A Randomized, Single-Blind, Crossover Study Evaluating the Impact of OnabotulinumtoxinA Treatment on Mood and Appearance During the COVID-19 Pandemic

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Abstract
Background: The emergence of COVID-19 led rapidly to one of the most severe disease outbreaks in modern history. This caused many aesthetic practices to close temporarily, providing a unique opportunity to evaluate the impact of neurotoxin use in the setting of an ongoing pandemic.

Objectives: The aim of this study was to examine whether administration of onabotulinumtoxinA (BOTOX Cosmetic, Allergan plc, Dublin, Ireland) to regular users synergistically amplifies the elevation in mood/happiness, self-satisfaction with appearance, and overall satisfaction in the context of the ongoing pandemic.

Methods: A randomized, single-blind, crossover study was designed to evaluate the impact of neurotoxin treatment in the upper third of the face on mood, self-satisfaction with appearance, and overall satisfaction. The placebo group crossed over to treatment after 1 month. Surveys evaluating patient happiness, self-satisfaction with appearance, and overall efficacy were completed by both groups, and again by the placebo group following crossover to treatment.

Results: Forty-five subjects were enrolled: 30 in the treatment group and 15 in the control/crossover group. The placebo group demonstrated no change in happiness or self-satisfaction in appearance until crossover to the treatment group. Both groups, once receiving onabotulinumtoxinA, reported increased happiness, self-satisfaction with appearance, and overall treatment satisfaction.

Conclusions: OnabotulinumtoxinA treatment to the upper face in the midst of the COVID-19 pandemic was found to increase patient happiness, self-satisfaction with appearance, and overall treatment satisfaction.

Level of Evidence: 2

The emergence of SARS-CoV-2 (COVID-19) in 2019 led rapidly to one of the most severe disease outbreaks in modern history. As the contagion spread out of control, hospitals in major disease hotspots began to experience shortages in staffing, personal protective equipment, and other hospital resources. On March 13, 2020, the American College of Surgeons became the first group to officially recommend reducing and canceling elective procedures to mitigate the strain on the healthcare system. Aesthetic procedure providers, including plastic surgeons, facial plastic surgeons, and dermatologists, also suspended many aspects of their practice in response to the pandemic.

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and dermatologists, all put their practices on hold in efforts to help conserve personal protective equipment supplies and limit unnecessary exposure of staff and patients to the new contagion. In a survey of American Council of Academic Plastic Surgeons providers, fewer than 10% of those offering aesthetic procedures prior to the pandemic were still offering those procedures in April.³

At the same time, the pandemic forced nonessential workers to transition to a virtual life, with many employers shifting to video calls, thereby putting their faces center screen to all their colleagues. Moreover, mask-wearing showcases the upper region of one’s face while hiding the bottom two-thirds. Facial rhytides in the upper facial region are often associated with signs of aging as well as signs of stress, anxiety, and anger.⁴ Potentially due to these effects, Google Trends (Mountain View, CA) analysis showed growing interest in aesthetic procedures, especially facial plastic surgery procedures, as stay-at-home orders were initially being lifted.⁵,⁶ Key trends in searches for neurotoxin treatments, in particular, noted a decrease over the first few months of the pandemic before rising to pre-pandemic levels immediately after stay-at-home orders were lifted.

The effects of the pandemic on non-naïve patient mood/happiness, self-satisfaction with appearance, and overall treatment satisfaction after neurotoxin treatment in the upper facial region have yet to be examined. Amidst the constraints of a global pandemic, many patients have exceeded their normal treatment interval and their glabellar wrinkles returned to baseline. This is a once-in-a-lifetime period during which regular users of neurotoxin are not able to receive their regular injections. It would not be surprising to find that these patients are experiencing a decrease in their mood secondary to weeks of social isolation and distancing.

This unique period offers the opportunity to evaluate the impact neurotoxin has on mood/happiness, self-satisfaction with appearance, and overall treatment satisfaction after neurotoxin treatment in the upper facial region in non-naïve patients in the setting of the COVID-19 pandemic. We primarily aimed to examine whether the administration of onabotulinumtoxinA (BOTOX Cosmetic, Allergan plc, Dublin, Ireland) to regular users synergistically amplifies their elevation in mood/happiness beyond what would be achieved had they not had treatment, in the context of the ongoing pandemic. We postulated that regular neurotoxin users have a secondary gain beyond wrinkle reduction, with the treatment also serving as a mood elevator.

