

# Comparative Study of Professional vs Mass Market Topical Products for Treatment of Facial Photodamage

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## ABSTRACT

**Summary Background:** Many over the counter topical products claim to reverse the signs of cutaneous photo-damage. To date, the two most studied ingredients for improving the texture, tone, and pigmentation of the skin are topical retinoids and hydroquinone.<sup>1</sup>

**Objective:** This split face study compares a mass market skincare regimen with a prescription skin care regimen for improvement in photo damaged skin.

**Methods:** Twenty-seven subjects with moderate photo damaged facial skin were enrolled. Each subject was consented and assigned with the mass market anti-aging system (Treatment A) to one side of the face and the prescription anti-aging system (Treatment B or Treatment C) to the other side of the face. Treatment B contained 13 subjects whom did not use 0.025% Retinol cream. Treatment C contained 14 subjects who used a 0.025% Retinol Cream. Subjects had 4 visits over 12 weeks for digital photography and surveys. Photographs were evaluated by blinded physicians.

**Results:** Physician objective analysis showed all three systems to have a statistically significant clinical improvement in photoaged skin seen in as little as 4 weeks of use. Participant's surveys rated the mass market system higher than both of the professional systems for visible skin changes, ease of use, and likelihood to recommend to a friend. Twelve of twenty-seven subjects preferred the mass market system for overall improvement while twelve thought each system gave the same improvement.

**Conclusion:** This study demonstrates that a mass marketed skin care system can give similar clinical improvements in photo-aged skin as a professionally dispensed prescription system and the majority of participants preferred the mass-marketed system.

*J Drugs Dermatol.* 2016;15(1):37-44.

## INTRODUCTION

Many topical products claim to reverse the signs of cutaneous photodamage, namely dyspigmentation and rhytid development. To date, the two most studied ingredients for improving the texture, tone, and pigmentation of the skin are topical retinoids and hydroquinone.

All-trans-retinoic acid (tretinoin), a naturally occurring metabolite of retinol, a form of Vitamin A, was the first retinoid to be synthesized, and has been used in topical skin care applications for acne reduction and treatment of photoaging since 1969.<sup>2</sup> Several strengths and formulations are commercially available in the US. Clinical studies have demonstrated efficacy of tretinoin, a prescription-strength retinoid, as a topical agent for the treatment of photodamaged skin,<sup>3</sup> but the potential for side effects such as dryness, scaling, erythema, itching, burning, and photosensitivity<sup>4</sup> may limit patient tolerance and duration of use.

Hydroquinone (1, 4 dihydroxybenzene) has long been used to treat cutaneous hyperpigmentation including melasma, solar and senile lentigines, ephelides, post-inflammatory hyperpigmentation, and other forms of dyschromia. Applied topically, hydroquinone acts as a tyrosine inhibitor to halt a critical step in melanogenesis.<sup>5</sup> Despite its effectiveness, hydroquinone

has several potential side effects including an irritant, allergic contact dermatitis, and exogenous ochronosis.<sup>6</sup> A variety of neoplasms have been reported in rodent studies where the animals received large systemic doses of the medication, but relevance to topical therapy in humans has not been determined.<sup>7</sup> Because of these concerns, hydroquinone has been removed from Japanese and European markets. In the US, 2% formulations are available over the counter, while 3% solution and 4% cream or gel require a prescription.

While tretinoin and hydroquinone are among the most commonly prescribed topical agents for treatment of cutaneous photoaging, several barriers to their use exist. Prescription strength hydroquinone and all tretinoin formulations require a physician assessment to obtain a prescription. Annual monitoring of retinoic acid and quarterly monitoring of 4% hydroquinone is the generally accepted protocol for safety and efficacy.

Other retinoids and hydroquinone formulations are available in over the counter cosmetic preparations. These products may be less irritating than their prescription-strength rival,<sup>8</sup> however, there are few, if any, clinical studies comparing over the counter versus prescription strength products. The objective of this



study is to compare the clinical effects of an over the counter mass-market anti-aging system to those of a professionally dispensed prescription anti-aging system.

"Other retinoids and hydroquinone formulations are available in over the counter cosmetic preparations. These products may be less irritating than their prescription-strength rival,"

## METHODS

This was a single site, blinded evaluator, split face study to compare a mass-market (available in mass retail) anti-aging skin care system (MD Complete, MD Professional, Minneapolis, MN) to a professionally dispensed prescription anti-aging skin care system. Subjects with moderate photo damaged facial skin, including fine wrinkles, lines, erythema, and mottled pigmentation, were consented and enrolled under IRB approval. Upon enrollment subjects were alternately assigned to either right or left sides of the face with the mass-market anti-aging skin care regimen (Treatment A) and the professionally dispensed anti-aging skin care regimen without the use of prescription tretinoin 0.025% cream (Treatment B), or with a prescription tretinoin 0.025% cream (Treatment C).

Standardized digital photography with Visia CR<sup>9</sup> (Canfield Scientific Inc, Fairfield, NJ) and 3D images with ANTERA 3D<sup>®</sup> device<sup>10</sup> (Miravex Limited, Dublin, Ireland) were obtained at baseline, 4-, 8-, and 12-week intervals. In addition, subjects completed online surveys and a global aesthetic improvement scale at each visit.

## Inclusion and Exclusion Criteria

This study was approved by the BioMedical IRB. Subjects with Fitzpatrick skin types I-IV, in good health with moderate hyperpigmentation and photodamage were eligible.

