Effectiveness of Using a Patient Simulator with Real-Time Feedback to Improve Light-Curing Skills of Dental Students

Tauböck, Tobias T.; Par, Matej; Attin, Thomas; Burrer, Phoebe

Source / Izvornik: Applied Sciences, 2020, 10

Journal article, Published version Rad u časopisu, Objavljena verzija rada (izdavačev PDF)

https://doi.org/10.3390/app10228269

Permanent link / Trajna poveznica: https://urn.nsk.hr/urn:nbn:hr:127:390945

Rights / Prava: Attribution 4.0 International/Imenovanje 4.0 međunarodna

Download date / Datum preuzimanja: 2025-03-01



Repository / Repozitorij:

University of Zagreb School of Dental Medicine Repository







Article Effectiveness of Using a Patient Simulator with Real-Time Feedback to Improve Light-Curing Skills of Dental Students

Tobias T. Tauböck ^{1,*}, Matej Par ^{1,2}, Thomas Attin ¹ and Phoebe Burrer ¹

- ¹ Department of Conservative and Preventive Dentistry, Center for Dental Medicine, University of Zurich, 8032 Zurich, Switzerland; mpar@sfzg.hr (M.P.); thomas.attin@zzm.uzh.ch (T.A.); phoebe.burrer@zzm.uzh.ch (P.B.)
- ² Department of Endodontics and Restorative Dentistry, School of Dental Medicine, University of Zagreb, 10000 Zagreb, Croatia
- * Correspondence: tobias.tauboeck@zzm.uzh.ch; Tel.: +41-44-634-32-84

Received: 5 October 2020; Accepted: 18 November 2020; Published: 21 November 2020



Abstract: The present study investigated the effectiveness of employing a patient simulator with an integrated visual feedback mechanism to improve the light-curing skills of dental students. A total of 44 third-year dental students were randomly divided into a control group (n = 22) and a training group (n = 22). Both groups light-cured a simulated restoration in tooth 27 in a patient simulator (MARC Patient Simulator, BlueLight Analytics, Halifax, Canada) by using the same curing device for 10 s. Delivered irradiances were recorded in real time by the built-in spectrophotometer. After measuring the baseline irradiances for both groups, the training group received detailed light-curing instructions and hands-on training with immediate visual feedback using the patient simulator. The irradiance of the training group was re-measured after the training. Both groups then attended a 26-day preclinical course, which involved placing 30 composite restorations. Upon completion of this course, the light-curing performance of both groups was re-assessed. The data were statistically analyzed using the Wilcoxon signed-rank test, Friedman's ANOVA, and the Mann-Whitney U-test at an overall level of significance of $\alpha = 0.05$. At baseline, the control and the training group delivered statistically similar irradiances with similar data scattering. In the training group, data scattering was considerably reduced after the hands-on training with the patient simulator. After the 26-day preclinical course, the irradiance of the training group was significantly higher and considerably less scattered compared to the control group. In conclusion, training with the patient simulator improved the light-curing performance of the dental students, mainly by helping them to deliver light energy more consistently.

Keywords: dental education; patient simulator; phantom course; light polymerization; dental curing lights

1. Introduction

Over the last quarter century, the teaching and placement of posterior resin composite restorations have steadily increased [1]. According to dental market data, more than 260 million direct composite restorations are nowadays placed each year worldwide [2]. Even though resin composites enable conservative, minimally invasive restorative therapy [3–6], a median longevity of only about six years has been reported for posterior composite restorations placed in general practice [7], with secondary caries and material fractures being the primary reason for failure [7,8].

The success of resin composite restorations is closely related to the degree of monomer conversion of the material, which in turn is determined by the amount of radiant energy applied by the operator



during light polymerization [9,10]. Inadequate resin polymerization has been shown to deteriorate the material's physico-mechanical properties [11,12], reduce its bond strength to the tooth [13,14], and increase wear [15] and bacterial colonization [16] of the restoration. Furthermore, insufficient curing may compromise the biocompatibility of the composite material due to the release of unreacted monomers [17–19].

A clinician's light-curing technique significantly affects the amount of light energy delivered to a restoration. In a previous study, Price et al. observed an up to 6-fold difference in the amount of radiant exposure applied by different operators, even when the same light-curing unit and the same irradiation time were used [20]. Even though a low radiant exposure may lead to a hard surface at the top of the composite restoration, it may simultaneously result in insufficient polymerization in deeper parts due to light scattering and absorption by the composite material [12,21–24]. Clinically, it is not possible for the practitioner to assess the depth of cure of the composite, so that insufficient polymerization of the material will remain unnoticed.