We secondarily aimed to examine the change in patient satisfaction and patient-reported efficacy in subjects returning for onabotulinumtoxinA treatment. Moreover, we aimed to examine these effects against a placebo treatment to ensure that the changes in patient satisfaction are due to the neurotoxin treatment itself rather than other variables associated with their visit, such as easing of local and national restrictions due to COVID-19. We hypothesized high patient satisfaction and efficacy.

**METHODS**

A total of 45 subjects were included: 30 in the treatment arm and 15 in the control arm. The study date range was from July 20, 2020 to September 3, 2020. Eligible subjects were enrolled in a cohort that included men and women between the ages of 18 and 75 years who were non-naïve neurotoxin users and were at least 20 weeks from their most recent neurotoxin treatment. Subjects were excluded if they had received neuromodulator injections in the glabellar region within 20 weeks prior to enrollment and did not have a glabellar wrinkle severity score of 2 to 3 on the Allergan Facial Wrinkle Scale (FWS). Exclusion criteria included diagnoses of severe depression or bipolar disorder, recent changes in antidepressant or antianxiety medications, or known allergy or sensitivity to study ingredients. Women who were pregnant, attempting to get pregnant, or breastfeeding were also excluded from this study. To complete enrollment, all subjects were expected to understand the aspects of this study, provide their consent, and complete the required treatment and follow-up visits. All study protocols were approved Advarra IRB (Columbia, MD).

Participation in the study occurred over the course of 3 to 4 visits and all procedures were performed by the senior author (S.H.D.). At the first visit, subjects were evaluated to confirm they met the criteria for inclusion and then randomly allocated by an online randomizer (https://www.random.org/lists/) to either a treatment or a control group. All 45 subjects were included in the randomization and the first 30 listed were then placed into the treatment group.

All subjects underwent standardized 2-dimensional photography and video at baseline. Subjects were photographed at rest and with maximal contraction (ie, while frowning) (Figure 1). Video was taken of the subjects while frowning, smiling, puckering, and reading a short rhyme. All subjects in both groups completed 2 questionnaires at baseline: FACE-Q Lines Between Eyebrows⁷ and the Subjective Happiness Scale (SHS).⁸ These were printed out and completed before any treatment or any contact with the study senior author (S.H.D.) to prevent any potential bias. The study coordinator distributed the survey.

Subjects in the treatment group received 20 to 64 units of onabotulinumtoxinA in the upper third of the face including glabella lines (GLs), forehead lines (FLs), and lateral canthal lines (LCLs). Subjects returned after 2 weeks and were assessed by the investigator to determine whether or not an optimal cosmetic result (OCR) had been achieved and whether subjects had experienced a reduction of at
least 1 point on the FWS. If an OCR was achieved, subjects completed the same FACE-Q Lines Between Eyebrows and SHS questionnaires they performed at baseline. They also completed the FACE-Q Outcome Satisfaction and a questionnaire comparing their perceived results of the onabotulinumtoxinA treatment to their prior neurotoxin treatments.

If additional correction was determined to be needed, then touch-up treatment of up to 20 units was administered to patients at the second visit. These subjects then returned 2 weeks later to complete the FACE-Q survey, the SHS, and the questionnaire comparing this neurotoxin treatment to previous treatments.

Subjects in the control group underwent a similar assessment. However, the control group was administered saline rather than onabotulinumtoxinA at their initial treatment. Investigators administered the FACE-Q Lines Between Eyebrows and Outcome Satisfaction surveys at 4 weeks post baseline. At this 4-week follow-up, all subjects in the control group crossed over to the treatment group. Investigators administered the onabotulinumtoxinA treatment according to the same technique as in the treatment arm. Once an OCR was achieved, investigators assigned patients a final FWS score. Four weeks after treatment, subjects completed the FACE-Q Lines Between Eyebrows survey, the FACE-Q Outcome Satisfaction survey, the SHS, and the questionnaire comparing current to previous treatments.

All statistical analyses, summary tables, and data listings were performed with Excel software (Microsoft, Redmond, WA). Comparison of pretreatment and posttreatment assessments, including both patient-reported measures and physician-determined facial wrinkle score, were analyzed through the use of paired t tests. A 2-sided P value of 0.05 was considered statistically significant. Indices that were only completed after the final treatment and an OCR had been achieved are reported through descriptive means and standard deviations.