Subjects were required to be non-lactating, non-pregnant, and to not use other topical skin care products on the face. Subjects were required to continue current cosmetic make up use and avoid introducing new cosmetics to their regimen for the duration of the study. Subjects were also required to not use systemic retinoids or steroids, and not to have chemical peels or any laser procedures on the treatment areas throughout the duration of the study. Subjects were instructed to only use the study skincare regimen provided, to avoid extended sun exposure and use of tanning beds.

Subjects were excluded for a known sensitivity or allergy to hydroquinone, retinoic acid, or alpha hydroxy acids. Subjects

receiving treatments with hydroquinone, retinoids, facial laser treatment, or peels within 6 months of starting the study were excluded. Subjects taking medications that may cause skin hyperpigmentation or subjects with active facial skin disease were also excluded.

## Study Procedure

Upon meeting the inclusion and exclusion criteria, subjects were assigned the mass-market skin care regimen (Treatment A) on one side of face and the professional prescription skin care regimen (Treatment B or C) to the other side of face. Baseline photography with Visia CR and 3D images with the ANTERA 3D<sup>®</sup> device were obtained. Subjects were instructed to cleanse the entire face immediately prior to photographs, at baseline and subsequent visits. Online surveys were obtained prior to subjects beginning skin care regimen and at the end of the study. At the baseline visit, subjects were dispensed Treatment A and Treatment B or C products with written instructions.

Subjects were given a generic moisturizer to be used in the morning after the Treatment A regimen if they experienced any dryness. Written instructions with directions for use were provided and reviewed with study staff at each visit. Subjects were provided with the option of an equalization treatment upon completion of the study at their discretion.

## ANALYSIS

Baseline and 12-week photographs of the subjects were evaluated by three blinded physician evaluators in regards to hyperpigmentation, erythema, fine-lines/wrinkles, global photo-aging, and physician global aesthetic improvement scale (PGAIS; See Tables 1-3). Additionally, they estimated the improvement from baseline to 12 weeks for Treatments A, B, and C with respect to the aforementioned attributes. The average of these scores were also expressed as percent of change from each variable.

## RESULTS

Twenty-seven female subjects 35-60 years of age (mean = 49 years) were enrolled. Thirteen were placed in Arm 1 and fourteen were placed in Arm 2.

TABLE 1.

Hyperpigmentation, Erythema and Fine Lines / Wrinkle Scale	
Number	Description
0	None
1	Trace involving small areas
2	Mild, with moderate involving small areas OR mild involving moderate areas
3	Moderate, with moderate involving moderate areas OR light involving all areas
4	Severe, with marked involving moderate to all areas



TABLE 2.

Global Photoaging Scale	
Number	Description
0	Smooth without significant fine lines or unevenness in pigmentation
1	Facial skin shows one area (cheeks, forehead, or the perioral area) of significant roughness, dyspigmentation (hypopigmentation or hyperpigmentation), or fine lines
2	Facial skin shows two areas of significant roughness, dyspigmentation, or fine lines or shows roughness, dyspigmentation, and fine lines in one area
3	Facial skin shows three areas with significant roughness, dyspigmentation, or fine lines or shows roughness, dyspigmentation, and fine lines in two areas
4	Facial skin shows any degree of photodamage greater than #3

TABLE 3.

Physician Global Aesthetic Improvement Scale (PGAIS) Score Ratings	
Number	Description
1	Very much improved
2	Much improved
3	Improved
4	No change
5	Worse than original condition

### Arm 1

The results of the physician assessments showed the both Treatment A and Treatment B having a statistically significant ( $P = 0.05$ ) improvement over baseline for hyperpigmentation, erythema and global photoaging. Treatment A also demonstrated statistically significant improvement in fine lines/wrinkles (Table 4, Figure 1). There was no statistically significant difference in improvement from baseline between Treatment A and Treatment B. However, Treatment A showed a trend of delivering slightly more improvement for most attributes based on the difference between scores as well as the physician assigned degree of improvement.

Using the PGAIS, both Treatment A and Treatment B regimes were shown to have similar and statistically significant improvement in hyperpigmentation, fine lines, wrinkles, erythema, and global photoaging. No significant difference noted between the two treatments on a two-tailed, unpaired T-test. Average PGAIS scores for Treatment A was  $2.85 \pm 1.01$ , and Treatment B was  $3.00 \pm 0.95$ . The percent improvement estimated by the physician's with respect to PGAIS was statistically similar between the two treatments,  $P = 0.491$ . Percent change in the PGAIS was

found to be  $27.05 \pm 24.97\%$  for Treatment A and  $22.56 \pm 21.91\%$  for Treatment B (Figure 2).

### Arm 2

Physician assessments showed the Treatment A and Treatment C having a statistically significant improvement over baseline for hyperpigmentation and global photoaging. Treatment A also showed significant improvement over baseline for fine lines, wrinkles (Table 4). Both Treatment A and Treatment C were associated with increased erythema, with Treatment C being greater than Treatment A. Treatment C had been found to be slightly more irritating than Treatment A based on subject feedback. Despite any variation in scores, there was no statistically significant difference between the two treatments (Table 5, Figure 3).

The PGAIS, global photoaging scoring showed the two treatment regimens to have statistically significant improvement over baseline for hyperpigmentation, fine lines, wrinkles, erythema, global photoaging, and that the improvement for both was statistically similar. There was no statistically significant difference noted between the two treatments on a two-tailed, unpaired T-test. Average PGAIS scores for Treatment A was  $2.88 \pm 0.92$ , and Treatment C was  $2.88 \pm 0.71$ . The percent improvement estimated by the physician's with respect to PGAIS was statistically similar between the two treatments:  $P = 1.000$ . The improvement of the subjects globally was found to be  $21.90 \pm 21.21\%$  for Treatment A and  $22.14 \pm 17.25\%$  for Treatment C (Figure 4).