Until recently, dental students and educators could not measure the light energy delivered to restorations. Hence, the problem of insufficient light-curing could not be addressed in practical dental education. Therefore, a patient simulator with light sensors inserted in typodont teeth has been introduced, which allows for the quantification of the applied irradiance by means of a built-in spectrophotometer and provides real-time feedback on light-curing performance [20]. Computer-assisted simulators can help identify operators who need instructional assistance, especially for technically demanding tasks [25]. Furthermore, it could be shown that training tools with digital visual feedback have great potential to optimize the learning process of students in case of complex practical operations [26]. While the relevance of hands-on training to acquire light-curing skills has been repeatedly reported in the literature [27,28], information on the retention of light-curing skills after individualized practical training is scarce.

The aim of this study was therefore to investigate the effectiveness of using a patient simulator to improve the ability of dental students to apply light energy from a light-curing device to a restoration, and to evaluate the effect of the simulator-based training on the retention of the light-curing skills. It was hypothesized that the students would deliver more radiant exposure after they received training with the patient simulator, including immediate visual feedback and individualized instructions.

2. Materials and Methods

A total of 44 third-year dental students who attended the preclinical phantom course in Conservative Dentistry at the University of Zurich participated in the study. Informed consent was obtained from the participants, and they were anonymized by individual codes. Under these terms, the study was exempted from the need to get ethical approval by the local ethics committee, and a declaration of non-jurisdiction was obtained from the Swiss Ethics Committees on Research (BASEC-Nr. 2020-01309). Before they attended the practical phantom course, all students had received a theoretical lecture on light-curing in the regular curriculum, which provided them with basic knowledge about light polymerization. The students were then randomly divided into a control group (n = 22) and a training group (n = 22).

At the start of the phantom course, the participants from both groups were asked to light-cure a simulated posterior restoration (tooth 27) in the MARC Patient Simulator (BlueLight Analytics, Halifax, Canada) in order to assess their baseline light-curing performance. All students used the same light-curing unit (SmartLight Pro, Dentsply Sirona, Bensheim, Germany), and the irradiation time was standardized to 10 s. The output irradiance of the light-curing unit was monitored for consistency throughout the whole study period using a calibrated FieldMaxII-TO power meter and PM2 thermopile sensor (Coherent, Santa Clara, CA, USA). The irradiance delivered to the simulated restoration in the MARC Patient Simulator was determined using a 3.9-mm diameter cosine-corrected light detector (CC3-UV, Ocean Optics, Dunedin, FL, USA) attached by a fiber-optic cable to a laboratory-grade spectrophotometer (USB4000, Ocean Optics, Dunedin, FL, USA) inside a mannequin head. The detector

was located at the bottom of a Class I cavity preparation in the upper left second molar, 2 mm below the cavosurface margin and 4 mm from the cusp tip.

In order to better imitate clinical conditions, the MARC Patient Simulator was fixed in a dental chair, and its mouth opening was limited to 40 mm. Furthermore, dental rubber dam, sectional matrices, and a separation ring (Palodent V3 Sectional Matrix System, Dentsply Sirona, Bensheim, Germany) were placed as in routine filling therapies. Prior to the light-curing procedure, the students were instructed to position the head of the patient simulator as they would do with a real patient. At their free disposal, various auxiliary tools lay in front of them on the tray of the dental chair, such as protective orange eyeglasses, standard protective glasses, an orange light shield, a mirror, and a probe.

After testing the baseline performance of both groups, the training group received a three-part training with the patient simulator: In the first part, the students were given a practical demonstration with the simulator on how to optimize the light-curing technique. For this purpose, they were taught how to correctly adjust the dental chair and position the head of the patient according to ergonomic aspects and in order to provide the light guide with a straight-line access to the restoration. The students were then shown how to position and stabilize the light-guide tip correctly, i.e., at right angles and as close as possible to the restoration surface. Furthermore, the relevance of wearing blue-light-blocking orange protective glasses was demonstrated to the students, which allow them to look directly at the restoration during the light-curing process and to stabilize the light guide with their free hand. During the practical demonstrations, the integrated visual feedback mechanism of the patient simulator allowed the students to follow in real time how small changes in the light-curing technique, such as changes in the position, distance, and tilt angle of the light guide, affect the amount of light delivered to a restoration.