RESULTS

Forty-five subjects who have had neurotoxin treatment in the past were enrolled in this study, 30 in the treatment group and 15 in the control/crossover group. All patients completed the treatment and follow-up period. Within the control group, 14 subjects identified as female, and 1 identified as male. The mean age of females in the control group was 49 years (range, 26-71 years) and the 1 male in the control group was 54 years of age. There were 26 females and 4 males enrolled in the control group. The females in the control group had a mean age of 48.8 years (range, 24-67 years), and males similarly had a mean age of 49.2 years (range, 49-63 years). The ages, along with other demographics, are listed in Table 1.

The mean duration from previous neurotoxin treatment was 6 months, and all subjects were required to have not received neurotoxin within 20 weeks of the study. There were no complications among either groups throughout the study.
Table 1. Subject Demographics

| Gender          | Treatment group | Control group |
|-----------------|-----------------|---------------|
| Males           | 4 (13.3)        | 1 (6.7)       |
| Females         | 26 (86.7)       | 14 (93.3)     |

| Age (years)     | Treatment group | Control group |
|-----------------|-----------------|---------------|
| Males           | 49.2 (49-63)    | 54.0 (54)     |
| Females         | 48.8 (24-67)    | 49.0 (26-71)  |

| Race/ethnicity  | Treatment group | Control group |
|-----------------|-----------------|---------------|
| Caucasian       | 27 (90)         | 12 (80)       |
| Hispanic American | 3 (10)     | 2 (13.3)     |
| Asian American  | 0 (0)           | 1 (6.7)       |

Values are n (%) or mean (range).

The senior author (S.H.D.) determined the FWS score of all subjects at baseline and after final treatment. In the control group, the mean FWS score at baseline was 2.56 and remained unchanged following saline treatment. After the control group crossed over to the treatment arm to receive onabotulinumtoxinA, the FWS score reduced from 2.56 to 0.47 ($P < 0.0001$) once an OCR had been achieved. The treatment arm had a baseline FWS score of 2.57 and reduced to 0.45 ($P < 0.0001$) once an OCR had been achieved.

The control group with 15 subjects received a mean of 1.03 mL of saline at the first treatment. All 15 subjects received touch-ups with an additional mean of 1.59 mL of saline. At the crossover, the control subjects received a mean of 30 units of onabotulinumtoxinA combined to the GLs, FLs, and LCLs. Fourteen subjects received touch-ups, with a mean of 13.8 units of onabotulinumtoxinA. A mean total of 42.9 units of onabotulinumtoxinA was used in the control group following crossover.

The treatment group of 30 subjects received 35.4 units of onabotulinumtoxinA at their first visit. There were 23 touch-ups with a mean of 141 units. A mean total of 46.2 units was used. When compared to the control group after crossover receiving onabotulinumtoxinA, there was no significant difference in mean volume at the initial treatment ($P = 0.08$). A comparison of the touch-up total between groups also showed no significant difference ($P = 0.88$). When comparing total units among initial treatment and touch-up between the control group after crossover with onabotulinumtoxinA to the treatment group, the mean total units showed no significant difference ($P = 0.27$).

Each subject completed the FACE-Q Lines Between Eyebrows assessment before and after treatment. The control group total FACE-Q score remained 23.58 out of a possible 28 at baseline and remained at 23.58 one month following saline treatment. Once the control group crossed over to the onabotulinumtoxinA treatment, FACE-Q scores reduced significantly in all categories (Table 2).

In the onabotulinumtoxinA treatment group, all 8 FACE-Q subscales showed significant improvement after treatment ($P < 0.0001$). The total score in the treatment group improved from 23.66 pretreatment to 10.56 posttreatment ($P < 0.0001$). Specific mean scores for each item are reported in Table 2. There were no significant differences between the FACE-Q scores from the control group after crossing over to the treatment arm compared to the initial onabotulinumtoxinA treatment group.

Subjects completed a FACE-Q satisfaction questionnaire at their final visit. No significant differences between satisfaction scores were reported between treatment and control groups following crossover to the treatment arm. The survey was not given to the control group following saline treatment. The treatment group reported an average FACE-Q satisfaction score of 21.43 and control group following crossover with onabotulinumtoxinA reported a score of 21.44. In comparison to previous neurotoxin treatments, 42 of 45 patients (93.3%) reported that they believed that the onabotulinumtoxinA treatment results had a faster onset during this round, whereas 2 of 45 patients reported that the time to results was no different to previous treatments and 1 reported slower onset. The equivocal result was originally in the control arm, whereas the slower result was in the treatment arm. Overall, patients reported a mean efficacy of 8.9 on a 10-point scale for the neurotoxin treatment. Subjects reported a mean onset time with onabotulinumtoxinA treatment of 2.87 days.