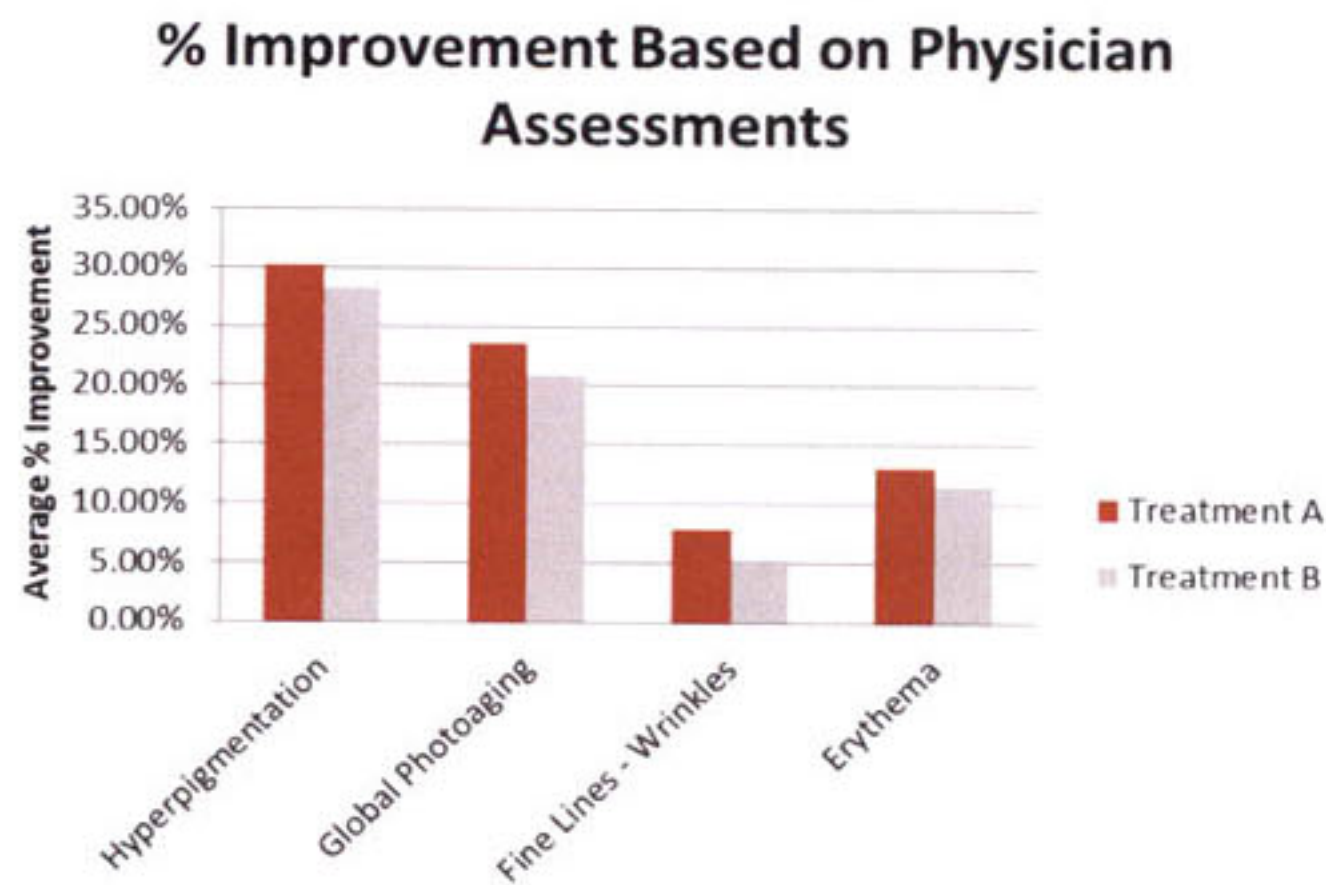
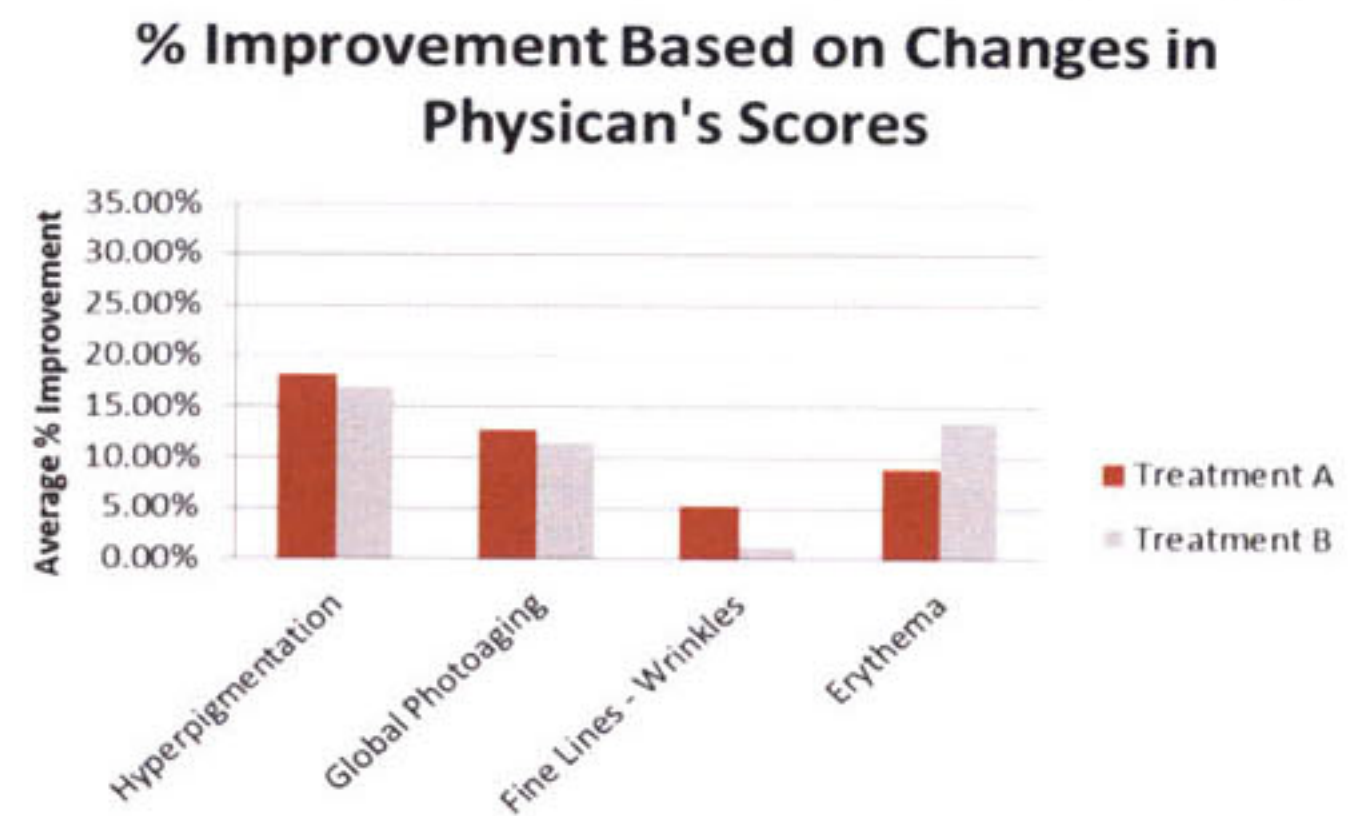
### Subject Surveys