In the second part of the training, the students were asked to light-cure the simulated restoration in tooth 27 of the MARC Patient Simulator. During light-curing, the students' technique and potential mistakes were observed. Based on the real-time irradiance profile recorded by the simulator's built-in software and the observations made, the students received individual instructions on how to improve their light-curing technique and correct detected mistakes. Subsequently, in the third part of the training, the students practiced light-curing twice on their own on the MARC Patient Simulator.

After training with the patient simulator, the light-curing performance of the training group was re-assessed under the same conditions as for the baseline testing. Both groups then attended the 26-day preclinical course, which involved placing 30 composite restorations. Upon completion of the preclinical course, the light-curing performance of both groups was re-assessed. The study protocol is summarized in Figure 1. After the final measurements of the study, the students in the control group received the same training with the patient simulator as those in the training group, in order to enable all course participants to practice with the simulator and thus ensure consistent education.

Due to significant deviations of the data from the normal distribution, non-parametric statistics were used in the statistical analysis. For the control group, the irradiance values recorded at baseline and after the 26-day preclinical course were compared using the Wilcoxon signed-rank test. For the training group, the irradiance values recorded at baseline, after training with the simulator, and after the 26-day preclinical course were compared using Friedman's ANOVA by ranks, which was followed by post-hoc comparisons using the Wilcoxon signed-rank test with Bonferroni adjustment. The comparisons between the control and the training group were performed using the Mann-Whitney U-test. The statistical analysis was conducted using SPSS version 20 (IBM, Armonk, NY, USA) at an overall level of significance of $\alpha = 0.05$.



Figure 1. Schematic representation of the study protocol.

3. Results

The irradiances delivered by the dental students at baseline, after training with the MARC Patient Simulator, and after the 26-day preclinical course, are presented in Figure 2. At baseline, the control and the training group delivered statistically similar irradiances. A similar data scattering at baseline was identified in the control and the training group, with interquartile ranges of 264 and 233 mW/cm², respectively.

In the training group, irradiance was not significantly increased compared to the baseline values after the students trained with the patient simulator; however, data scattering was considerably reduced, as evidenced by a 4.7-fold lower interquartile range compared to that at baseline. After the 26-day preclinical course, data scattering in the training group decreased further (7.5-fold lower than at baseline), and a significant improvement in the delivered irradiance compared to the baseline values was identified.

In the control group, the irradiance values measured after the 26-day preclinical course were not significantly different from the baseline values. Furthermore, data scattering in the control group after the 26-day preclinical course remained similar to that at baseline, with interquartile ranges of 255 and 264 mW/cm², respectively.

The comparison of the training and the control group after the 26-day preclinical course indicates that the irradiance values of the training group were significantly higher (median values of 1147 and 1061 mW/cm², respectively) and considerably less scattered (interquartile ranges of 31 and 255 mW/cm², respectively).



Time of evaluation

Figure 2. Irradiance (mW/cm²) delivered by the dental students at baseline, after training with the MARC Patient Simulator, and after the 26-day preclinical course. The boxplots show the medians (black lines) with 25% and 75% percentiles (boxes); the whiskers represent $1.5 \times IQR$ (interquartile range), or minima and maxima of the distribution if below $1.5 \times IQR$; outliers are shown as circles, and extreme outliers are shown as asterisks. Same lowercase letters indicate statistically similar values within the control group, whereas same uppercase letters indicate statistically similar values within the training group. *p*-values for comparisons between the control and the training group are indicated above the corresponding boxes.

4. Discussion

Appropriate light-curing is crucial for the long-term success of direct resin composite restorations because it determines the physico-mechanical and biological properties of the material [17,18,29]. The present study revealed that before receiving detailed light-curing instructions and hands-on training, the dental students delivered a wide range of radiant exposure between 1.9 and 12.5 J/cm² during the 10-s irradiation time, representing a more than 6-fold difference between the minimum and maximum amount of light energy applied. This suggests that clinically relevant properties of composite restorations such as wear resistance, depth of cure, and hardness may differ considerably after light-curing [11,12,15]. Indeed, several studies on the longevity of composite restorations showed that operator factors significantly affected the results [30,31].

