases rate, to secure safe dental care provision [42].

Click or tap here to enter text.Biosafety protocols applied a year after pandemics outbreak are not significantly different from the ones effective today, albeit the virus transmissibility and symptoms changed significantly. This work introduces a prospective setting of a combination of field-tested technologies for enhanced clinical biosafetyof orthodontic workflow in confrontation with surging cases of Omicron variant infections [80,84–86,88]. Effectivity and sustainability of this protocol lies in its simplicity and realization of the fact that despite new variants are more invasive to human immunity, their air-borne pathway is equally obstructed with masks, and indoor biosafety measures. People infected with Omicron variant might have clinical symptoms and significant viral load despite hight titres of neutralisation antibodies. It is important to realize that development of either multicomponent vaccines or vaccines against currently circulating virus variants can bring an effective last line of our defense. Vaccines work after the virus has entered the body. The safety protocol presented in this work is focused on earlier parts of the virus path before it enters the body. The protocol provides a multilevel system of defenses represented as mostly airborne protections.

Omicron SARS-CoV-2 (B.1.1.529) and its sublineage BA.2 remain a variant of concern [70,89] and define a new chapter in the COVID-19 pandemic. This highly mutated strain has more than 30 mutations, several of which overlap with those in the Alpha, Beta, Gamma, or Delta variants of concern. These mutations and deletions are known to lead to increased transmissibility, higher viral binding affinity, and higher antibody escape. The long-term potential of the new variants is not certain yet [80–82,85,88,90–93] and preliminary research publications suggest it is from 2 to 4,2 times more infectious than Delta variant [88]. BA.2 more transmissible, more replicative in human nasal epithelial cells and more fusogenic than BA.1 [89]. It evades not only human natural im-

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munity as well as it evades immunity from vaccines [85] and as number of laboratory studies have previously shown a reduced ability of approved vaccines to neutralize the new variant, the picture on treatments had been less clear.Click or tap here to enter text.Click or tap here to enter text.

Click or tap here to enter text.Click or tap here to enter text.Click or tap here to enter text.Click or tap here to enter text.Click or tap here to enter text.Click or tap here to enter text.The ability of this variant to evade immunity from previous infections in contrast to Delta and Alpha variants was presented in population-level evidence [93] and thus make this suggestion epidemiologically important in countries with huge amounts of previously infected cases, as Slovakia is. An increased risk of reinfection of Omicron variant is known according to preliminary evidence [90][100],[101] and probably caused by Omicron escape of neutralization antibodies [102]. Even after two doses of mRNA vaccines, higher transmissibility of Omicron was observed also in Norway [103]. The booster dose may not prevent getting infected, but observed symptoms were mild or moderate [104–106]. The time since second or booster vaccination plays role in effectiveness against symptomatic disease, as noticed in United Kingdom [102].

Click or tap here to enter text.Click or tap here to enter text.Based on these evaluations of Omicron strains, each new VOC results in uncertainty - struggling about transmission reduction, discussing vaccines efficacy, supplying elective-care and preventing long COVID complications. Thus, not only vaccines play a key role in preventing COVID-19 spread, but solutions also such as biosafety protocols are complementary and highly demanded.

The risk for transmission of pathogens in a dental office resulting in an infectious disease is still unknown; it seems to be limited in developed countries, but it cannot be considered negligible [111]. Current bio-safety settings organize in five distinct areas of pandemic control, comprising:

(1) planning and protocols,
(2) patient screening,
(3) preparation of facilities,
(4) PPE and infection control,
(5) aerosol control;

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Research published by Estrich et al. 2020 showed that dental professionals have enhanced their infection control practices in response to COVID-19 and have benefited from greater availability of personal protective equipment. Most practicing dentists (72.8%) used personal protective equipment according to interim guidance from the Centers for Disease Control and Prevention [72].

As the pandemic situation will develop towards more infectious variants, new considerations, new protocols, and new mechanisms will be implemented in the dentistry profession including tele-dentistry approach [113].

Possibly lower lethality of Omicron variant in combination with significantly higher ability to infect and create asymptomatic carriers might be dangerous. The effects of COVID-19 are very diverse and vary from individual to individual. Many patients, develop long-term disabilities, such as pulmonary, cardiovascular, hematological, renal, gastrointestinal, reproductive, psychological and the central nervous system problems, that can last from months to years [114]. Click or tap here to enter text.The blood-brain barrier pathway can let the virus into the neural system and cause neuronal damage as well as neurodegeneration or long-term neurological and psychosocial consequences [117–120]. Cardiovascular problems (e.g., myocarditis, arrhythmias, myocardial damage) are quite common too [121] and recent studies have shown that SARS-CoV-2 infection also affects the human reproductive system, especially the male reproductive system also via the ACE2 receptor [122,123].

This work introduces a novel combination of biosafety measures for dental workflow adaptation to preserve the biosafety in dental care confronted with highly trans-

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missible air-borne viruses. Combination of described procedures and technologies, especially setting with UVC and virucidal air-dispersed oils, can suppress the air-borne translation of the virus and has not been investigated yet. We hypothesized that this biosafety protocol could provide a simple and long-term sustainable model for a biosafe dental workflow. That it can manage renewed and increased risks brought by more infectious Omicron variant carried with asymptomatic infectious patients. We aimed, in the present study, to determine its clinical reliability with retrospective identification of events where dental procedure was performed unknowingly on an infected patient, their frequency and cross infection incidents.

2. Materials and Methods

2.1. Main objective and study design

The main goal of this patient-centered study was to evaluate introduced biosafety measures for orthodontic workflow as a prospective setting for prevention of in-office infections with air-borne SARS-CoV-2 variants. The secondary goal was to provide preliminary data for a larger study.

The study objectives were to answer if under this prospective setting infected patients were treated and if any infection with SARS-CoV-2 occurred in the monitored clinical environment.

This was a single arm, single center small-scale study set up in a particular clinic. Data was collected after 18 months of protocol in place with pseudonymous online form. Everyone treated in the clinic within this period experienced the same conditions.

The primary planned outcome of the study was confirmation of exposure of the environment and personnel to infected patients with no cross infections.