For this analysis, a two-tailed T-test of Treatment A vs Treatment B or Treatment C was performed. A number 1 was assigned to

TABLE 4.

Physician Assessment, P-values of 12-week Final Assessment Over Baseline					
Arm	Treatment Group	Hyperpigmentation	Global Photoaging	Fine Lines	Erythema
1	A	0.007E-2	0.007E-1	0.044	0.011
1	B	0.003E-1	0.001	0.323	0.004E-1
2	A	0.004E-3	0.005	0.044	0.133
2	C	0.019E-4	0.010	0.323	0.014



**FIGURE 1.** Arm 1 physician assessment of improvement at 12-weeks.**FIGURE 2.** Average percent change from baseline in PGAIS for hyperpigmentation, fine lines/wrinkles, erythema, and global photoaging.**TABLE 5.****Arm 2 Physician Assessment P-values over Baseline**

Arm	Treatment Group	Hyperpigmentation	Global Photoaging	Fine Lines	Erythema
2	A	4.29E-06	0.0052	0.0441	0.1333
2	C	1.91E-06	0.0097	0.3232	0.0145

the treatment the subject preferred while the non-preferred treatment was assigned a number 0. Responses where the subject reported "No Improvement" were not assigned a value.

### Arm 1

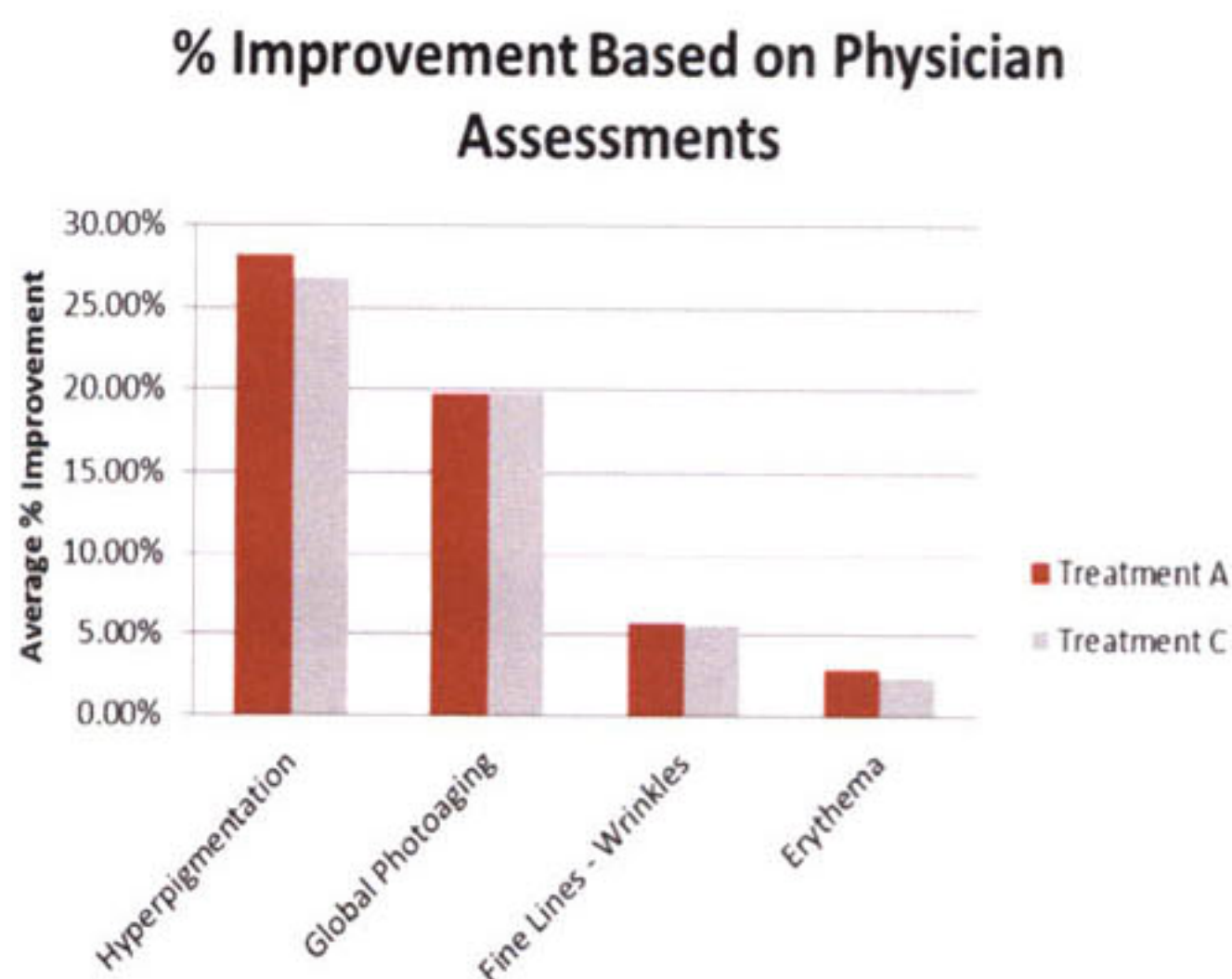
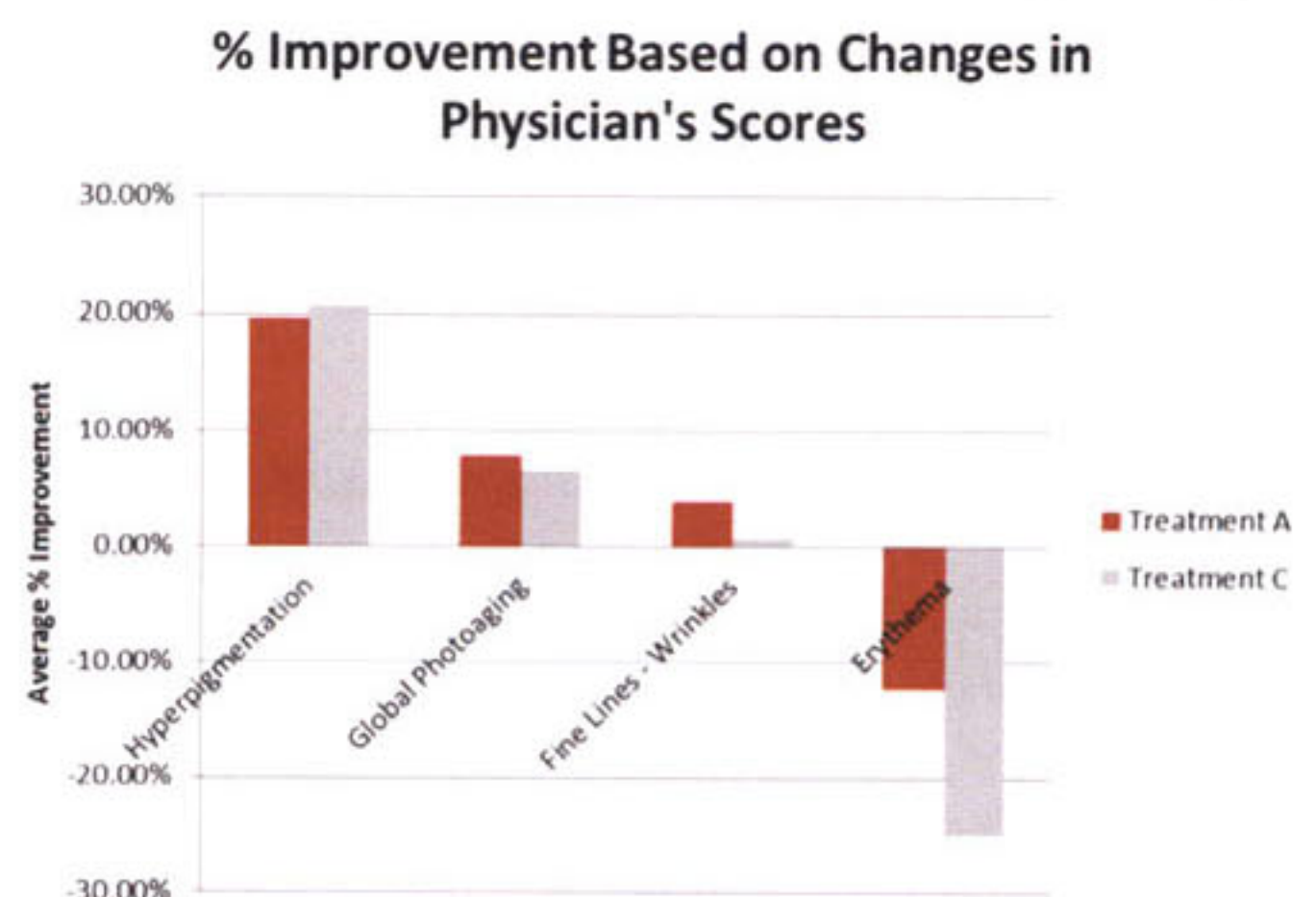
Participants rated Treatment A higher than Treatment B for a number of attributes including softer skin, reduction in pore size, improvement in skin texture and firmness, brighter complexion, and changes in age spots (Figures 5 and 6).