The light energy necessary to adequately polymerize a resin composite depends on the brand type, increment thickness, translucency, and shade of the material [32,33], but a radiant exposure of 10 J/cm² is usually regarded as the critical minimum threshold [20,27]. Before training, 15 out of 22 students

(68%) in the training group delivered irradiances above that threshold, while after the training, all students (100%) were able to deliver irradiances above the critical minimum. After completion of the 26-day preclinical course, 21 out of 22 students (95%) in the training group were able to surpass the stipulated threshold. These results indicate that the individualized simulator training with immediate visual feedback helped to enable a higher percentage of students to deliver clinically relevant radiant exposures. On the other hand, in the control group, the number of students able to deliver radiant exposures above the stipulated threshold remained unchanged after the 26-day preclinical course compared to the evaluation at baseline (14 out of 22; 64%). This suggests that a certain number of worse-performing students were unable to improve their light-curing skills by attending the 26-day preclinical course alone, clearly indicating the benefit of the individualized training with the patient simulator.

The main benefit of the training with the patient simulator was that radiant exposures delivered by students to a simulated posterior restoration became considerably more consistent. This finding is clinically more important than a statistically significant improvement of 5% in the training group identified after the preclinical course, and an 8% significantly better performance of the training group compared to the control group after the preclinical course. Although deemed significant by the formal statistical analysis, such relatively small improvements in light-curing performance are of secondary relevance compared to the considerably narrowed distributions of irradiance values after the training with the patient simulator.

Before receiving detailed instructions and training, most students chose an orange light shield to protect their eyes from the bright blue light emitted by the light-curing device. A disadvantage of using shields is that they must be handheld, which leaves no hand free to stabilize the curing light tip while light-curing. This may have caused displacements in the position or tilt angle of the light-guide tip during the curing procedure and may explain the relatively high percentage of students who failed to meet the target radiant exposure of 10 J/cm² at baseline. In the practical demonstrations and hands-on training with the simulator, the students were advised to wear blue-light-blocking orange protective glasses so that the position of the light-guide tip over the restoration can be safely monitored. They were also advised to wear such glasses so that they could carefully stabilize the curing light tip with their free hand. This might have contributed to the improved light-curing performance after the simulator training.

A limitation of the present study is that the students knew that their light-curing performance was measured with the patient simulator. This circumstance might have masked the effect of the simulator training, since all students were likely more cautious about light-curing than usual, knowing that their performance was recorded. Future studies should investigate whether patient simulator-based training on light-curing would actually improve material properties of composite restorations.

5. Conclusions

Within the limitations of the present study, it is concluded that training with the patient simulator significantly improved the light-curing performance of dental students. The individualized training with the patient simulator was most beneficial for the subgroup of worse-performing students, helping them to perform light-curing procedures more consistently.

Author Contributions: Conceptualization, T.T.T.; methodology, T.T.T.; formal analysis, M.P.; investigation, T.T.T. and P.B.; resources, T.T.T. and T.A.; writing—original draft preparation, T.T.T.; writing—review and editing, T.T.T., M.P., T.A. and P.B.; visualization, T.T.T. and M.P.; supervision, T.T.T. and T.A.; project administration, T.T.T. and T.A.; funding acquisition, T.T.T. All authors have read and agreed to the published version of the manuscript.

Funding: The purchase of the MARC Patient Simulator (BlueLight Analytics, Halifax, Canada) was funded by a grant of the Foundation for Research in Science and the Humanities at the University of Zurich.

Conflicts of Interest: The authors declare no conflict of interest.