Due to known limitations of single arm studies, conclusions of this study can be limited. On the other hand, such design was the only viable choice for investigating biosafety measures as non-application of any preventive measures in pandemic would not be ethical. Alternatives for external control group for this single arm trial were considered, however there is no comparative data available about how frequently patients get infected during orthodontic appointments.

2.2. Participants and the environment

The protocol was applied and evaluated in the clinical environment of dental clinic with 4 doctors, 4 dental nurses and one manager.

During an eighteen-month evaluation period approximately 2500 appointments were scheduled in digital calendar for 160 different patients not including their accompanying persons. Approximately 2230 appointments took place (other were cancelled or postponed mostly due to pandemic health precautions or travel complications).

The environment for dental care consists of fully separable rooms with independent air processing and separate Ultraviolet - C light (UVC) air sterilization systems. Each of the three rooms have an independent dental unit with separate nurse position.

2.3. Brief description of the protocol

The key attributes of this biosafety protocol are:

- Efficient
- Sustainable
- Simple
- Applicable in other dental specialties (despite orthodontic customization)

The fundamental backbone of this protocol is a combination of air treatment and new technologies. Air treatment is performed with a combination of hooded UVC sterilization and air disinfection with creation of virucidal air puffer made by certified virucidal oil nebulizer/diffuser. Key technologies implemented as part of this protocol in the workflow are: artificial intelligence in patient diagnostics, continuous and post-

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treatment monitoring, smart mobile patient coaching, 3D printing for aerosol control and some other techs.

The set-up of this protocol might be considered as a biosafety overkill, however the current risks of airborne infection that could come from an asymptomatic carrier and circumvent immune defenses causing a permanent health damage to someone else, is not negligible. With a future more transmissible variants to come and professional dedication to preserve highest biosafety level of dental office an efficient air processing protocols will be needed.

This working protocol is intended as a possible complement to existing methodologies. It represents more than a year of our interdisciplinary efforts dedicated to clinical testing and the implementation of various new technologies and working procedures to maintain the biosafety of dental healthcare. Dental care must be provided regarding the patient safety as well as safety of healthcare professionals.

This protocol was created in interdisciplinary cooperation of epidemiologists, infectologists, dental surgeons, general dentists, orthodontists, and other healthcare professionals. It provides inspiration for wider clinical implementation and assessment. It is our contribution to solving this historical situation affecting safety and availability of oral care.

The fundamental principle of this protocol is full room volume air treatment with a combination of UVC and virucidal oil diffusion. Sterilization of the entire volume of air (for each patient) of the given treatment unit (room) by a combination of UVC light with a created permanent virucidal buffer of certified disinfectant oils and special active FFP3 protective aids. The key additions to the protocol are fundamental changes in working practices in the provision of artificial intelligence and telemedicine. There are two main parts of the permanent daily protocol:

- Full room-volume air UVC sterilization for each patient *total air volume per dental unit (separated room)
- Permanent air dispersed super small droplets of virucide oil - a protective puffer in recommended concentrations, created with disinfectant fogging machine (nebulizer)

Complementary technologies for digital workflow:

- AI video-scan evaluation (common checkups rendered obsolete) - Dental Monitoring
- custom made IOS/Android app coaching the proper habits - StrojCHECK [11]
- 3D printed aerosol vacuum pump ending, that supports aerosol dispersion during dental procedures and other customized 3D printing allowing more

2.4. Comprehensive Biosafety Protocol Description

2.4.1. Introduction of the protocol

The aim of this protocol was to define safe and at the same time physically and economically sustainable measures for a longer period of the pandemic with the minimization of the impact on the provided health care in dental practice. With objectives to maintain high quality of care provided, without significant increase of the costs and with no tolerance to any exposure of the staff or patients.

We began work on this protocol on the 6th of February 2020, and it took us more than 9 months to experiment, test, and implement various new practices, technologies, and modifications to existing practices. Through final consultations with experts, it has taken on its present form. We currently consider this protocol to be useful and inspiring for clinicians looking for cost-effective solutions that can be sustainable in the long run. Despite all our staff is vaccinated, with Omicron variant, they might be infectious and without clinical symptoms at the same time [80–84,88,90–93].

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In order to develop this protocol, we have implemented new and improved several existing procedures in cooperation with renowned infectologists, epidemiologists and other experts. Example of some implemented technological innovations:

1. Click or tap here to enter text.On-line dynamic anamnestic forms (effectively replacing part of 4D clinical examinations)
2. Tele-dentistry Tele-orthodontics—Dental Monitoring® (DM) (Dental Monitoring Co., Paris, France) / https://dental-monitoring.com/ (accessed on 1 December 2021) and (StrojCHECK®, Bratislava, Slovakia, 3Dent Medical, www.osim.sk (accessed on 1 December 2021) [11]
3. Artificial intelligence in tele-diagnostics - active screening of patients in tandem with the doctor
4. Special medical devices - active FFP3 shield respirator – BioVYZR - Toronto USA based Vyzr Technologies, a shield that covers the wearer's face and protects against droplets and pathogens. Powered Air Purifying Respirator (PAPR), a device typically used only in industrial and healthcare settings.
5. 3D printing of sterilizable devices (aerosol aspirators for surgical aspirators or individualized handles)
6. Two-phase air sterilization (diffusers of biocidal oils with UVC, NewAroma.sk)

2.4.2. The protocol principles

This protocol does not inevitably change the procedures already established so far for sterilization of dental instruments, disinfection of surfaces and other routinely applied rules of each dental clinic. These remain, as current pandemic is just one of the many infections we fight in asepsis in the dental clinic environment. Its key set of differences from HIV, EBV, HSV and other common viruses is period of possible asymptomatic air-borne transmissibility. The advantage of modern orthodontic therapy with clear aligners is the relatively rare occurrence of the need for urgent treatment. In the case of urgent orthodontic treatment of a confirmed infectious COVID-19 patient, a biohazard protocol is applied as in HIV patients, in COVID19 with an emphasis on the prevention of airborne spread. Regardless of whether the treatment involves aerosol dispersion (e.g., removal of attachments or fixed retainer or orthodontic auxiliaries like distalizer, power-arms [125,126] or power caps), the treatment procedure differs from the standard protocol only in the fact the patient has the last appointment of the day shift - as the last procedure on a given day.

