Mini-CAT: Final (Rotation 5 Week 2) **Name: Jordan Villaruel**

CLINICAL QUESTION:

A 30-year-old male complains of loss of smell for the past 2 months. His medical history is positive for a previous COVID-19 infection and he admits the loss of smell started at the same time. Patient denies any improvement in sense of smell since it began. Post COVID-19 anosmia usually resolves spontaneously, however the ENT PA wants to know if intranasal corticosteroids is a viable treatment option to improve sense of smell.

PICO QUESTION:

In the adult population, do intranasal corticosteroids improve post-viral olfactory dysfunction?

PICO SEARCH TERMS:

P	**I**	**C**	**O**
Adults	Intranasal Corticosteroids	Placebo	Sense of smell
Post-viral anosmia	Nasal Steroids	No intervention	Improved olfactory dysfunction
Post-COVID anosmia	Paracervical block	Alternatives	Improved anosmia
Post-viral olfactory loss	Topical steroids		Recovered olfaction
Post-COVID olfactory dysfunction			No improvement

SEARCH STRATEGY:

Database Results:

1. PubMed
    - Intranasal Corticosteroids for Post COVID anosmia → 178
        - Filters: 5 years, meta-analysis, systematic review, RCT → 178
        - Filters: 10 years, meta-analysis, systematic review, RCT → 178
    - Intranasal Corticosteroids for post-viral anosmia → 60
        - Filters: 5 years, meta-analysis, systematic review, RCT → 55
        - Filters: 10 years, meta-analysis, systematic review, RCT → 60
2. Google Scholar
    - Intranasal Corticosteroids for Post COVID anosmia → 4,020
        - Filters: 5 years, sort by relevance, review article → 1,220
    - Intranasal Corticosteroids for post-viral anosmia → 163
        - Filters: 5 years, sort by relevance, review article → 127
3. ScienceDirect
    - Polypharmacy reduction for medication compliance in geriatrics → 49
        - Filters: 5 years, sort by relevance, research article → 38
    - Intranasal Corticosteroids for post-viral anosmia → 164
        - Filters: 5 years, sort by relevance, research article → 27
4. Wiley Online Library
    - Intranasal Corticosteroids for Post COVID anosmia → 44
        - Filters: 5 years, journal articles → 42

Selection Process:
I narrowed down the results by looking for studies that focused on the efficacy of intranasal corticosteroids in treating post COVID-19 anosmia. I screened for articles that gave special attention to the adult patient population, so that it is more relevant to my clinical scenario. Furthermore, I sought for articles were recent within the last 5 years and were either meta-analysis, systematic review, or RCT. I began to narrow down my selection by seeking articles with relevant titles and briefly assessing the abstract. I wanted studies that were relevant to my scenario, therefore I focused on studies that were performed in the U.S. with a population of those suffering from post-COVID olfactory dysfunction. My selection process was directed to include the most relevant and highest level of evidence to determine if intranasal corticosteroids improve sense of smell in those with post COVID-19 anosmia.

ARTICLES CHOSEN:

Article #1 Interventions for the Treatment of Persistent post-COVID-19 Olfactory Dysfunction

Citation: O'Byrne L, Webster KE, MacKeith S, Philpott C, Hopkins C, Burton MJ. Interventions for the treatment of persistent post-COVID-19 olfactory dysfunction. *Cochrane Database of Systematic Reviews 2021*, Issue 7. Art. No.: CD013876. DOI: 10.1002/14651858.CD013876.pub2.
Type of Study: Systematic Review
Abstract: ***Background*:** Olfactory dysfunction is an early and sensitive marker of COVID-19 infection. Although self-limiting in the majority of cases, when hyposmia or anosmia persists it can have a profound effect on quality of life. Little guidance exists on the treatment of post-COVID-19 olfactory dysfunction, however several strategies have been proposed from the evidence relating to the treatment of post-viral anosmia (such as medication or olfactory training). ***Objectives*:** To assess the effects (benefits and harms) of interventions that have been used, or proposed, to treat persisting olfactory dysfunction due to COVID-19 infection. A secondary objective is to keep the evidence up-to-date, using a living systematic review approach. ***Methods*:** The Cochrane ENT Information Specialist searched the Cochrane COVID-19 Study Register; Cochrane ENT Register; CENTRAL; Ovid MEDLINE; Ovid Embase; Web of Science; ClinicalTrials.gov; ICTRP and additional sources for published and unpublished studies. The date of the search was 16 December 2020. ***Main Results:*** We included one study with 18 participants, which compared the use of a 15-day course of oral steroids combined with nasal irrigation (consisting of an intranasal steroid/mucolytic/decongestant solution) with no intervention. Psychophysical testing was used to assess olfactory function at baseline, 20 and 40 days. ***Conclusions:*** There is very limited evidence available on the efficacy and harms of treatments for persistent olfactory dysfunction following COVID-19 infection. However, we have identified other ongoing trials in this area. As this is a living systematic review we will update the data regularly, as new results become available.
Link: https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD013876.pub2/full

