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Global facial rejuvenation with hyaluronic acid: a safe set of directives to whole-approach of the aging-changes evaluated by magnetic resonance imaging

Abstract

Background: Face rejuvenation with hyaluronic acid (FR-HA) through a global approach was performed in a single session, by using a safe set of directives targeted for each facial zone.

Methods: FR-HA was performed with products of the QTFill Signature® range all of them with same HA-concentration and molecular-weight, with two crosslinking technologies, the own Ultra-High-Density™ crosslinking and BDDE-crosslinking with tree degrees of BDDE, resulting in high-, medium- and low-G', and 3.0% of lidocaine hydrochloride. Bolus injection with needle and retrograde-backflow injection with microcannula or needle were directed to specific facial zones. A safe FR-HA protocol based on HA-products, fat layers and vasculature, and points and techniques of injection recovered the face youthful appearance.

Results: FR-HA was made for eleven facial zones, patient average of 6.95±1.30, average of 30.55±0.74 injections-points per facial-zone and of 16.80±0.83 injections-points per patient. The volume of HA injected was 49.50 ml, average of 4.50±0.37 ml per facial zone and 2.48±0.12 ml per patient. From one-month to twelve-months there was no significant differences on the face appearance and on density of the gel-diffusion displayed by MRI in T2-weighted with fat suppression on axial and coronal planes, which were endorsed by the Facelift Outcomes Evaluation questionnaire scores.

Conclusions: Minimal changes on clinical outcomes and slow degradation of gel-diffusion on MRI in T2-weighted with fat suppression on axial and coronal planes from one-month to twelve-months showed that the HA-products remained stable in the injection site without evidence of significant resorption or loss of correction, indicating FR-HA efficacy and long-lasting.

Keywords: aging, filler, facial rejuvenation, hyaluronic acid, nonsurgical, facial zone

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Introduction

Facial rejuvenation with hyaluronic acid (FR-HA) is a nonsurgical alternative to surgical facelift, according to concentration, molecular-weight and crosslinking technology of the HA.[1] HA-gel has properties as elasticity or G', cohesivity and viscosity accountable for its firmness, projection capacity and long-lasting. To act in specific facial zones a single HA range with different G' values is limited for products manufactured by different degrees of same crosslinking technology and same HA-concentration.[2] Knowledge of facial anatomy, mostly fat layers and vasculature, allows to guide specific treatment of each facial zone. The superficial fat layer comprises the subcutaneous fat of the glabella, crow's feet, marionette line, chin and lip, and fat compartments as central and middle-lateral forehead, infraorbital, nasolabial, zygomatic-malar, middle, lateral-temporal, and jowls.[3] The superficial fat layers are a safe location for fillers, avoiding the muscle dynamics pressure over the gel, preserving its original shape after injection. Moreover, the evaluation by Doppler ultrasound detected the ophthalmic, infraorbital and facial arteries running under the superficial fat layers.[4] Danger zones for injection are related to the vessels depth and location in each facial zone. They are located on the superomedial aspect of the orbit, infraorbital zone, and nasolabial fold and antero-inferior angle of the masseter.[5] Major complications arise secondary to injury, compression and cannulation of the vessels, and gel migration. Needle and microcannula are used according to the facial zone.[6] Magnetic resonance imaging (MRI) in T2-weighted with fat suppression on axial and coronal planes allows identifies placement, longevity and localization of the HA-gel in facial rejuvenation.[7] Facelift Outcomes Evaluation (FOE) questionnaire measures the patient's concept of their self-image, quantifying FR-HA efficacy and long-lasting.[8]

FR-HA is described using products of a single HA range with same HA-concentration, same molecular-weight and three G' values to restore the aged-face to their youthful appearance in a single session. FR-HA efficacy and long-lasting is appraised comparing the patient appearance that was monitored by MRI before, from one-month to twelve-months after HA-injection, and by FOE scores at the same period.