Oral rinsing is not routinely recommended in our protocol for all patients. Only in the patients where intra-oral procedure is planned, a iodine prerinse for 30 seconds is indicated. Rinsing is not addressing the nasopharyngeal region with the largest "virus load" (reported in the nasopharynx). From our practical experience, the recommended 30-second rinsing often led to a "run-in" and subsequent coughing of the patient and thus unnecessary contamination of the space. This protocol only recommends rinsing with careful rinsing only during attachments replacement or cleaning, bio3dir removal and “powerCaps”, “powerArms” removal, interproximal recontouring or dental hygiene procedures. Prior to these procedures, the patient rinses the mouth for 30 seconds.

This protocol works with the premise that either patient, nurse or doctor are infectious. This is the reason why as a part of the protocol is introduced:

1. minimization of time exposure (shortened duration of treatment, replacement of unnecessary physical visits of the patient via AV technologies, ordering for the exact time with preparation of everything necessary for the procedure in advance)
2. mechanical and physic-chemical prevention in the dispersion of the virus and its carriers into the space resp. decontamination (PPE, continuous sterilization of the air and virucide "puffer" in the air), et ...

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3. preventive (patient input filter - symptoms, smart-App tracking, continuous testing of healthcare professionals *)

A slightly elevated temperature that is acceptable under this protocol is 37.8 ° C (originally taken from CDC). The uniforms of the medical staff are rotated daily. They include all surface clothing including shoes and socks. No hazmat suits are used.

2.4.3. Brief description of technologies utilized in the protocol

The protocol implements the following technologies and practices:

1. On-line dynamic anamnestic forms
2. Artificial intelligence in dental monitoring
3. Robotization of automatic surface disinfection
4. A.I. smart patient app for treatment coaching
5. 3D printing of sterilizable devices
6. Regular COVID testing of personnel
7. UVC and diffused virucidal oil air treatment

1. Click or tap here to enter text.The use of on-line dynamic anamnestic smart forms like Typeform - www.typeform.com brings interactivity and order to communication with patients at home. Online dynamic anamnestic forms: use the patient's own mobile phone not only for video communication (WhatsApp, facetime), but also for outsourcing part of the examination. For example with the proper instructions, a short selfie - video sequence of a natural smile can be captured by the patient and provided within online smart-form. The anamnesis itself is very important in reducing the risk of transmission, the proportion of asymptomatic patients with COVID-19 was less than 30% in the number of children with the highest proportion of asymptomatic infection. Identification of symptomatic patients is the first and relatively effective method of risk reduction. Since the anamnesis is taken remotely, neither staff nor co-patients are exposed to the risk of infection, nor is there any contamination of the surfaces in the waiting room. We use dynamic forms from Typeform company for this protocol. Remote screening of COVID-19 symptoms by application has been identified as a suitable method for detecting COVID-19 infection. Even the survey form for this biosafety protocol clinical evaluation was created as a smart form. Asking a set of questions that differs according to the answers. Logic behind is shown on **Figure 1**.

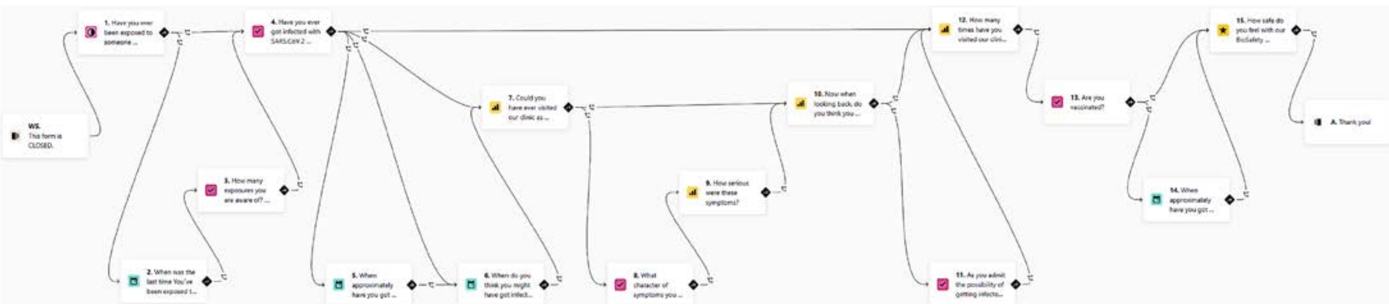

Figure 1. Example of logic behind the Smart on-line form – English version of survey evaluation this protocol. URL: https://sangreazul.typeform.com/BioSafety-ENG (Accessed on 15th of December 2021)

2. The technology of artificial intelligence implemented in the form of the Dental monitoring software is using the patient's mobile phone for regular "scanning" either to assess the course of treatment or screening a growing patient with monitoring of development or. monitoring retention stability after cessation of treatment. A special holder allows you to record a video of your own teeth. It allows paradoxically more regular and even more thorough inspection using

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A.I. Artificial intelligence allowed us to summon the patient to an appointment only when necessary (**Figure 2**). Each video scan first evaluates A.I. and alerts the doctor only to the monitored situations. The form of our workflow has thus changed fundamentally, and healthcare professionals spend a large part of the day reviewing the outputs of artificial intelligence, which in turn extremely efficiently evaluates huge volumes of data - video scans of our patients' oral cavities. It is not humanly possible to evaluate the hundreds of video scans that patients regularly make. The "brute force" of this technology is ideal for identifying situations requiring human intervention.

Figure 2. First Dental monitoring session is patient educated with the nurse how to use the free app in his/her own mobile in combination to “scanbox” holder. Published with written consent of the person.