Statistical analysis of the subjective responses show there was a statistical significant preference seen with Treatment A in respect to skin firmness, brighter complexion, reduction

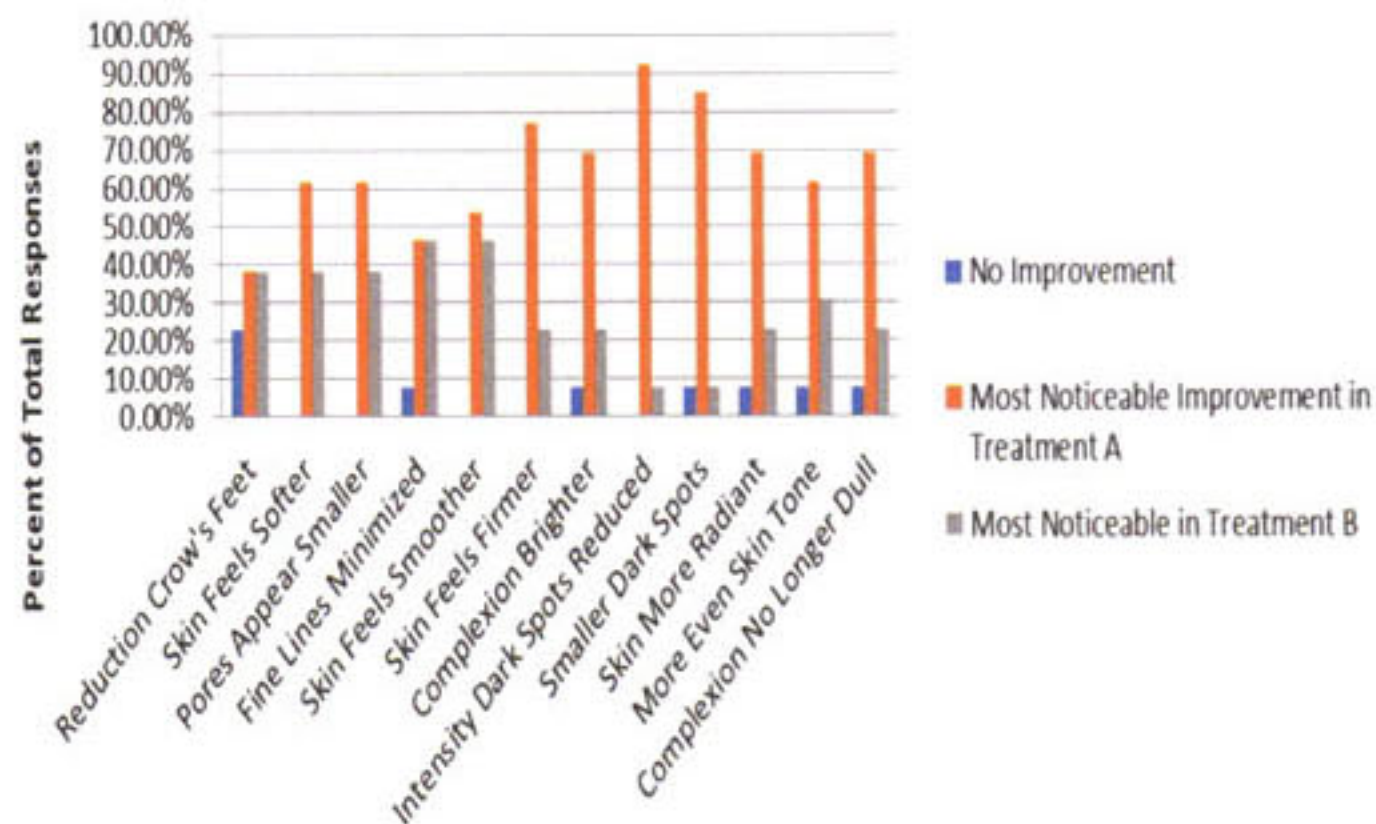
in the intensity of dark spots, reduction in size of dark spots, more radiant skin, and decrease in the dullness of complexion (Table 6).

Subjects, on average, noticed results around the same time (4 weeks) for both treatments. In addition, the majority of subjects reported more visible results with either the Treatment A or Treatment B system compared to previous treatments they may have utilized in the past.

Subjects reported more irritation associated with the Treatment A system, yet the application times for this particular regimen were less than those of Treatment B for both morning and nighttime applications (Table 7). Overall Treatment A

**FIGURE 3.** Arm 2 physician assessment of improvement at 12-weeks.**FIGURE 4.** Average percent change from baseline in PGAIS for hyperpigmentation, fine lines/wrinkles, erythema, and global photoaging.