Article # 2 Clinical Olfactory Working Group Consensus Statement on the Treatment of Post-infectious Olfactory Dysfunction

Citation: Addison AB, Wong B, Ahmed T, et al. Clinical Olfactory Working Group consensus statement on the treatment of post-infectious olfactory dysfunction. *J Allergy Clin Immunol*. 2021;147(5):1704-1719. doi:10.1016/j.jaci.2020.12.641

Type of Study: Systematic Review

Abstract:
Background: Respiratory tract viruses are the second most common cause of olfactory dysfunction. As we learn more about the effects of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), with the recognition that olfactory dysfunction is a key symptom of this disease process, there is a greater need than ever for evidence-based management of post-infectious olfactory dysfunction (PIOD).
Objectives: Our aim was to provide an evidence-based practical guide to the management of PIOD (including post–coronavirus 2019 cases) for both primary care practitioners and hospital specialists.
Methods: A systematic review of the treatment options available for the management of PIOD was performed. The written systematic review was then circulated among the members of the Clinical Olfactory Working Group for their perusal before roundtable expert discussion of the treatment options. The group also undertook a survey to determine their current clinical practice with regard to treatment of PIOD.
***Results*:** The search resulted in 467 citations, of which 107 articles were fully reviewed and analyzed for eligibility; 40 citations fulfilled the inclusion criteria, 11 of which were randomized controlled trials. In total, 15 of the articles specifically looked at PIOD whereas the other 25 included other etiologies for olfactory dysfunction.
***Conclusions*:** The Clinical Olfactory Working Group members made an overwhelming recommendation for olfactory training; none recommended minocycline antibiotics. The diagnostic role of oral steroids was discussed; some group members were in favor of vitamin A drops. Further research is needed to confirm the place of other therapeutic options.

Link: https://pubmed.ncbi.nlm.nih.gov/33453291/

Article # 3 Effect of Nasal Corticosteroid in the Treatment of Anosmia Due to COVID-19: A Randomized Double-Blind Placebo-Controlled Study

Citation: Rashid RA, Zgair A, Al-Ani RM. Effect of nasal corticosteroid in the treatment of anosmia due to COVID-19: A randomised double-blind placebo-controlled study. *Am J Otolaryngol*. 2021;42(5):103033. doi:10.1016/j.amjoto.2021.103033

Type of Study: Randomized Controlled Trial

Abstract:
Objectives: Anosmia is a common debilitating symptom of the novel coronavirus disease 2019 (COVID-19). Currently, there is no satisfactory treatment of anosmia. Therefore, this study was conducted to evaluate the therapeutic effect of nasal betamethasone drops in the recovery of olfaction in COVID-19-associated anosmia.
Methods: The study was designed as a randomized, double-blind, placebo-controlled clinical trial. In total, 276 PCR-confirmed COVID-19 patients who were presented to the outpatient clinic with anosmia were enrolled in the study. In the betamethasone group, 138 participants received nasal