3. Technology of robotized around-the-clock surface disinfection. It should respect all existing guidelines with an emphasis on consistency and differentiation of surfaces and a higher frequency of cleaning (after each patient). After entering, the patient shall be in contact only with the necessary surfaces, first disinfecting her/his hands. Frequent cleaning of surfaces in the clinic, after each procedure, should include frequently inspected surfaces such as door handles, keyboards and mice. Addition of floor cleaning by robotic vacuuming with disinfection mop - in our case iRobot Braava jet m6 suitable for up to 100 m^2 (**Figure 3**). The CDC recommends applying standard virucidal disinfectants to potentially contaminated surfaces to prevent the spread of SARS-CoV-2 infection. The work on the susceptibility of human coronaviruses and SARS-CoV is expected to be highly effective in SASRS-CoV-2that is relatively resistant to environmental conditions and remains infectious on smooth surfaces such as metal and plastic for many days.

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Figure 3. Robotized cleaning of surfaces like floor after each procedure can free the professional staff for other duties. Using smart robots managed with mobile application proved useful during pandemic.

4. Technology of self-developed smart mobile applications for patient treatment coaching and remote discipline support (**Figure 4**). Authors of this paper have been gradually developing iterations of the free tele-health smart patient application for patients in orthodontic treatment with clear aligners, to support the proper habits - stereotypes. Such an app allows better remote management of the patient and possible reduction of the frequency for visits to the dental office. The application educates and motivates the patient to behave responsibly [11]. For example, the app provides motivation and coaching for more frequent cleaning of teeth and aligners and in general it improved patient compliance.

Figure 4. Patient with installed free smart mobile app developed by doctors for remote behavioral coaching improves compliance of patient especially during pandemics.

5. 3D printing technology supports the presented biosafety protocol with specific sterilizable aerosol aspirators (**Figure 5a-d**). These devices are printed by a Multijet Fusion 3D Pro Printer and are sterilizable at 121°C in autoclave. This aerosol interception device is called "SUR-FACE" was developed by an Italian orthodontist because of Coronavirus pandemic. It connects to a conventional 16 mm suction device. The material is polyamide and is compatible with any retractor with thickness ≤ 2mm. The material is recyclable and supplied with 5 additional rubber seals. The one-time use of suction cup attachments minimizes the risk of transmitting infection with this tool. The sterilizability of these handpieces is critical. From clinical experience it is very effective in containing aerosols produced during clinical procedures.

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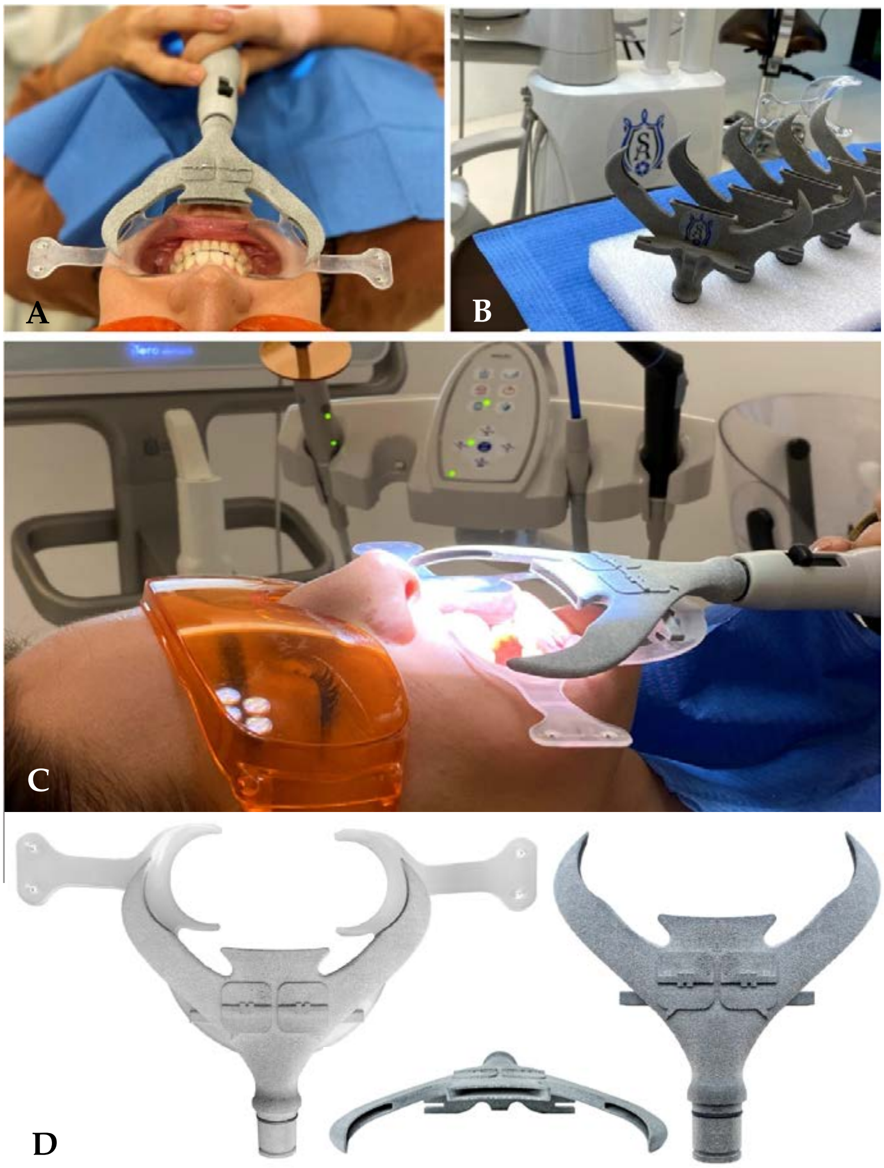

Figure 5. 3D printed aerosol interception device. A) Frontal view of 3D printed aerosol suction attached to surgical suction system and oral retractor; B) With 3D printing each office can be supported with adequate quantities; C) Lateral view of "SUR-FACE" attached to conventional retractor; D) View of "SUR-FACE" with and without cheek retractor and view of three suction openings

6. Regular antigen testing from saliva or other convenient form of testing for possible infectiousness of everybody in the team, shall be employed as with arrival of Omicron-like strains it is even more likely that a vaccinated healthcare professional would become a "supercarrier."
7. Air-processing technologies are key to the presented biosafety protocol with two-phase air treatment: room air is the most likely vector and therefore a key element in the stopping of transmission of infection. (**Figure 6**). The transmission of SARS-CoV-2 infection occurs mainly through droplets that fall relatively rapidly to the ground. However, aerosolized particles smaller than 5 µm contaminate the air and can levitate indoors where the air is not exchanged and disinfected for several hours. In addition to PPE, aerosol extractors and other elements preventing significant air contamination in the clinic, it is therefore appropriate to include other forms of air conditioning, in our case hooded UVC

emitters combined with diffusers of biocidal oils, suitable for combination with UVC sterilization.