References

- 1. Wilson, N.H.; Lynch, C.D. The teaching of posterior resin composites: Planning for the future based on 25 years of research. *J. Dent.* **2014**, *42*, 503–516. [CrossRef]
- 2. Heintze, S.D.; Rousson, V. Clinical effectiveness of direct class II restorations—A meta-analysis. *J. Adhes. Dent.* **2012**, *14*, 407–431.
- 3. Körner, P.; El Gedaily, M.; Attin, R.; Wiedemeier, D.B.; Attin, T.; Tauböck, T.T. Margin integrity of conservative composite restorations after resin infiltration of demineralized enamel. *J. Adhes. Dent.* **2017**, *19*, 483–489.
- 4. Wiegand, A.; Credé, A.; Tschammler, C.; Attin, T.; Tauböck, T.T. Enamel wear by antagonistic restorative materials under erosive conditions. *Clin. Oral Investig.* **2017**, *21*, 2689–2693. [CrossRef]
- Körner, P.; Sulejmani, A.; Wiedemeier, D.B.; Attin, T.; Tauböck, T.T. Demineralized enamel reduces margin integrity of self-etch, but not of etch-and-rinse bonded composite restorations. *Odontology* 2019, 107, 308–315. [CrossRef] [PubMed]
- Tauböck, T.T.; Jäger, F.; Attin, T. Polymerization shrinkage and shrinkage force kinetics of high- and low-viscosity dimethacrylate- and ormocer-based bulk-fill resin composites. *Odontology* 2019, 107, 103–110. [CrossRef] [PubMed]
- Sunnegårdh-Grönberg, K.; van Dijken, J.W.; Funegård, U.; Lindberg, A.; Nilsson, M. Selection of dental materials and longevity of replaced restorations in Public Dental Health clinics in northern Sweden. *J. Dent.* 2009, *37*, 673–678. [CrossRef] [PubMed]
- 8. Beck, F.; Lettner, S.; Graf, A.; Bitriol, B.; Dumitrescu, N.; Bauer, P.; Moritz, A.; Schedle, A. Survival of direct resin restorations in posterior teeth within a 19-year period (1996–2015): A meta-analysis of prospective studies. *Dent. Mater.* **2015**, *31*, 958–985. [CrossRef] [PubMed]
- Calheiros, F.C.; Daronch, M.; Rueggeberg, F.A.; Braga, R.R. Influence of irradiant energy on degree of conversion, polymerization rate and shrinkage stress in an experimental resin composite system. *Dent. Mater.* 2008, 24, 1164–1168. [CrossRef] [PubMed]
- Par, M.; Spanovic, N.; Bjelovucic, R.; Skenderovic, H.; Gamulin, O.; Tarle, Z. Curing potential of experimental resin composites with systematically varying amount of bioactive glass: Degree of conversion, light transmittance and depth of cure. J. Dent. 2018, 75, 113–120. [CrossRef]
- Sobrinho, L.C.; Goes, M.F.; Consani, S.; Sinhoreti, M.A.; Knowles, J.C. Correlation between light intensity and exposure time on the hardness of composite resin. *J. Mater. Sci. Mater. Med.* 2000, *11*, 361–364. [CrossRef] [PubMed]
- 12. Tarle, Z.; Attin, T.; Marovic, D.; Andermatt, L.; Ristic, M.; Tauböck, T.T. Influence of irradiation time on subsurface degree of conversion and microhardness of high-viscosity bulk-fill resin composites. *Clin. Oral Investig.* **2015**, *19*, 831–840. [CrossRef] [PubMed]
- Staudt, C.B.; Krejci, I.; Mavropoulos, A. Bracket bond strength dependence on light power density. *J. Dent.* 2006, 34, 498–502. [CrossRef] [PubMed]
- 14. Yamamoto, A.; Tsubota, K.; Takamizawa, T.; Kurokawa, H.; Rikuta, A.; Ando, S.; Takigawa, T.; Kuroda, T.; Miyazaki, M. Influence of light intensity on dentin bond strength of self-etch systems. *J. Oral Sci.* **2006**, *48*, 21–26. [CrossRef] [PubMed]
- 15. Ferracane, J.L.; Mitchem, J.C.; Condon, J.R.; Todd, R. Wear and marginal breakdown of composites with various degrees of cure. *J. Dent. Res.* **1997**, *76*, 1508–1516. [CrossRef] [PubMed]
- 16. Brambilla, E.; Gagliani, M.; Ionescu, A.; Fadini, L.; Garcia-Godoy, F. The influence of light-curing time on the bacterial colonization of resin composite surfaces. *Dent. Mater.* **2009**, *25*, 1067–1072. [CrossRef] [PubMed]
- 17. Peutzfeldt, A. Resin composites in dentistry: The monomer systems. *Eur. J. Oral Sci.* **1997**, *105*, 97–116. [CrossRef] [PubMed]
- 18. Wegehaupt, F.J.; Tauböck, T.T.; Attin, T.; Belibasakis, G.N. Influence of light-curing mode on the cytotoxicity of resin-based surface sealants. *BMC Oral Health* **2014**, *14*, 48. [CrossRef]
- 19. Tauböck, T.T.; Marovic, D.; Zeljezic, D.; Steingruber, A.D.; Attin, T.; Tarle, Z. Genotoxic potential of dental bulk-fill resin composites. *Dent. Mater.* **2017**, *33*, 788–795. [CrossRef]
- 20. Price, R.B.; McLeod, M.E.; Felix, C.M. Quantifying light energy delivered to a Class I restoration. *J. Can. Dent. Assoc.* **2010**, *76*, a23.