Overall, both groups reported significant changes in overall happiness/mood scores as judged on the SHS following onabotulinumtoxinA treatment. The control SHS pretreatment score remained unchanged following saline treatment alone. Once the control group crossed over to the treatment arm with onabotulinumtoxinA, SHS scores improved significantly (Table 3). The treatment arm also reported significant improvements for all questions on the SHS (Table 3). A higher score in questions 1 to 3 indicated greater happiness, whereas a lower score on question 4 indicated greater happiness. The control group SHS scores following onabotulinumtoxinA treatment showed no significant differences compared with the treatment group scores (Table 3).

**DISCUSSION**

To the authors’ knowledge, this is the first trial to examine the direct effects of onabotulinumtoxinA treatment in non-naive users on mood/happiness, self-satisfaction of...
Table 2. FACE-Q Appraisal of Lines Between Eyebrow Scores

| FACE-Q question | Control group following crossover with OnabotulinumtoxinA treatment | Treatment group |
|-----------------|---------------------------------------------------------------------|-----------------|
|                 | Mean pretreatment | Mean posttreatment with onabotulinumtoxinA | P value | Mean pretreatment | Mean posttreatment with onabotulinumtoxinA | P value |
| Question A      | 3.26               | 1.44                          | <0.0001 | 3.25               | 1.43                          | <0.0001 |
| Question B      | 3.40               | 1.47                          | <0.0001 | 3.41               | 1.48                          | <0.0001 |
| Question C      | 3.28               | 1.42                          | <0.0001 | 3.27               | 1.41                          | <0.0001 |
| Question D      | 3.33               | 1.53                          | <0.0001 | 3.36               | 1.52                          | <0.0001 |
| Question E      | 3.35               | 1.51                          | <0.0001 | 3.36               | 1.52                          | <0.0001 |
| Question F      | 3.44               | 1.56                          | <0.0001 | 3.45               | 1.57                          | <0.0001 |
| Question G      | 3.53               | 1.65                          | <0.0001 | 3.55               | 1.63                          | <0.0001 |
| Total           | 23.58              | 10.58                         | <0.0001 | 23.66              | 10.56                         | <0.0001 |

Table 3. Subjective Happiness Scale Scores

| SHS item | Control group following crossover with onabotulinumtoxinA treatment | Treatment group | Control post onabotulinumtoxinA vs treatment arm |
|----------|---------------------------------------------------------------------|-----------------|-------------------------------------------------|
|          | Mean pretreatment | Mean posttreatment with onabotulinumtoxinA | P value | Mean pretreatment | Mean posttreatment with onabotulinumtoxinA | P value | P value |
| Question 1 | 6.0               | 6.6                          | 0.007 | 5.43               | 6.21                          | 0.01 | 0.06 |
| Question 2 | 6.08              | 6.53                         | 0.05 | 5.54               | 6.21                          | 0.008 | 0.10 |
| Question 3 | 5.77              | 6.33                         | 0.022 | 5.07               | 6.18                          | 0.0005 | 0.51 |
| Question 4 | 2.67              | 1.6                          | 0.026 | 3.21               | 1.75                          | 0.0009 | 0.72 |

appearance, and overall treatment satisfaction in relation to a pandemic. This study was performed to take advantage of the once-in-a lifetime opportunity offered by the COVID-19 pandemic: the scenario in which aesthetic clinics are closed and regular neurotoxin patients are unable to receive their treatment at the scheduled time may never occur again. Normally neurotoxin treatment effects last about 3 to 4 months in the upper face before experiencing a relapse of facial wrinkles. Moreover, patients must continually return to the office for touch-up procedures and maintenance treatments. During initial stay-at-home orders, this was not possible because clinics were shut down.