Materials and method

Twenty females, age from 45- to 52-year-old, average of 50.15-year-old, underwent FR-HA to improve the aging-changes. All patients used the products of the QTFill Signature® range (S. THEPHARM Co. Ltd., Seoul, Korea) that associated own Ultra-High-Density Technology® crosslinking to the BDDE-crosslinking with tree BDDE degrees, resulting in high-, medium- and low-G', corresponding to SubQ, Deep and Fine products, respectively, with same HA-concentration of 24 mg/ml and same molecular-weight of 1,570 kDa, incorporated with 0.3% lidocaine hydrochloride. They were applied in specific facial zones, according to the G'

values. Exclusion criteria included males, smokers, allergy, bleeding disorders, facial trauma and aesthetic surgery. Patients were followed for twelve months. All patients signed an informed consent form agreeing to the proposed treatment that was performed according to the 1964 Helsinki Declaration and Medical Research Involving Human Subjects.

Injection procedure

Topical anesthesia with lidocaine hydrochloride cream was applied on the facial zones for five minutes and cleaned with alcoholic chlorhexidine solution before the injection. Pinching-lifting the skin using the thumb and index to lift subcutaneous tissue away from the muscle layer were made to prevent vascular injury (Figure 1). Bolus injection used a 27G½ needle in a perpendicular transcutaneous approach to inject a high-G' product, creating a pillar to project and lifting the central facial triangle. Retrograde-backflow injection used a 25G50mm blunt-tip cannula, excepting in glabella, philtral ridge and white roll where was used a 27G½ needle, to inject high-, medium- and low-G' products to volumetric expansion and modeling the face. The volume of HA per facial zone varied as the aging-changes.

Figure 1 Bolus injection by pinching the skin to lift subcutaneous tissue away from the muscle layer.

Facial approach

An individual approach for each facial zone related to points, technique and location of the injections, and adequate HA-products created a safety protocol for FR-HA (Figure 2).

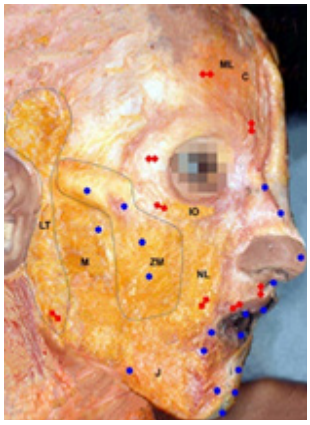

Figure 2 Blue points indicate bolus injection. Red points and lines retrograde-backflow injection.

Superficial fat compartments: middle-lateral (ML) and central (C), infraorbital (IO), nasolabial (NL), zygomatic-malar (ZM), middle (M), lateral-temporal (LT), and jowls (J).

Forehead: Retrograde-backflow technique pointed on each horizontal line injected SubQ-product in the superficial central and middle-lateral fat compartments.

Glabella: Retrograde-backflow technique pointed on the caudal end of vertical line injected Fine-product intradermally.

Crow's feet: Retrograde-backflow technique pointed on the lateral end of each wrinkle injected Deep-product subcutaneously.

Tear trough and Nasojugal groove: Retrograde-backflow technique pointed 1 cm below the inferior-lateral orbital rim injected Fine-product in the superficial infraorbital fat compartment.

Cheek: Bolus technique pointed on the zygomatic arch, zygomatic prominence, antero-medial cheek, lateral-cheek and buccal zone injected SubQ-product in the superficial zygomatic-malar and middle fat compartments.

Nasolabial fold: Retrograde-backflow technique pointed on the caudal end of the nasolabial fold injected SubQ-product along the superficial nasolabial fat compartment.

Marionette lines: Bolus technique pointed on the modiolus, and middle of the hollow injected SubQ-product subcutaneously.

Chin: Retrograde-backflow technique pointed on mental crease end and bolus technique pointed on the lateral borders and midpoint of the chin injected Deep-product subcutaneously.

Jowls: Bolus technique pointed on the jowls sulcus injected Deep-product in the superficial jowls fat compartment.

Jawline: Retrograde-backflow technique pointed at the jaw angle injected SubQ-product downward in the superficial middle fat compartment and upward in the superficial lateral-temporal fat compartment.

Lip: Retrograde-backflow technique pointed on white roll injected Deep-product, in the philtral ridge, subcutaneously, and Fine-product in white roll and cupid's bowl by retrograde-backflow technique, subcutaneously, and as bolus technique in the vermillion submucosa.