drops of betamethasone 3 times daily until recovery for a maximum of one month. Similar dose of 9% NaCl drops was administered to 138 participants in the placebo group.
Results: The median age of participants was 29 years (IQR 23–37). Among them, 198 (71.7%) were females. Ageusia was co-presented with anosmia in 234 (84.8%) of participants. In this study, 83% of participants had recovered from anosmia within 30 days, with a median recovery time of 13 days (IQR 8–18). Compared to placebo, nasal application of betamethasone drops has no significant effect on the recovery time of anosmia (hazard ratio 0.88; 95% CI 0.68–1.14; P = 0.31).
Conclusions: The use of nasal betamethasone to facilitate the recovery time of acute anosmia is not advised. In addition, age, smoking status, the duration of anosmia at presentation, and the co-presentation of ageusia with anosmia are important determinant covariates for the recovery time of anosmia. Further clinical trials, which take these covariates into account, will need to be undertaken. The trail has been registered at ClinicalTrails.gov, NCT04569825.

Link: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8024226/

Article # 4 Treatment of Post-Viral Olfactory Dysfunction: An Evidence-Based Review with Recommendations

Citation: Hura N, Xie DX, Choby GW, et al. Treatment of post-viral olfactory dysfunction: an evidence-based review with recommendations. *Int Forum Allergy Rhinol*. 2020;10(9):1065-1086. doi:10.1002/alr.22624

Type of Study: Systematic Review

Abstract:
Background: Post-viral olfactory dysfunction (PVOD) is one of the most common causes of olfactory loss. Despite its prevalence, optimal treatment strategies remain unclear. This article provides a comprehensive review of PVOD treatment options and provides evidence-based recommendations for their use.
***Methods*:** A systematic review of the Medline, Embase, Cochrane, Web of Science, Scopus, and Google Scholar databases was completed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. Studies with defined olfactory outcomes of patients treated for PVOD following medical, surgical, acupuncture, or olfactory training interventions were included. The Clinical Practice Guideline Development Manual and Conference on Guideline Standardization (COGS) instrument recommendations were followed in accordance with a previously described, rigorous, iterative process to create an evidence-based review with recommendations.
Results: From 552 initial candidate articles, 36 studies with data for 2183 patients with PVOD were ultimately included. The most common method to assess olfactory outcomes was Sniffin' Sticks. Broad treatment categories included: olfactory training, systemic steroids, topical therapies, a variety of heterogeneous non-steroidal oral medications, and acupuncture.
***Conclusion*:** Based on the available evidence, olfactory training is a *recommendation* for the treatment of PVOD. The use of short-term systemic and/or topical steroids is an *option* in select patients after careful consideration of potential risks of oral steroids. Though some pharmacological investigations offer promising preliminary results for systemic and topical medications alike, a paucity of high-quality studies limits the ability to make meaningful evidence-based recommendations for the use of these therapies for the treatment of PVOD.

Link: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7361320/

Article # 5 Corticosteroid Nasal Spray For Recovery Of Smell Sensation In COVID-19 Patients: A Randomized Controlled Trial

Citation: Abdelalim AA, Mohamady AA, Elsayed RA, Elawady MA, Ghallab AF. Corticosteroid nasal spray for recovery of smell sensation in COVID-19 patients: A randomized controlled trial. *American Journal of Otolaryngol*. 2021;42(2):102884. doi:10.1016/j.amjoto.2020.102884

Type of Study: Randomized Controlled Trial

Abstract:
Objective: To evaluate the role of the topical corticosteroid, mometasone furoate, nasal spray in the treatment of post COVID-19 anosmia.
Methods: A prospective, randomized, controlled trial was conducted among patients with post COVID-19 anosmia. One hundred patients were randomly assigned to two groups; group I included 50 patients received mometasone furoate nasal spray in an appropriate dose of 2 puff (100 μg) once daily in each nostril for 3 weeks with olfactory training, group II included 50 patients were advised to keep on olfactory training only. The assessment of smell was done using (Visual Analog Scale from 0 to 10). All patients were initially evaluated after their recovery from COVID-19 and followed up for 3 weeks. The smell scores were recorded weekly and the duration of smell loss was recorded from the onset of anosmia till the full recovery.
Results: In both groups, the smell scores significantly improved by the end of the third week ($P < 0.001$). By comparing smell scores between both groups after 1 week, 2 weeks, and 3 weeks of treatment, there were no statistically significant differences between both groups. In group I, (62%) of patients completely recovered their sense of smell after 3 weeks of treatment, compared to (52%) of patients in group II ($P = 0.31$).
Conclusion: The results suggested that using mometasone furoate nasal spray as a topical corticosteroid in the treatment of post COVID-19 anosmia offers no superiority benefits over the olfactory training, regarding smell scores, duration of anosmia, and recovery rates.
Trial registration: ClinicalTrials.gov ID: NCT04484493