**FIGURE 5.** ARM 1 subject survey responses regarding product efficacy for a number of attributes.**FIGURE 6.** Treatment A vs Treatment B baseline and 12 week follow up. Treatment A on left side of face. Treatment B to right side of face.**TABLE 6.**

**P-values Comparing Number of Subject Responses for Product Preference of Each Treatment for ARM 1 and 2 Using Two-Tailed T-Test ( $\alpha$  of 0.05).**

Parameter	P-Value Arm 1	P-Value Arm 2
Reduction Crow's Feet	1	0.0128
Skin Feels Softer	0.2567	0.4683
Pores Appear Smaller	0.2567	2.29E-05
Fine Lines Minimized	1.000	0.4363
Skin Feels Smoother	0.7088	0.1405
Skin Feels Firmer	0.0045	0.1114
Complexion Brighter	0.0128	0.1405
Intensity Dark Spots Reduced	5.17E-08	0.0524
Smaller Dark Spots	4.30E-07	4.30E-07
Skin More Radiant	0.0128	0.0524
More Even Skin Tone	0.1114	8.90E-05
Complexion No Longer Dull	0.0128	0.2195

took 37% and 41% less time in the morning and 17% and 23% less time in the evening than Treatment B and Treatment C, respectively (Table 7). This equates to about 2 minutes less each morning and 1 minute less each evening. Aside from a decrease in application times, subjects found the Treatment A system easier, less complicated, and more convenient to use.

Sixty to ninety percent of the subjects preferred Treatment A to Treatment B for a number of attributes evaluating overall user experience (Figure 7). Forty six percent of subjects rated the efficacy of the Treatment A system higher than the Treatment B while only fifteen percent rated Treatment B better in efficacy (Figure 8). Likewise, a greater number of participants would continue using Treatment A and recommend it to a friend compared to Treatment B (Figures 9 and 10).

## Arm 2

Participants rated the Treatment A higher than Treatment C for 11 of 12 attributes including softer skin, reduction in pore size, improvement in skin texture and firmness, brighter complexion, and changes in age spots (Figures 11 and 12). For this analysis, a two-tailed T-test of Treatment A versus Treatment B was performed. A number 1 was assigned to the Treatment the subject preferred while the non-preferred Treatment was assigned a number 0. Responses where the subject reported "No Improvement" were not assigned a value. Based on the findings, there was statistically significant improvement seen regarding the reduction in crow's feet, reduction in the size of pores, decrease in the size of dark spots, and a more even skin tone for Treatment A over Treatment C, while Treatment C showed no parameter with a statistically significant improvement compared to Treatment A (Table 6).

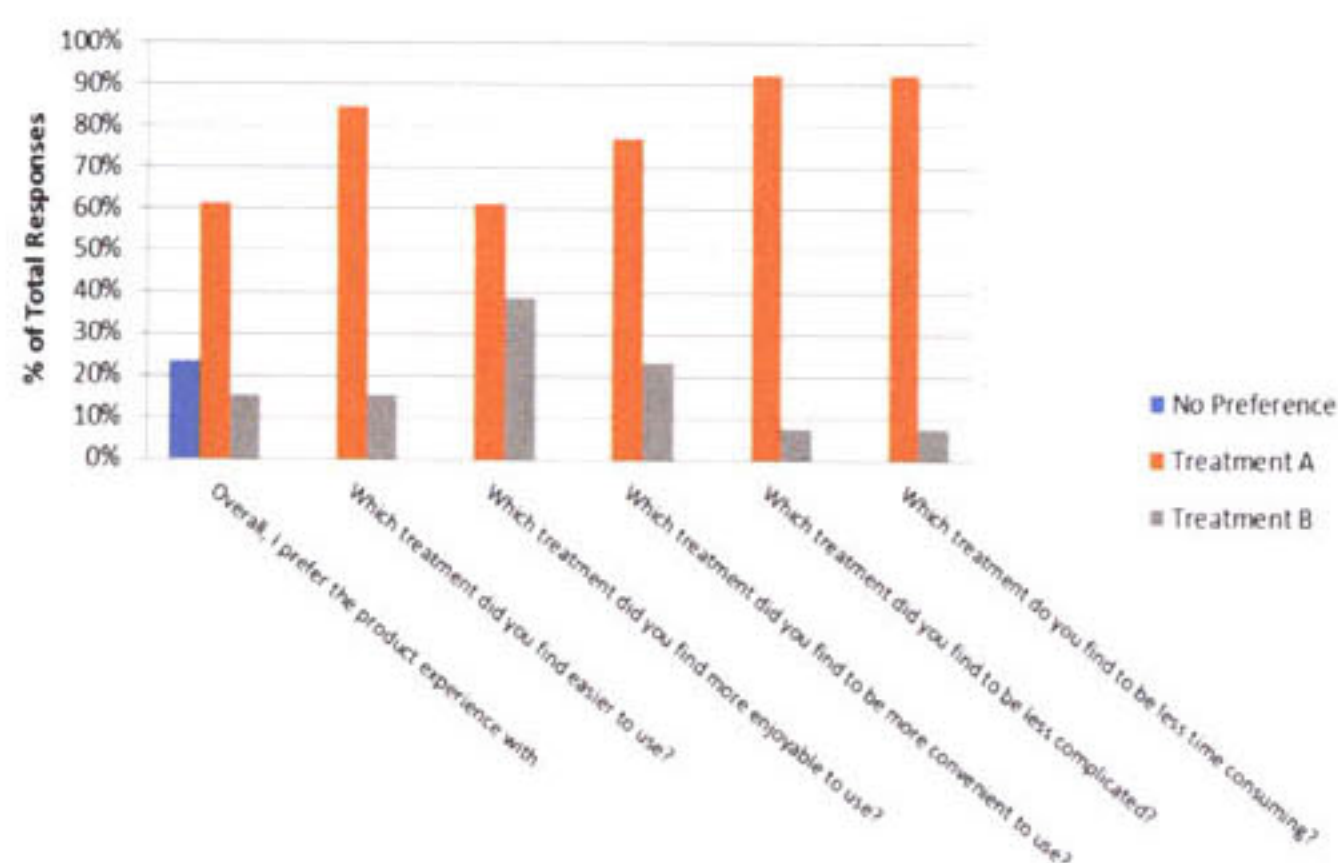
A greater percentage of participants reported some degree of irritation with Treatment C with one participant noting that it was "too drying". As for the Treatment A system, one subject commented that there was "some redness, itching, and peeling".