MRI assessment

MRI in T2-weighted with fat suppression on axial and coronal planes detailed the gel-diffusion symmetry, migration and progressive degradation for twelve-months. Fat suppression extinguish the fat layers signal, making them dark, with HA hyperintense signal.[9] The fat suppression displayed the HA-gel-diffusion as a dense, homogeneous and bright spindle. The axial plane displayed the gel-diffusion transversely as a nodule, mostly on cheek and nasolabial fold. The coronal plane displayed the gel-diffusion longitudinally, transversely and nodular along the face.

Quantitative assessment

The FOE questionnaire for facelift was adapted to nonsurgical facial rejuvenation, an instrument designed to evaluate patient-reported outcomes before and after FR-HA. Each question was scored from 0, most negative response, to 4, most positive response. The values were added, divided by 24 and multiplied by 100, with 0 representing the least satisfied possible and 100 most satisfied possible. Patients with scores over 50% were considered satisfied.

Results

Twenty females underwent FR-HA in a single session for up to eleven facial zones, average of 6.95±1.30 facial zones per patient and

average of 30.55±0.74 injection points per facial zone. Each patient received an average of 16.80±0.83 injections points per treatment. Table 1 detailed number of injection points and volume of HA-injected in eleven facial zones for each patient. The volume of HA injected was 49.50 ml, average of 4.50±0.37 ml per facial zone and 2.48±0.12 ml per patient. The volume of SubQ-product was 29.15 ml to forehead, cheek, nasolabial fold, marionette lines and jawline; of Deep-product was 11.00 ml to crow's feet, lip philtral ridge, chin and jowls; and of Fine-product was 9.35 ml to glabella, tear trough, and lip vermillion, cupid's bow and white roll. Table 2 exhibited for each facial zone the number of patients and injection points, and distribution of injection technique and volume of the HA-products. FR-HA through volumetric expansion, projection and lifting provided by SubQ, Deep and Fine products in eleven facial zones recovered the forehead, glabella and crow's feet wrinkles; lid-cheek junction, cheek, nasolabial fold, marionette line, chin and mandible contour; and lip fulness, contour and philtral ridge, reaching a youthful appearance for the aging-face (Figure 3).

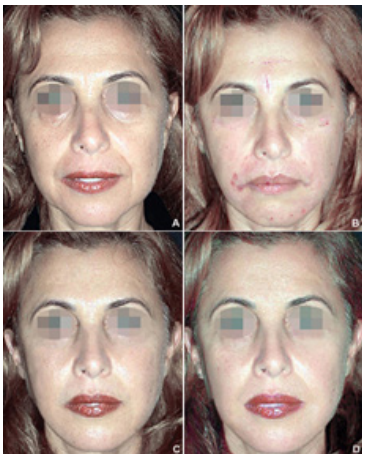

Figure 3

(A) At baseline, 51-year-old female with aging-changes of whole face.

(B) Twenty-four hours after injection of 3.60 ml of HA-products in eleven facial zones, being 2.15 ml for SubQ-product, 0.75 ml for Deep-product and 0.70 ml for Fine-product.

(C) At one-month, recovery of the more youthful face appearance.

(D) No significant changes from one-month to twelve-months, with an even younger appearance than that at baseline.

Volumetric augmentation of the cheek induced a lifting of lid-cheek junction, nasolabial fold and marionette line, well-evidenced through clinical outcomes and noticeable projection and symmetry of midface displayed in MRI on axial plane at one-month (Figure 4). Efficacy and long-lasting of FR-HA by using the SubQ, Deep and Fine products in specific facial zones were evidenced by noticeable recovery of the symmetry and balance of the youthful appearance from one-month to twelve-months, displayed in MRI on coronal plane with no significant changes in density, size and symmetry of the gel-diffusion, indicating that the HA-products injected remained stable in the facial zones with no significant resorption or loss of the correction in the same period (Figure 5). Minimal differences on clinical outcomes and no significant changes of the gel-diffusion in MRI on coronal plane were endorsed by FOE scores of 74.38% at one-month and 71.13% at twelve-months. Table 3 exhibited the FOE questionnaire scores of the patient's perception of its facial appearance before and after FR-HA. Side effects as erythema, bruising and swelling regressed within days. No major complications as asymmetry, granuloma, gel migration, infections, and harm of the facial nerve, skin necrosis or blindness occurred in this series of patients.