Link: https://www.sciencedirect.com/science/article/pii/S0196070920305780

SUMMARY OF THE EVIDENCE:

Author (Date)	Level of Evidence	Sample/Setting (# of subjects/ studies, cohort definition etc.)	Outcome(s) studied	Key Findings	Limitations and Biases
Article 1: O'Byrne L, et al. (2021)	Systematic Review	Authors used RCTs including participants who had symptoms of olfactory disturbance following COVID-19 infection. Only individuals who	Primary: Recovery of sense of smell Serious adverse effects Secondary: Change in sense of smell	Overall, there is very limited evidence available on the efficacy and harms of treatments for persistent olfactory dysfunction following COVID-19 infection.	This review is inherently limited by only having one complete study included. Furthermore, this study only included 18

		had symptoms for at least 4 weeks were included in this review. Studies compared any intervention with no treatment or placebo. Selection criteria: Adult participants (18 and older) with persisting abnormalities of their sense of smell as a consequence of COVID-19. 18 participants, 9 enrolled in the 15-day course of steroids combined with nasal irrigation, the other 9 had no intervention. Psychophysical testing was used to assess baseline olfactory function at 20 and 40 days.	Overall, generic quality of life Presence of parosmia Systemic corticosteroids plus intranasal steroid/mucolytic/decongestant compared to no intervention	Recovery of sense of smell was assessed after 40 days using the Connecticut Chemosensory Clinical Research Center (CCCRC) score. 5 out of 9 participants had normal olfactory function in the intervention group compared to 0 out of 9 - no participants with normal olfactory function in the control group. No adverse events were not identified by any of the patients in this study. This study reported an improvement in sense of smell in the intervention group from baseline (median improvement in CCCRC score 60, interquartile range (IQR) 40) compared to the control group (median improvement in CCCRC score 30, IQR 25).	patients (nine randomized to treatment and nine to no treatment). This study provided only a small amount of evidence regarding the use of intranasal corticosteroids in the recovery of, or change in, olfactory function post-COVID-19 infection.
Article 2: Addison AB, et al. (2021)	Systematic Review	Authors conducted a systematic search of electronic databases (PubMed, Google Scholar, Cochrane database, Web of Science, Scopus, and Embase) Selection criteria: Comparative studies of any design examining the outcome of management of patients with	Olfactory function using different interventions. Assessed different interventions for post-covid olfactory loss in recent literature. The weighed the benefits of non-pharmacological (olfactory	Although there is lack of evidence for using steroids in post–COVID-19 PIOD, there is increasing support for the use of corticosteroids to treat respiratory distress or systemic cytokine storm in severe cases. One study showed that the combination of oral and topical steroids or an oral steroid as monotherapy significantly improves olfactory function versus	Although there is limited evidence for the treatment options available, some treatment options have shown promise and may be useful in selected patients.