- Dieckmann, P.; Mohn, D.; Zehnder, M.; Attin, T.; Tauböck, T.T. Light transmittance and polymerization of bulk-fill composite materials doped with bioactive micro-fillers. *Materials* 2019, 12, 4087. [CrossRef] [PubMed]
- 22. Par, M.; Spanovic, N.; Tauböck, T.T.; Attin, T.; Tarle, Z. Degree of conversion of experimental resin composites containing bioactive glass 45S5: The effect of post-cure heating. *Sci. Rep.* **2019**, *9*, 17245. [CrossRef] [PubMed]
- Par, M.; Marovic, D.; Attin, T.; Tarle, Z.; Tauböck, T.T. The effect of rapid high-intensity light-curing on micromechanical properties of bulk-fill and conventional resin composites. *Sci. Rep.* 2020, *10*, 10560. [CrossRef] [PubMed]
- 24. Par, M.; Spanovic, N.; Mohn, D.; Attin, T.; Tauböck, T.T.; Tarle, Z. Curing potential of experimental resin composites filled with bioactive glass: A comparison between Bis-EMA and UDMA based resin systems. *Dent. Mater.* **2020**, *36*, 711–723. [CrossRef] [PubMed]
- 25. Urbankova, A.; Engebretson, S.P. Computer-assisted dental simulation as a predictor of preclinical operative dentistry performance. *J. Dent. Educ.* **2011**, *75*, 1249–1255. [CrossRef] [PubMed]
- 26. Nagy, Z.A.; Simon, B.; Tóth, Z.; Vág, J. Evaluating the efficiency of the Dental Teacher system as a digital preclinical teaching tool. *Eur. J. Dent. Educ.* **2018**, 22, e619–e623. [CrossRef]
- 27. Price, R.B.; Felix, C.M.; Whalen, J.M. Factors affecting the energy delivered to simulated class I and class V preparations. *J. Can. Dent. Assoc.* **2010**, *76*, a94.
- 28. Federlin, M.; Price, R. Improving light-curing instruction in dental school. J. Dent. Educ. 2013, 77, 764–772. [CrossRef]
- 29. Zorzin, J.; Maier, E.; Harre, S.; Fey, T.; Belli, R.; Lohbauer, U.; Petschelt, A.; Taschner, M. Bulk-fill resin composites: Polymerization properties and extended light curing. *Dent. Mater.* **2015**, *31*, 293–301. [CrossRef]
- 30. Demarco, F.F.; Corrêa, M.B.; Cenci, M.S.; Moraes, R.R.; Opdam, N.J. Longevity of posterior composite restorations: Not only a matter of materials. *Dent. Mater.* **2012**, *28*, 87–101. [CrossRef]
- Laske, M.; Opdam, N.J.; Bronkhorst, E.M.; Braspenning, J.C.; Huysmans, M.C. Longevity of direct restorations in Dutch dental practices. Descriptive study out of a practice based research network. *J. Dent.* 2016, 46, 12–17. [CrossRef] [PubMed]
- Fan, P.L.; Schumacher, R.M.; Azzolin, K.; Geary, R.; Eichmiller, F.C. Curing-light intensity and depth of cure of resin-based composites tested according to international standards. *J. Am. Dent. Assoc.* 2002, 133, 429–434. [CrossRef] [PubMed]
- 33. Karacolak, G.; Turkun, L.S.; Boyacioglu, H.; Ferracane, J.L. Influence of increment thickness on radiant energy and microhardness of bulk-fill resin composites. *Dent. Mater. J.* **2018**, *37*, 206–213. [CrossRef] [PubMed]

Publisher's Note: MDPI stays neutral with regard to jurisdictional claims in published maps and institutional affiliations.



© 2020 by the authors. Licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (http://creativecommons.org/licenses/by/4.0/).