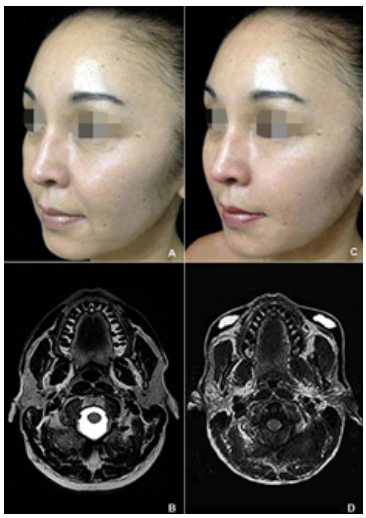

Figure 4

(A) 52-year-old female with midface deflation.

(B) At one-month, recovery of the midface youthful appearance with 2.20 ml of HA-products, being 1.60 ml for SubQ-product, 0.20 ml for Deep-product and 0.40 ml for Fine-product.

(C) MRI in T2-weighted with fat suppression on axial plane showing no zygomatic-malar projection.

(D) At one-month, symmetrical midface projection by a gel-diffusion pillar in the cheek displayed through transverse section of the gel-diffusion.

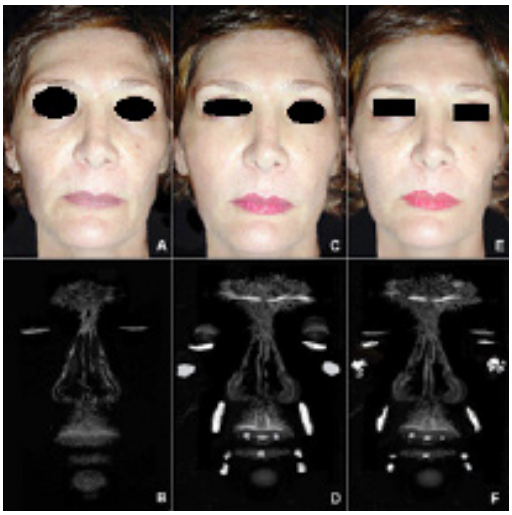

Figure 5

(A) 52-year-old female with a flaccid and hanging face. Patient requested a HA-rhinoplasty twenty-days after FR-HA, not considered in the study protocol.

(B) At one-month, recovery of the youthful appearance with 3,55 ml of HA-products, being 2.50 ml for SubQ-product, 0.20 ml for Deep-product and 0.85 ml for Fine-product.

(C) At twelve-months, no significant changes on the face appearance.

(D) MRI on coronal plane at baseline.

(E) At one-month, distribution of the gel-diffusion on the facial zones.

(F) No significant HA-degradation at month-twelve, corroborating with no significant changes on the face appearance.

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Table 1 Patient distribution, injection points and volume of HA injected per facial zone/patient