All of the study subjects presented to the clinic with a moderate-to-severe glabellar wrinkle score and experienced a clinically and statistically significant reduction in FWS score following onabotulinumtoxinA treatment. The control group, who received placebo saline, showed no changes in their FWS score until after crossover and receiving onabotulinumtoxinA. These results support previous evidence regarding the efficacy of neurotoxin for treatment of GLs, LCLs, and FLs. Some of the most important outcomes of aesthetic treatment are not only clinical improvement of a treatment’s effects, but also the patient’s self-reported mood/happiness, satisfaction, and appraisal of treatment. Our results demonstrated a significant increase in patient mood/happiness following onabotulinumtoxinA treatment (Table 3). The control group did not experience an increase in happiness with placebo saline alone, indicating the powerful effect of onabotulinumtoxinA on their happiness. This is a meaningful result particularly in the setting of the COVID-19 pandemic which has placed numerous stressors on patients. Previous studies have demonstrated the powerful effects neurotoxins have on improving quality of life, self-esteem, and even as a treatment for depression. Many studies trial neurotoxin treatments on naive subjects. This current study demonstrated that regular, non-naïve users of neurotoxin will continue to experience an increase in mood/
happiness, self-satisfaction of appearance, and overall treatment satisfaction, despite an ongoing pandemic. It would not be surprising to find that many patients have decreased moods during the pandemic due to the long-term social isolation and distancing. This study was able to distinguish between an elevation in mood/happiness due to the neurotoxin treatment or to the simple fact that the aesthetic office had been reopened through the use of the placebo saline injection. The saline did not increase mood/happiness, self-satisfaction of appearance, or overall treatment satisfaction. Once given onabotulinumtoxinA, all of these increased significantly. This demonstrates that easing of COVID-19 restrictions alone did not improve patient happiness and self-satisfaction of appearance, or overall treatment satisfaction. Thus, these improvements can be ascribed to the onabotulinumtoxinA treatment.

Our study results demonstrated improvements in patient-reported FACE-Q Lines Between Eyebrows appraisal compared with placebo. The control group in this study reported no changes from baseline in their eyebrow appraisal scores following administration of the saline placebo. After crossover and administration of the onabotulinumtoxinA treatment, the control group reported improvements similar to the primary treatment group across all criteria of eyebrow appraisal.

Charles Darwin first noted the link between facial expression and mood in a seminal work in 1872. The “omega” sign, a term he coined to describe the contraction of the corrugator muscles, was associated with melancholy and a depressed mood. After its disappearance, subject mood improved without the associated melancholic features. This observation of Darwin’s, now termed the “facial feedback hypothesis,” has become an important field of interest in psychology and aesthetic medicine. Injection of neurotoxin to paralyze the upper face, including the GLs, FLs, and LCLs, may increase mood by acting on this effect, as demonstrated in this study. The paralysis of these muscles prevents extended periods of a contracted upper facial region, inhibiting the effects of facial feedback. This effect has been previously reported in the literature by a study showing that treating facial lines with onabotulinumtoxinA prevents frowning increases, inducing a similar feeling in the individual. Paralysis of the upper glabellar region with neurotoxin may induce a greater sense of positive emotion due to the inability to gauge negative facial emotions.

Subjective evaluations such as in this study have several limitations that deserve mentioning. The study was performed at a single site. The small sample with predominantly Caucasian female subjects is noted. Further study is warranted, although the unique time period of clinic shutdowns has passed in most areas.

CONCLUSIONS

OnabotulinumtoxinA treatment to the upper face in the midst of the COVID-19 pandemic was found to increase patient happiness, self-satisfaction with appearance, and overall treatment satisfaction. As the COVID-19 pandemic continues, aesthetic providers can offer the benefit of neurotoxin treatment to elevate mood/happiness and provide a sense of normalcy to our patients during these stressful times.

Disclosures

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REFERENCES

1. Schuchat A, CDC COVID-19 Response Team. Public health response to the initiation and spread of pandemic COVID-19 in the United States, February 24-April 21, 2020. MMWR Morb Mortal Wkly Rep. 2020;69(18):551-556.
2. COVID-19: recommendations for management of elective surgical procedures. American College of Surgeons. Published March 13, 2020. https://www.facs.org/covid-19/clinical-guidance/ elective-surgery. Accessed October 16, 2020.
3. Sarac BA, Schoenbrunner AR, Wilson SC, Chiu ES, Janes JE. The impact of COVID-19-based suspension of surgeries on plastic surgery practices: a survey of ACAPS members. Plast Reconstr Surg Glob Open. 2020;8(8). doi:10.1097/GOX.0000000000003119.
4. Stotland MA, Kowalski JW, Ray BB. Patient-reported benefit and satisfaction with botulinum toxin type A treatment of moderate to severe glabellar rhytides: results from a prospective open-label study. Plast Reconstr Surg. 2007;120(5):1386-1393.