		postviral olfactory loss were included. 2352 patients with post-viral anosmia, 40 citations fulfilled inclusion criteria, 11 RCTs In total, 15 of the articles specifically looked at PIOD and the other 25 included other etiologies for olfactory dysfunction.	training, acupuncture) versus pharmacological treatment (nasal steroids, theophylline, antibiotics, vitamin A).	monotherapy with topical steroids. It has been suggested that the favorable effect of oral corticosteroids in PIOD could be attributed to their efficacy on any underlying sinonasal inflammation, possibly because of the mucosal effects of an upper respiratory tract infection. Patients with COVID-19 and other infection-related olfactory dysfunction should be guided through olfactory rehabilitation and be signposted to specialists for other treatments in refractory cases. There is good evidence to suggest that olfactory training (OT) improves olfactory function in patients with PIOD.	
Article 3: Rashid RA, et al. (2021)	Randomized Controlled Trial	Authors used as designed as a randomized, double-blind, placebo-controlled clinical trial. 276 total PCR-confirmed COVID patients who were presented to the outpatient clinic with anosmia were enrolled in the study. 138 participants in the betamethasone group, 138 placebo group Selection criteria:	Primary outcome was the time taken for anosmia to resolve, in days, following the initiation of treatment.	Nasal application of betamethasone had no significant effect on the recovery time of anosmia in COVID-19 patients. Overall, 83% of participants had recovered from anosmia within the follow-up period; 82% in the betamethasone group versus 84% in the placebo group. The evidence from this study suggests that the use of nasal betamethasone to facilitate the recovery time of acute anosmia is not advised.	Limitations of this study include the use self-reported assessment of smell, short term follow-up, and the relatively small sample size. Further clinical trials, which take these covariates (anosmia and ageusia) into account, will need to be undertaken.

		PCR-confirmed SARS-CoV-2 infection, age ≥ 18 years, and recent developed of anosmia. Exclusion criteria included pregnancy, the presence of psychological disorders, history of anosmia before COVID-19 era or sinonasal diseases.			
Article 4: Hura N, et al. (2020)	Systematic Review	Authors searched Medline, Embase, Cochrane, Web of Science, Scopus, and Google Scholar databases Selection criteria: Studies with defined olfactory outcomes of patients treated for PVOD following medical, surgical, acupuncture, or olfactory training interventions were included. 36 studies with data for 2183 patients with PVOD were ultimately included.	Primary outcomes are subjective olfactory measurements and objective olfactory scores Investigates the efficacy steroid treatments versus non-steroidal treatments and reported the olfactory outcomes after losing smell before a viral infection.	The use of short-term systemic and/or topical steroids is an *option* in select patients after careful consideration of potential risks of oral steroids. Despite an encouraging safety profile of topical steroid application and perceived potential of olfactory function after, the heterogeneous data presented here makes conclusions regarding their use challenging. An evidence-based treatment algorithm of patients with PVOD includes a recommendation of the use of olfactory therapy, as it has shown to have improvement in olfaction.	No limitations or bias reported.
Article 5: Abdelalim AA, et al. (2021)	Randomized Controlled Trial	Authors conducted a prospective, randomized, controlled trial among patients with post COVID-19 anosmia. Selection criteria:	The assessment of smell was done using (VAS from 0 to 10). All patients were initially evaluated after their recovery from COVID-19	The results of our study suggest that using mometasone furoate nasal spray as a topical corticosteroid therapy in the treatment of post COVID- 19 anosmia offers no benefits over the olfactory training. This	No limitations or bias reported.

		Adults 18 years or older, confirmed case (positive PCR), recovered/discharged (2 negative PCR), suffering from sudden recent anosmia or hyposmia with or without loss of taste. 100 patients, 50 patients in each group, all patients suffered from post COVID-19 olfactory dysfunction (anosmia/hyposmia). Experimental group received ICS and control group received olfactory training	and followed up for 3 weeks. The smell scores were recorded weekly and the duration of smell loss was recorded from the onset of anosmia till the full recovery.	topical corticosteroid nasal spray shows no superiority regarding the smell scores over the period of the study, the duration of anosmia/hyposmia, and the recovery rates. Administering topical nasal corticosteroids in post COVID-19 anosmia remains controversial because more larger studies need to be conducted.	

CONCLUSIONS:

Article 1:

Intranasal corticosteroids with nasal irrigation showed a very small percentage in recovery of sense of smell compared no treatment for anosmia. Due to low quality evidence of this systematic review, there is very limited evidence regarding the efficacy of different interventions at preventing persistent olfactory dysfunction following COVID-19 infection.

Article 2:

This systematic review demonstrated a more favorable improvement in post-infectious olfactory dysfunction with non-pharmacologic treatments, such as olfactory training, compared with pharmacological treatment including intranasal corticosteroids.

Article 3:

Intranasal application of betamethasone exhibited no significant statistical effect on the recovery time of post-viral anosmia compared to the placebo.