Facial zones																						
Age	**Forehead**		**Glabella**		**Crow's feet**		**Nasojugal**		**Cheek**		**Nlf**		**Marionette**		**Chin**		**Jowl**		**Jawline**		**Lip**	
	ip	**vol**	**ip**	**vol**	**ip**	**vol**	**ip**	**vol**	**ip**	**vol**	**ip**	**vol**	**ip**	**vol**	**ip**	**vol**	**ip**	**vol**	**ip**	**vol**	**ip**	**vol**
49	-	-	2	0,10	4	0,50	2	0,30	8	1,00	2	0,20	2	0,30	-	-	2	0,20	-	-	-	-
51	-	-	-	-	2	0,60	2	0,30	4	0,70	2	0,20	2	0,20	-	-	2	0,40	2	0,20	-	-
50	-	-	1	0,10	3	0,40	2	0,30	4	0,40	1	0,15	3	0,50	-	-	2	0,35	-	-	-	-
52	3	0,35	-	-	2	0,25	2	0,30	4	0,60	2	0,35	1	0,20	1	0,10	2	0,20	2	0,25	4	0,55
51	3	0,50	2	0,20	1	0,15	2	0,30	4	0,55	2	0,20	1	0,10	2	0,25	2	0,35	2	0,25	2	0,50
50	-	-	-	-	-	-	1	0,20	4	0,60	2	0,30	2	0,40	-	-	2	0,20	2	0,30	-	-
48	-	-	-	-	2	0,35	1	0,20	4	0,70	-	-	-	-	-	-	2	0,30	-	-	2	0,20
49	2	0,40	2	0,30	3	0,20	2	0,50	6	0,60	-	-	1	0,20	-	-	2	0,20	2	0,35	-	-
52	-	-	1	0,10	-	-	2	0,30	4	0,65	2	0,40	2	0,20	-	-	2	0,20	2	0,35	-	-
50	-	-	1	0,20	2	0,20	-	-	6	0,90	-	-	1	0,15	-	-	2	0,20	-	-	3	0,50
50	-	-	-	-	4	0.2	1	0,20	4	0,70	2	0,40	2	0,10	-	-	2	0,40	2	0,45	-	-
52	3	0,80	-	-	-	-	1	0,20	4	0,60	2	0,20	2	0,30	-	-	2	0,20	1	0,15	-	-
49	-	-	-	-	2	0,25	-	-	5	0,90	2	0,40	-	-	-	-	2	0,20	2	0,20	3	0,45
49	-	-	-	-	4	0,50	2	0,40	2	0,35	2	0,20	-	-	1	0,25	-	-	-	-	2	0,45
51	-	-	-	-	4	0,55	1	0,15	4	0,75	2	0,45	-	-	-	-	-	-	2	0,25	-	-
51	2	0,20	2	0,20	2	0,25	2	0,30	8	1,00	2	0,20	2	0,20	1	0,15	2	0,15	2	0,55	3	0,40
50	-	-	1	0,10	-	-	-	-	4	0,70	2	0,20	-	-	-	-	2	0,20	2	0,35	2	0,50
48	-	-	2	0,40	-	-	-	-	4	0,50	2	0,25	2	0,40	-	-	2	0,20	-	-	3	0,20
51	2	0,25	-	-	-	-	4	0,50	5	0,80	2	0,50	4	0,45	-	-	-	-	2	0,50	4	0,55
50	-	-	2	0,20	-	-	1	0,20	4	0,60	2	0,25	2	0,35	3	0,60	-	-	-	-	-	-

ip: injection points

vol: volume (ml) of HA injected per injection point

Table 2 Distribution of patient's, injection technique and points, and volume of HA-product, per facial zone

	Patients	**Injection technique**		**Injection points**	**HA-product (ml)**		
		Bolus	**Retrograde**		**SubQ**	**Deep**	**Fine**
forehead	6	-	+	15	2.5	-	-
glabella	7	-	+	11	-	-	1.5
crow's feet	12	-	+	31	-	4	-
tear trough + nasojugal	14	-	+	22	-	-	4
cheek	20	+	-	92	14	-	-
nasolabial fold	14	-	+	28	4.5	-	-
marionette lines	13	+	-	21	3.5	-	-
lip	9	+	+	25	-	2.5	1.5
chin	3	+	+	5	-	1	-
jowl sulcus	12	+	-	24	-	3.5	-
jawline	11	-	+	22	3.5	-	-

Table 3 FOE questionnaire to assess patient's perception of its facial appearance before and after FFR-HA

Questions	**Answers**		
	Pre FFR	**01 month after FFR**	**12 months after FFR**
1. How well do you like the appearance of your face?*	0.50±0.13	3.80 ±0.50	3.70 ± 0.29
2. How much do your current facial wrinkles and tone bother you?**	1.95±0.29	2.50±0.28	2.65±0.32
3. Do you think your current facial appearance makes you look old in other's eyes? **	0.90±0.10	3.70 ± 0.29	3.60 ±0.08
4. Do you think your current facial appearance limits your social or professional activities?***	1.05±0.36	3.65 ± 0.32	3.55 ± 0.43
5. How confident are you that your facial appearance is the best that it can be?*	0.75±0.10	3.55 ± 0.35	3.45 ±0.43
6. Would you like to alter the appearance of your face non-surgically with hyaluronic acid?****	0.80±0.01	0.65 ± 0.33	0.60 ± 0.09

*Answer ranged from 0 (Not at all) to 4 (Completely)