(**a**)

(**b**)

Figure 6. Key element of this biosafety protocol is combination of diffusers of biocidal oils combined with UVC emitters; (**a**) Certified mini diffuser/nebulizer for virucidal aromatic oils for air-conditioning installation (up to1000 m^3) www.NewAroma.sk; (**b**) Certified hooded UVC Germicidal radiator PROLUX G30W A / SPH01, wall mounted.

2.4.4 Air-processing elements (UVC + virucidal difusers)

Sterilization of the entire air volume of one separate room in clinic with volume of 13 m^3 will take approximately 25~30 minutes (time intervals between patients). SARS-CoV-2 virus particles are rapidly inactivated by UVC radiation. Two hardware key elements of the presented prospective biosafety setting are UVC and Diffuser:

A) Germicidal radiator PROLUX G30W A / SPH01
- UVC lamp life of 8,000 hours
- for two-shift operation endurance 550 days (2 x 7.5 h)
- 1 emitter cycle is sufficient to sterilize a volume of 5.5 m x 4 m x 3.0 m

B) Aroma Pro Mini - professional diffuser (aroma atomizer)
- for air conditioning
- capacity up to 1000 m^3 (www.NewAroma.sk accessed 15th December 2021)
- possibility to choose from several certified disinfectant oils
- disinfectant is present in the mixture in 3 weight percent at an emission of 5 ml per hour (adjustable) to form an invisible aerosol dispersion in the air

2.5. Protocol development and evaluation

The protocol has been in development from 8th of February 2020 until 1st of June 2020 (5 months). The unchanged protocol in place was from 1st of June 2020 until 30th of November (18 months). The protocol evaluation with auto-locked smart on-line forms was performed between 1st of December and 12th of December.

2.6. Protocol strengths and weaknesses

Strengths:
- low cost, affordable, effective, sustainable
- does not require specific rebuilding of the current dental set-ups
- dimensioned for highly transmissible strains coming after Omicron
- not dependable on vaccination status or unreliable testing results

Weaknesses:
- Difficult to clinically evaluate clinical reliability
  - Only possible way is feedback form (bias)
  - Larger sample needed
  - Other studies for comparison are needed
- Requiring extra time gaps between patients in the same room
- Possible biosafety overkill
- Unknown performance under unexplored highly transmissible variants

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3. Results

3.1. Descriptive results

From 160 relevant patients, the smart online form has been filled out and submitted 115 times. 8 responses in English language the rest is in Slovak. The special fingerprint feature identified 3 duplicate answers that were removed. The result is 111 valid responses (69.37%). All answers are in the table that is available online in the public repository.

Approximately half of the responding patients were exposed to an infected person with Covid-19 (**Figure 7**). Exactly from 111 patients were 56 (50,5%) directly exposed to SARS-Co-2 infection and 55 (49,5%) were not (during the last 18-months). Dates of these exposures shows **figure 8**.

90 (81%) of responding patients were vaccinated (**Figure 9** and **Table 1**), however, only 14 had Pfizer booster (3rd) shot.

58 were vaccinated with two shots of Pfizer, 7 with Moderna, 4 with Janssen and 8 with AstraZeneca.

45 (50%) of all vaccinated received their last shot until June 2021.

9 patients reported the possibility of being infectious during their visit at the clinic.

38 responders got infected with the SARS.CoV.2 virus.

37 responders rejected the possibility they got infected at the clinic under evaluated protocol. Only one of them considered this as the possibility with lowest offered level of confidence.

Regarding question for biosafety feeling of patient during the dental procedure, (**Figure 10**) the feeling of patients was evaluated on the scale 1-5, where the 1 represents „no safety feeling “to 5 „very safe “. From 111 patients mean feeling was M= 4.59, SD= 0.732.

37 patients answered the question „Could you have ever visited our clinic as already infected? “ (**Figure 11**). The scale available was from 1 (*no, there were no chance to be infectious during the visit*), to 5 (*yes, I was infectious during the visit*). M= 1. 32, SD = .818. All the infectious patients visiting the clinic were asymptomatic as they would not get through initial entry filter (**Figure 12**).

3.2. Graphical interpretation of clinical evaluation of the protocol

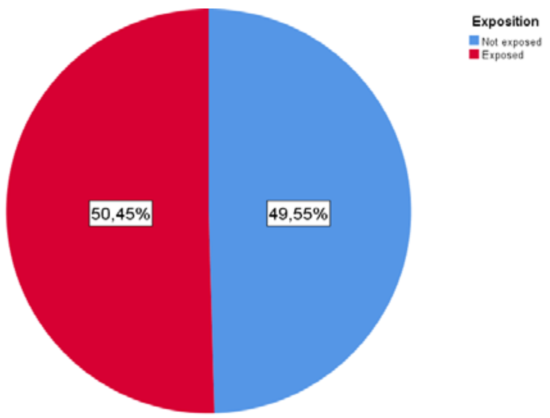

Figure 7. This graph represents distribution of exposed vs non exposed patients to someone diagnosed with Covid-19 during the last 18 months.

From 111 patients were 56 (50,5%) exposed to SARS-Co-2 infection and 55 (49,5%) were not (**Figure 7**). The incidence of exposure to an infected person is in **Figure 8**.