Article 4:

Outcomes in post-COVID olfactory function revealed no difference when treated with intranasal corticosteroids versus placebo. This systematic review recommends topical steroids as a possible option for treating post-viral anosmia only after careful consideration of potential risks and limited evidence.

Article 5:

The results suggested that using corticosteroid nasal spray as a topical corticosteroid in the treatment of post COVID-19 anosmia offers no superiority benefits over the olfactory training, regarding smell scores, duration of anosmia, and recovery rates.

Overarching**:**

Anosmia is a common debilitating symptom of the novel coronavirus disease 2019. Currently, there is no satisfactory treatment of anosmia. It is thought that oral corticosteroids in post-viral olfactory dysfunction could be a viable treatment option to target any underlying sinonasal inflammation, which is a common sequalae of upper respiratory tract infection. Overall, the articles overarchingly concluded that intranasal corticosteroids do not improve post-viral olfactory dysfunction compared to placebos. Non-pharmacological treatment, such as olfactory training is preferred.

CLINICAL BOTTOM LINE:

The clinical bottom line is intranasal corticosteroid is **not** a satisfactory treatment option in improving post-viral olfactory dysfunction. Articles 1, 2, 3, 4, and 5 were RCTs or systematic reviews that provided viable evidence to support this conclusion. These studies demonstrate that application of intranasal corticosteroids had no difference in olfactory outcomes compared to placebos and non-pharmacological treatments. Currently, there is no standard practice of care for this issue due to lack of robust data. Overall, the evidence presented here is applicable to my clinical scenario and all other patients suffering from post-COVID anosmia. The significance of this data can be used to clinically recommend against intranasal corticosteroids to recover sense of smell.

Weight of Evidence:

Article 1:

This American conducted 2021 review was selected because it assessed the effects (benefits and harms) of interventions to treat olfactory dysfunction in adults with COVID-19 infection. The article looked at intranasal steroid/mucolytic/decongestant compared to no intervention. The interventions included intranasal steroids (drops / rinses / sprays), systemic steroids, olfactory training, vitamin A, zinc, antioxidants, antivirals, monoclonal antibodies, and xanthine derivatives. Primary outcomes studied were recovery of sense of smell, diseased related quality of life, adverse effects, and change in sense of smell. Overall, this article carries weight because evaluated the interventions, such as intranasal steroids compared to no intervention, in the recovery of sense of smell related to COVI-19 sequalae.

Article 2:

This 2020 meta-analysis was chosen because it investigated viable treatment options for post infectious olfactory dysfunction. The study gathered evidence from 40 RCTs and cohort studies with 2352 patients. The authors assessed different interventions for post-covid olfactory loss in recent literature. The valued the benefits of non-pharmacological (olfactory training, acupuncture) versus pharmacological treatment (nasal steroids, theophylline, antibiotics, vitamin A). Overall, this article carries weight because it examined the outcomes of nasal steroid treatment in comparison to others for post-viral olfactory loss.

Article 3:

This 2021 RCT from the American Journal of Otolaryngology was chosen because it studied the use of betamethasone to treat anosmia in confirmed COVID-19 patients. Although this study was performed in the Middle East, it carries reverence because it is a registered clinical trial under the US Federal Government. The trial included 276 participants that were randomized equally and split into a betamethasone group or placebo group who was given normal saline. Overall, this article carries weight because it compared remission rates of post viral anosmia with betamethasone versus placebo.

Article 4:

This 2020 Johns Hopkins systemic review was chosen because comprehensive review of the supporting evidence for the treatment of post viral olfactory dysfunction with accompanying, evidence-based recommendations when possible. This review investigated the efficacy steroid treatments versus non-steroidal treatments and reported the olfactory outcomes after losing smell before a viral infection. Overall, this article carries weight because it demonstrated the negative impact on quality of life of olfactory dysfunction and researched viable methods to improve olfaction.

Article 5:

This 2021 randomized controlled trial from the American Journal of Otolaryngology was selected since it evaluated the role of the topical corticosteroid, mometasone furoate, nasal spray in the treatment of post COVID-19 anosmia. As such, the evidence is certainly current. 100 patients with confirmed post-COVID-19 loss of smell were randomized into receiving intranasal corticosteroids or underwent olfactory training. Overall, this RCT carries weight because it is relevant to the target population and it determined the clinical efficacy of intranasal corticosteroids in treating post-viral olfactory loss.