**Answer ranged from 0 (Completely) to 4 (Not all)

***Answer ranged from 0 (Always) to 4 (Never)

****Answer ranged from 0 (Definitely) to 4 (No)

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Discussion

FR-HA was an attractive alternative for facial surgery to patients concerned with immediate results, downtime, surgical and anesthetic risks, and financial expense. The study protocol included only females since they showed a significantly greater superficial cheek fat volume than males.[10] The protocol adjusted the assessment from one-month due to the hydrophilic property of HA fillers enabled them to increase correction from 15% in the first-month after HA-injection. MRI in T2-weighted with fat saturation on axial and coronal planes showed that the volume gain after HA-injection is maximal in the first month and remained more or less stable for the next twelve-months.[11] FR-HA was a global approach creating harmony, symmetry and balance through volumetric expansion, projection and lifting of the facial zones. The degree/technology of crosslinking, concentration and molecular-weight of the HA defined the final product features.[12] The own manufacturing technique of the QTFill Signature®, or Ultra-High-Density™ Technology, through vibration compressor, from KIPO™ equipment, further intertwined the molecules already entangled by BDDE-crosslinking, creating an ultra-high-density for the gel.[13] The high density of the SubQ-product, Deep-product and Fine-product provided by HA-concentration of 24 mg/ml, HMW-HA of 1,570 kDa and own crosslinking technology increased its resistance to degradation. This can be explained by densely packed HA-molecules in the gel structure, which retarded the penetration of enzymes inside it.[14] Moreover, HMW-HA of the SubQ-product, Deep-product and Fine-product induced anti-inflammatory activities and inhibited phagocytosis, enhancing its resistance to degradation by limiting the enzymatic activity.[15]

The high cohesivity, or the internal adhesion forces among individual crosslinked HA units within the gel, provided by HA-concentration of 24 mg/ml of the QTFill Signature® range, also increased the resistance to degradation. HA-fillers with concentration of 24mg/ml were most resistant to degradation than those with lower HA-concentrations.[16] The products viscosity of the QTFill Signature® range due to high gel-cohesivity, avoided the gel to spread, maintaining its volumization capacity. Moreover, the high cohesivity and viscosity of the SubQ, Deep and Fine products avoided gel migration in a site remote from the primary injection.[17] Long-lasting of the QTFill Signature® range was demonstrated by no significant changes on the face appearance and by density and homogeneity of the gel-diffusion displayed in MRI, showing that the products remained stable in the injection site without significant evidence of resorption or loss of correction, from month-one to month-twelve. The products with high-G', medium-G' and low-G' of the QTFill Signature® range created by tree BDDE degrees, own crosslinking technology and same HA-concentration targeted them to specific facial zones. The G' values established the gel firmness of the products, or their ability to resist deformation.[18]

The SubQ-product with high-G' was firm and more elastic, supporting shearing forces and vertical compression projecting and lifting facial zones, Deep-product with medium G' was less elastic and firm, volumizing and modeling facial zones, and Fine-product with low-G' was soft, filling superficial lines and grooves. Bolus injection through a perpendicular approach created pillars of gel-diffusion to support and project the central facial triangle.[19] Retrograde-backflow injection allowed uniform distribution of the gel, volumizing and modeling facial zones submitted to less strain forces. Outcomes on FR-HA were usually based on subjective evaluation of the facial appearance, therefore was pertinent to quantify the patient's perspective of achieved results based on evidence.[20] The FOE questionnaire quantified the influence of the patient self-consciousness of its appearance and quality of life before and after FR-HA. The FOE scores exhibited a significant positive correlation between the increases of patient satisfaction, with the improvement of the facial appearance for twelve-months.

Conclusion

An individual and safe approach for each facial zone remodeled the face in a single session based on HA-products, facial fat layers and vasculature, and points and techniques of the injection. The SubQ, Deep and Fine products of the QTFill Signature® range resultants from own crosslinking technology with tree G' values, same HA-concentration of 24 mg/ml and molecular-weight of 1,570 kDa injected in specific facial zones recovered the youthful appearance of the face. Minimal changes on the patient appearance displayed on MRI in T2-weighted with fat suppression on axial and coronal planes showed the gel-diffusion stability in the injection site without evidence of significant resorption or loss of volume correction from one-moth to twelve-months, indicating efficacy and long-lasting for FR-HA. The results were corroborated by the FOE questionnaire scores for twelve-months.

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Conflicts of interest

The authors declare no conflict of interest.

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