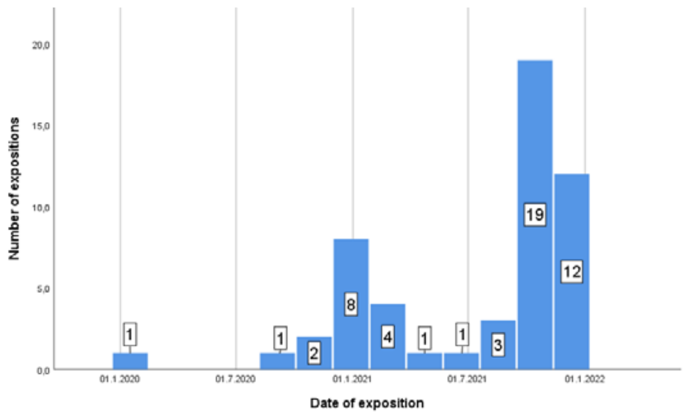

Figure 8. Frequency of exposure to an infected person by the date.

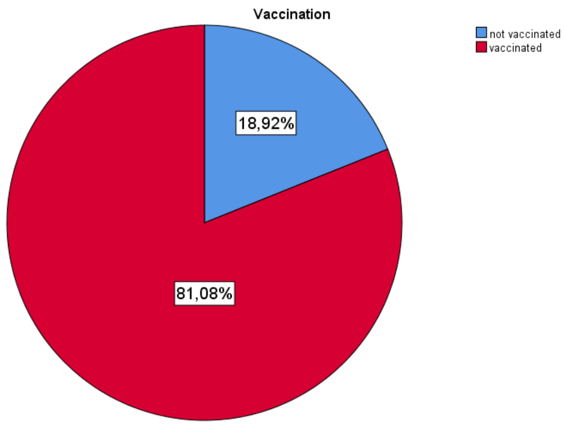

Figure 9. Vaccination distribution in patients.

Table 1. Vaccination status of all responses.

Status	Frequency	Percent
not vaccinated	21	18,9
vaccinated	90	81,1
Total	111	100,0

One-sample t-test revealed the significant difference in distribution of the exposures t(51)= 7103,185, p<0.001 during the time. (M=14.7.2021; SD= 162 d).

Independent sample t test showed the significant higher number of exposures in the unvaccinated group (N=11, M=3.91, SD= 1.3) and vaccinated group (N=45; M = 2.42, SD = 1.438) t (54) = 3.127, p= .003.

There was no significant and low Pearson's correlation (almost significant) between the date of exposition and number of the protentional contacts with SARS-Co-2 r= 0.265, N=52, p=0.058.

3.3. Biosafety protocol

The records of safety feeling of patients was on the scale 1-5, where the 1 represents „no safety feeling "to 5 „very safe ", from 111 patients mean feeling was M= 4.59, SD= 0.732 (**Figure 10**, and **Table 2**).

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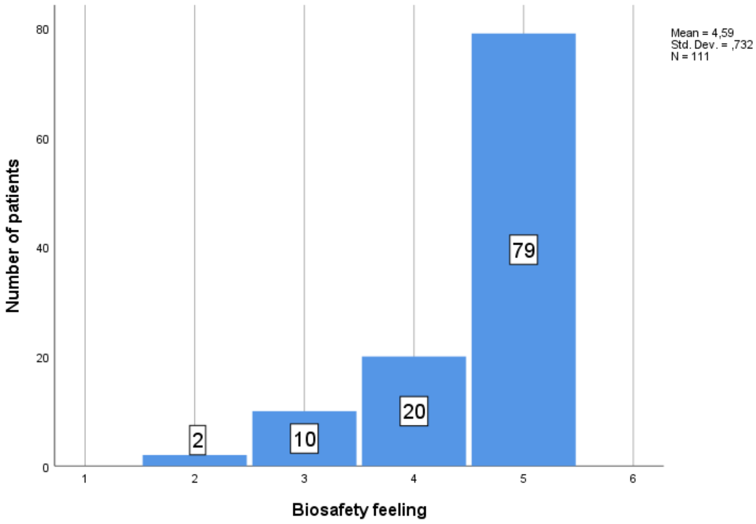

Figure 10. Number of the biosafety feeling records by value.

Table 2. Biosafety feeling of patient during dental procedures.

	N	**Mean**	**Std. Deviation**	**Std. Error**	**95% Confidence Interval for Mean** Lower Bound	**95% Confidence Interval for Mean** Upper Bound	Minimum	Maximum
disease free	74	4,55	,743	,086	4,38	4,73	2	5
Ab+	3	4,67	,577	,333	3,23	6,10	4	5
PCR/Ag +	30	4,73	,583	,106	4,52	4,95	3	5
multiple	3	3,67	1,528	,882	-,13	7,46	2	5
other	1	5,00	.	.	.	.	5	5
Total	111	4,59	,732	,069	4,45	4,72	2	5

Between the groups of unvaccinated patients, which one was declared as „Never got the vaccine against SARS-Co-2“(N=5, M= 5, SD=0) and the second group was „Unvaccinated, but still waiting“ (N=16, M=4.5, SD= .730), there was no significant difference between the biosafety feeling t(19)= -1.504, p=.149

There was no statistical difference in biosafety feeling between in the group of vaccinated patients between the patients without booster dose (N=78, M=4.56, SD= .783) and with booster dose (N=12, M= 4.67, SD=.492).

37 patients answered the question „Could you have ever visited our clinic as already infected? “, there was scale, which divided the risk of infectious status to 1 no, there were no chance to be infectious during the visit, until 5 – yes, I was infectious during the visit. M= 1. 32, SD = .818.

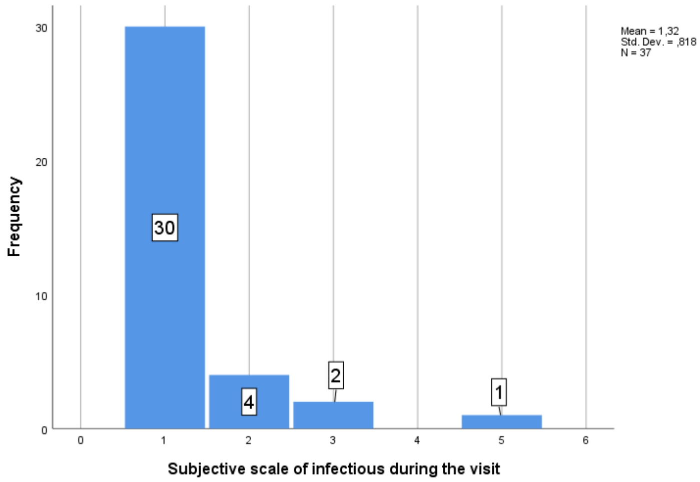

Figure 11. Number of subjective infectious status during visit.