5. Dhanda AK, Leverant E, Leshchuk K, Paskhover B. A Google Trends analysis of facial plastic surgery interest during the COVID-19 pandemic. Aesthetic Plast Surg. Published online August 5, 2020:1-3. doi:10.1007/s00266-020-01903-y.

6. Chandawarkar A, Jenny H, Kim R. Data-driven insights on the effects of COVID-19 on aesthetics: part I (passive analysis). Aesthet Surg J. 2021;41(3):NP65-NP74.

7. Klassen AF, Cano SJ, Scott A, Snell L, Pusic AL. Measuring patient-reported outcomes in facial aesthetic patients: development of the FACE-Q. Facial Plast Surg. 2010;26(4):303-309.

8. Lyubomirsky S, Lepper HS. A measure of subjective happiness: preliminary reliability and construct validation. Soc Indic Res. 1999;46:137-155.

9. Abramo AC. Muscle insertion and strength of the muscle contraction as guidelines to enhance duration of the botulinum toxin effect in the upper face. Aesthetic Plast Surg. 2018;42(5):1379-1387.

10. Flynn TC. Botulinum toxin. Am J Clin Dermatol. 2010;11(3):183-199.

11. Carruthers J, Rivkin A, Donofrio L, et al. A multicenter, randomized, double-blind, placebo-controlled study to evaluate the efficacy and safety of repeated onabotulinumtoxinA treatments in subjects with wry’s feet lines and glabellar lines. Dermatol Surg. 2015;41(6):702-711.

12. Jandhyala R. Impact of botulinum toxin A on the quality of life of subjects following treatment of facial lines. J Clin Aesthet Dermatol. 2013;6(9):41-45.

13. Wang J, Rieder EA. A systematic review of patient-reported outcomes for cosmetic indications of botulinum toxin treatment. Dermatol Surg. 2019;45(5):668-688.

14. Ogilvie P, Rivkin AZ, Dayan S, Yoelin SG, Weichman BM, Garcia JK. OnabotulinumtoxinA for treatment of forehead and glabellar lines: subject-reported satisfaction and impact from a phase 3 double-blind study. Dermatol Surg. 2019;45(5):689-699.

15. Dayan SH, Arkins JP, Patel AB, Gal TJ. A double-blind, randomized, placebo-controlled health-outcomes survey of the effect of botulinum toxin type A injections on quality of life and self-esteem. Dermatol Surg. 2010;36(Suppl 4):2088-2097.

16. Finzi E, Wasserman E. Treatment of depression with botulinum toxin A: a case series. Dermatol Surg. 2006;32(5):645-649; discussion 649.

17. Darwin C, Prodger P. The Expression of the Emotions in Man and Animals [1872]. New York: Oxford University Press; 1998.

18. Jack RE, Schyns PG. The human face as a dynamic tool for social communication. Curr Biol. 2015;25(14):R621-R634.

19. Gottin LO, Cohen IG, Koplan JP. Universal masking in the united states: the role of mandates, health education, and the CDC. JAMA. 2020;324(9):837.

20. Lyu W, Wehby GL. Community use of face masks and COVID-19: evidence from a natural experiment of state mandates in the US. Health Aff (Millwood). 2020;39(8):1419-1425.

21. Rader B, White LF, Burns MR, et al. Mask wearing and control of SARS-CoV-2 transmission in the United States. medRxiv. Published online September 1, 2020:2020.08.23.20078964. doi:10.1101/2020.08.23.20078964.

22. Pritzker JB. COVID-19 Executive Order No 30. 2020. https://www2.illinois.gov/Pages/Executive-Orders/ExecutiveOrder2020-32.aspx. Accessed December 15, 2020.

23. Nestor MS, Fischer D, Arnold D. “Masking” our emotions: botulinum toxin, facial expression, and well-being in the age of COVID-19. J Cosmet Dermatol. 2020;19(9):2154-2160.

24. Wegrzyn M, Vogt M, Kireclioğlu B, Schneider J, Kissler J. Mapping the emotional face. How individual face parts contribute to successful emotion recognition. PLoS One. 2017;12(5):e0177239.

25. Pfefferbaum B, North CS. Mental health and the COVID-19 pandemic. N Engl J Med. 2020;383(6):510-512.

26. Brooks SK, Webster RK, Smith LE, et al. The psychological impact of quarantine and how to reduce it: rapid review of the evidence. Lancet. 2020;395(10227):912-920.