Magnitude of Any Effects:

Article 1:

At the 20-day control there was no significant improvement in olfactory function (p = 0.053). The improvement in olfactory performance became significant at the 40-day follow-up compared to baseline scores [60 (IQR 60) versus 20 (IQR 30); p = 0.009]. However, at end of the observation period, no patient presented with normal olfactory function

Article 2:

Various comparative studies have shown improvement in olfactory function in 25% to 55% of patients following treatment with steroids. Evidence for using steroids in post–COVID-2019 PIOD is lacking and there is the confounding problem of steroid administration in severe disease. Whether the improvement in olfactory function after the 8-month follow-up was due to spontaneous recovery or steroid effect was not clear from this study.

Article 3:

83% of participants had recovered from anosmia within 30 days, with a median recovery time of 13 days (IQR 8–18). Compared to placebo, nasal application of betamethasone drops has no significant effect on the recovery time of anosmia (hazard ratio 0.88; 95% CI 0.68–1.14; $P = 0.31$).

Article 4:

All 133 patients had a PVOD etiology of OD, with improvement seen in 49.6% of patients using T&T olfactometry, and an average improvement of 10.2 to 39.5 points on VAS, after injection of dexamethasone or betamethasone into the olfactory cleft. A directed beclomethasone spray therapy demonstrated that 2/8 PVOD patients had TDI score improvement of greater than 6 points. However, TDI improvement > 6 seen in 67.8% of PVOD patients undergoing olfactory training vs. 33% of PVOD controls who did not undergo OT($p < 0.05$)

Article 5:

In both groups, the smell scores significantly improved by the end of the third week ($P < 0.001$). By comparing smell scores between both groups after 1 week, 2 weeks, and 3 weeks of treatment, there were no statistically significant differences between both groups. In group I, (62%) of patients completely recovered their sense of smell after 3 weeks of treatment, compared to (52%) of patients in group II ($P = 0.31$).

Clinical Significance:

Olfaction, 1 of the 5 principal human senses, serves a variety of critical health-related roles ranging from the ability to detect health hazards such as fire or toxic fumes, to psychosocial implications such as the ability to enjoy food. It is estimated that 60% of COVID-19 positive patients suffer olfactory dysfunction at the onset of the infection and at least 10% of these go on to experience post-viral anosmia. Although the prevalence of olfactory dysfunction may be small as they tend to resolve, the growth in global infections increase the number of individuals suffering from post-COVID-19 anosmia. Overall, current literature shows there is not enough rigorous evaluation to exhibit the benefits of nasal corticosteroid in post-viral smell dysfunction. Most research demonstrates topical corticosteroids have little to no improvement in post-viral olfactory impairment compared to placebos Despite the lack of demonstrated efficacy for the use of ICS, there is known evidence to support its use as a first-line treatment of these symptoms in the setting of chronic rhinosinusitis. Currently, olfactory training is the only disease-specific intervention with demonstrated efficacy for the treatment of post-viral anosmia. It is believed that

repeated stimulation of olfactory neurons with clearly defined odorants increases both the regenerative ability and the neuroplastic potential. Moreover, it is thought that intranasal corticosteroids would be successful because it can target underlying sinonasal inflammation. The evidence gathered here should warrant future implications for ICS, since anosmia symptoms can occur among other viral infections beyond COVID-19. In any case, the decision to initiate steroid therapy should be based on a multidimensional risk-benefit assessment and a detailed discussion with the patient regarding respiratory failure that includes consideration of existing comorbidities, imaging findings, and the implications of taking a short course of steroids.

Other Considerations:

Further research should conduct rigorous studies to assess the true nature of nasal corticosteroid sprays and rinses in patient with post-infectious symptoms, as there is no clear recommendation. Current literature should also employ more higher quality articles to include more randomized controlled trials with larger populations. It would be useful to study the effects of optimal timing for the initiation of olfactory training because it can curtail potential long-term anosmia.