For the patients, who answered the question of possible infectious status during the visit (N=6) (scale of potential risk was higher than 1), they recorded the most no symptoms during the visit N=3 (50%), headache N=2 (33,3%) and pain of joints N=1 (16,67%) (**Figures 11** and **12**).

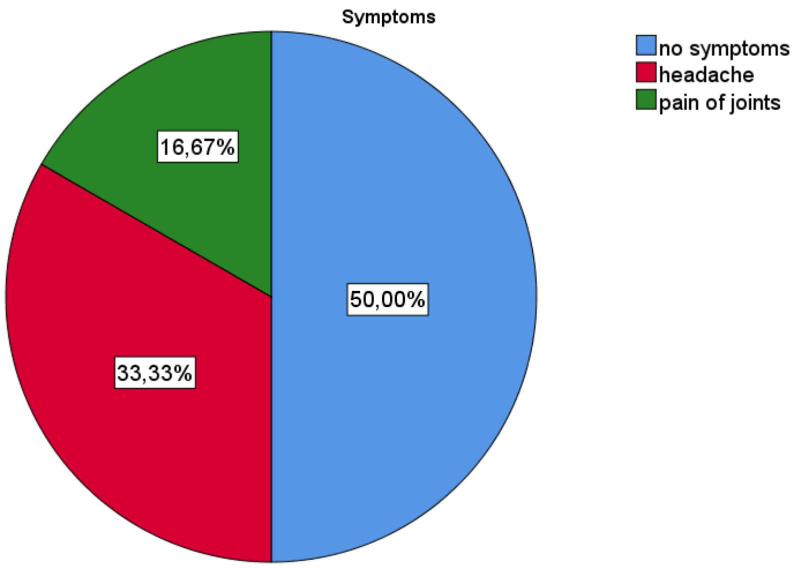

Figure 12. Potential infectious patients during the visit and spectrum of their symptoms.

There was medium correlation between number of exposures and potentially infectious patients r (28) = .402; p= .034.

4. Discussion

Evaluated prospective setting for orthodontic workflow is based on combination of well researched technologies with known virucidal effects. Together this combination is simple and sustainable. Despite the results, preliminary suggest its virucidal effectivity of such prospective setting, these shall be considered as preliminary data for a larger study.

Evaluated subjective feedback from pseudonymous questionnaires showed that under this prospective setting infected patients were treated with high probability. Also, data suggest that chances of SARS-CoV-2 cross infection occurrence in the monitored clinical environment were extremely low.

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With awareness of limitations of single arm, single center studies, we shall emphasize that practice guidelines should rarely, if ever, be based on evidence from single-center trials and this study shall encourage clinicians from dental community to engage in further and wider evaluation of such prospective settings. Combination of UVC and dispersed oil in virucidal air-processing might evolve in the very near future to a sustainable model for biosafe dental care. Dispersion of aerosols during dental therapy and other procedures and technologies to reduce the contagion among dentists are well researched [7,127,128]. However, there is currently no comparative data available about how frequently patients get infected during orthodontic appointments or other biosafety efficiency.

Further interpretation of the study results shows, that from 115 on-line form responses one was probably intentionally invalid as it repeatedly referred triple vaccination even before 3rd shots were available in EU as well references events out of the observed 18-month period and entered various other oxymorons. This response has been evaluated as invalid.

Approximately every second responder had a history of recent Covid-19 exposition. Dates of these exposures (**Figure 8**) correlate with Slovak regional pandemic situation and is obvious difference between previous and the current wave.

45 (50%) of all vaccinated received their last shot until June 2021, so with over 6 months since last vaccination their immunity from vaccines against Omicron variant will not be probably relevant.

The evaluation of the protocol reveals 9 patients reporting the possibility of them being infectious during their visit to the clinic. There was no incident of personnel getting infected from patients or within work. Only two of the personnel got infected with covid in the past. Both cases were from well-known family sources.

37 from 38 infected responders rejected the possibility they got infected at the clinic in the monitored period. Only one of them considered this as the possibility with the lowest offered level of confidence. There were five levels of confidence of this parameter:

1 - Certainly not! 0%
2 – 25%
3 - maybe 50%
4 – 75%
5 - Sure I've got it there 100%

37 patients answered the question „Could you have ever visited our clinic as already infected? ", (**Figure 11**) All the infectious patients visiting the clinic were asymptomatic as they would not get through initial entry filter (**Figure 12**).

In this article authors have presented a biosafety protocol with further context to orthodontic care facing Omicron variant with new epidemiological properties. With this new variant we anticipate a higher transmissibility and lower protection from vaccines, albeit with milder clinical symptoms [80–86,88,90,92,93]. So, there is more likely to have an asymptomatic carrier on dental procedure in the near future than is today.

The results of the survey have demonstrated that patient entry-symptomatic-screening prevented symptomatic patients present in the dental procedures. Survey also revealed that most of the vaccinated patients have probably very low or nearly no protection from vaccines [42,48,78,80,82].

The weakness of this study is the clinical evaluation of clinical performance of the true safety of this biosafety protocol. On-line survey does not represent representative sample, it depends on the self-assessment of the responders. As well there is a high probability that responders are more responsible part of the targeted group.

The results can be interpreted from the perspective of previous studies presented in the Introduction chapter as supporting the validity of the protocol, albeit not proving him safe rather proving him not unsafe. Wider and multicentric research is necessary to

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prove reliability of this settings. Ideally with similar clinic not following the protocol, however working in the similar geographical location and intensity.

Approximately half of the responding patients were exposed to an infected person with Covid-19, however this is self-assessment evaluation. It is interesting that dates of these exposures correlate with Slovak regional pandemic situation in those times. It is also obvious difference between the previous and the current wave. The frequency of exposures during the current wave is higher than in the previous when more strict lockdowns were implied. 50% of all vaccinated patients have received their last shot before June 2021, so with over 6 months since the last vaccination their immunity from vaccines against Omicron variant will not be probably relevant [42,82].

More transmissible Omicron variant defines a new chapter of COVID-19 pandemics. As it is spreading at a rate we have not seen with any previous variants, there is a concern that people are dismissing omicron as mild, not learning from the recent past. Even if Omicron does cause less severe disease, the sheer number of cases could once again overwhelm unprepared health systems [129].

Omicron contains mutations associated with higher levels of immune escape, higher transmissibility, and an improved ability to bind cells. But there are also many mutations within the new variant that are not yet understood. As we have no idea what these new mutations do yet, it is logical to stay cautious and responsible [129].

Predictions of practicality and efficiency of this prospective setting for dental care are difficult, as they face only the preliminary findings about Omicron variant and society attitudes are changing. We are currently facing considerations of Omicron as a possible pandemic-ender, with some people including some politicians willing to take the risk for the sake of the economy. Some people are willing to get even voluntarily infected despite the Omicrons's c. The known risks of the infection with impact on the nervous system, heart tissue or the risk of long covid are known. It remains unclear whether Omicron will have any of the "silent" effects seen with earlier variants, such as self-attacking antibodies, sperm impairments and changes in insulin-producing cells.

Only time will reveal if there were other hidden risks for our health. In this regard, only recently have researchers found strong evidence that it's an infection with the Epstein-Barr virus - a particularly ubiquitous member of the herpesvirus family, best known for causing mononucleosis, triggers multiple sclerosis (MS). Infection with Epstein-Barr increased the likelihood of developing multiple sclerosis, by more than 32-fold [130].

However, as this new era puts current vaccines into different perspective, masks, ventilation, and hygiene stay again unaffected. Vaccines are tools that have the greatest impact when they are used to protect those who are most at risk. They are the last line of our defense. Vaccines cannot be today considered as substitute for masks, distancing, ventilation, or hand hygiene. It also seems logical that Omicron-like strains are here to stay. It can be fought with measures that work today and that must be sustainable. This presented biosafety protocol addresses higher risks suggested by preliminary observations that indicate Omicron spreads faster and escapes antibodies more readily than previous variants. Loss of smell and taste is clinically frequent in older variants, now with Omicron, Sore throat and night sweats are reported frequently. The protocol anticipates the increase of reinfections and cases of mild breakthrough infections in people who are vaccinated is highly probable [92].

5. Conclusions

Results of this study suggest perspective application of combined procedures and technologies focused particularly on virucidal air-processing with UVC and oil dispersion as well as other technologies like AI and telemedicine in confrontation with airborne SARS-CoV-2 variants.

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Presented prospective setting in prevention of COVID-19 was evaluated with 111 responses that suggest that 9 patients were treated as infectious asymptomatic carriers (with high probability), however, no cross infection has been identified.

Despite the results suggesting virucidal effectivity of this sustainable biosafety prospective setting, these shall be considered only as preliminary data for a larger study. With awareness of limitations of single arm, single center studies, it shall be highlighted that practice guidelines should rarely, if ever, be based on evidence from single-center trials and this study shall encourage clinicians from dental community to engage in further and wider evaluation of described technologies and procedures.

While more infectious Omicron-like strains does appear to be clinically less severe compared to Delta, its long-term effects are yet unknown and dental profesionals must not risk patients` infection [131].

Supplementary Materials: The following are available online at https://docs.google.com/spreadsheets/d/1lznYWB32gTb282v4HJbQRY_Uw42xXnBhNj-vnmvJvKE/edit?usp=sharing

Author Contributions:

Conceptualization, Martin Smatana, Georgia Fountoulaki and Bohuslav Novák; Data curation, Andrej Thurzo, Peter Sabaka, Ivan Varga, Ladislav Czakó and Branislav Gális;

Formal analysis, Andrej Thurzo, Alexandra Bražinová, Iveta Waczulíková, Martin Smatana, Veronika Kurilová, Branislav Gális and Bohuslav Novák;

Funding acquisition, Helena Kosnáčová; Investigation, Iveta Waczulíková and Ladislav Czakó; Methodology, Andrej Thurzo, Iveta Waczulíková, Martin Smatana, Veronika Kurilová, Jana Kaiferová, Bela Mriňáková, Branislav Gális and Georgia Fountoulaki;

Project administration, Peter Sabaka and Bohuslav Novák; Resources, Andrej Thurzo, Wanda Urbanová and Peter Sabaka; Software, Andrej Thurzo, Iveta Waczulíková and Bela Mriňáková;

Supervision, Alexandra Bražinová, Neda Markovská, Iveta Waczulíková and Bohuslav Novák; Validation, Peter Sabaka, Helena Kosnáčová and Branislav Gális;

Visualization, Andrej Thurzo, Iveta Waczulíková, Bela Mriňáková, Ladislav Czakó and Branislav Gális;

Writing – original draft, Andrej Thurzo, Wanda Urbanová, Helena Kosnáčová, Bela Mriňáková, Ivan Varga, Ladislav Czakó and Branislav Gális;

Writing – review & editing, Andrej Thurzo, Alexandra Bražinová, Iveta Waczulíková, Wanda Urbanová, Martin Strunga, Veronika Kurilová, Jana Kaiferová, Peter Sabaka, Helena Kosnáčová, Bela Mriňáková and Ivan Varga.

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Institutional Review Board Statement: The study was conducted according to the guidelines of the Declaration of Helsinki, and no approval was necessary by the Ethics Committee. Ethical review and approval were waived for this study, since no experimental materials or approaches were used. All used materials and machines were fully certified and are still available on the market.

Informed Consent Statement: Written informed consent was obtained from all subjects involved in the study.

Data Availability Statement: We fully adhere to Data Availability Statements in section "MDPI Research Data Policies" at https://www.mdpi.com/ethics.

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