**TABLE 7.**

**Number of Subjects Reporting Length of Morning (AM) and Evening (PM) Application Times for Arm 1 and Arm 2**

Subject response	Arm 1 AM A/B	Arm 2 AM A/C	Arm 1 PM A/B	Arm 2 PM A/C
1-3 minutes	8/2	12/5	7/5	8/3
4-6 minutes	4/7	1/6	4/4	5/7
7-9 minutes	0/3	1/3	1/4	1/3
10+ minutes	1/1	0/0	1/0	0/1
Total	13/13	14/14	13/13	14/14
Avg. time ( min.)	3.4/5.4	2.6/4.4	3.8/4.6	4.0/5.2



**FIGURE 7.** Subject responses various product attributes for ARM 1.

As seen with Arm 1, subjects found the Treatment A regimen easier to use and more enjoyable and overall subjects preferred this product's experience compared to Treatment C (Figure 13).

Overall, subjects rated the efficacy of the Treatment A system higher than the Treatment C (Figure 14). Based on product performance, a higher percentage of participants would prefer to continue using the Treatment A system and recommend to a friend (Figures 15 and 16).

### Side Effects

One subject withdrew consent due to irritation of both Treatment A and Treatment B, this subject was instructed to discontinue both treatment A and B for 2 weeks. Upon return to clinic, the subject was instructed to perform a patch test. The subject called to report she did not perform the patch test and withdrew consent. Two subjects withdrew consent due to the time required to participate in the study and one subject was lost to follow up.

## DISCUSSION

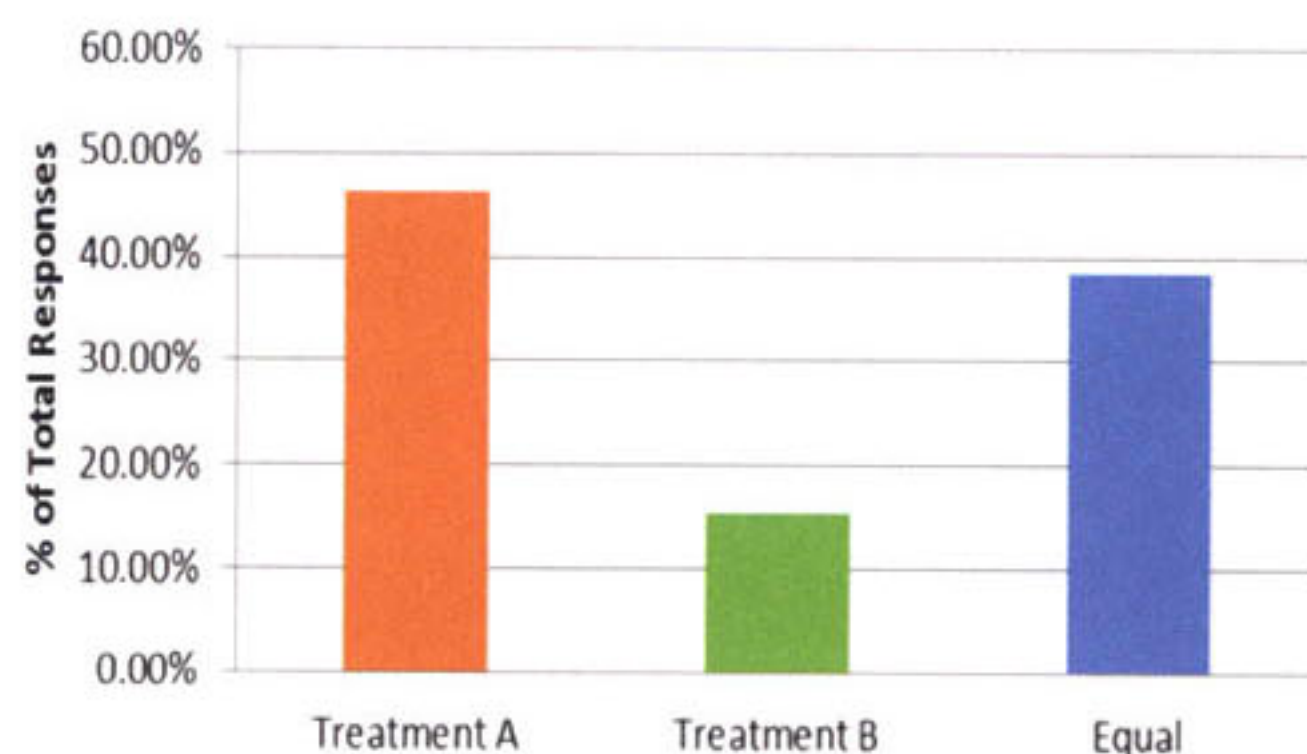
The design of this comparison study was to compare results of a mass-market anti-aging skin care system with a professional prescription based anti-aging skin care system with and without a prescription strength retinoic acid.

The results of this study show that all three treatment systems give rise to a significant clinical improvement in photoaged skin seen in as little as 4 weeks of use. This study demonstrates that a mass-marketed skin care system can give similar clinical improvements in photoaged skin as a professionally dispensed prescription based system with and without a prescription strength retinoic acid. It also showed that not only were the objective and subjective results better in many categories but that more subjects preferred the mass-marketed system.

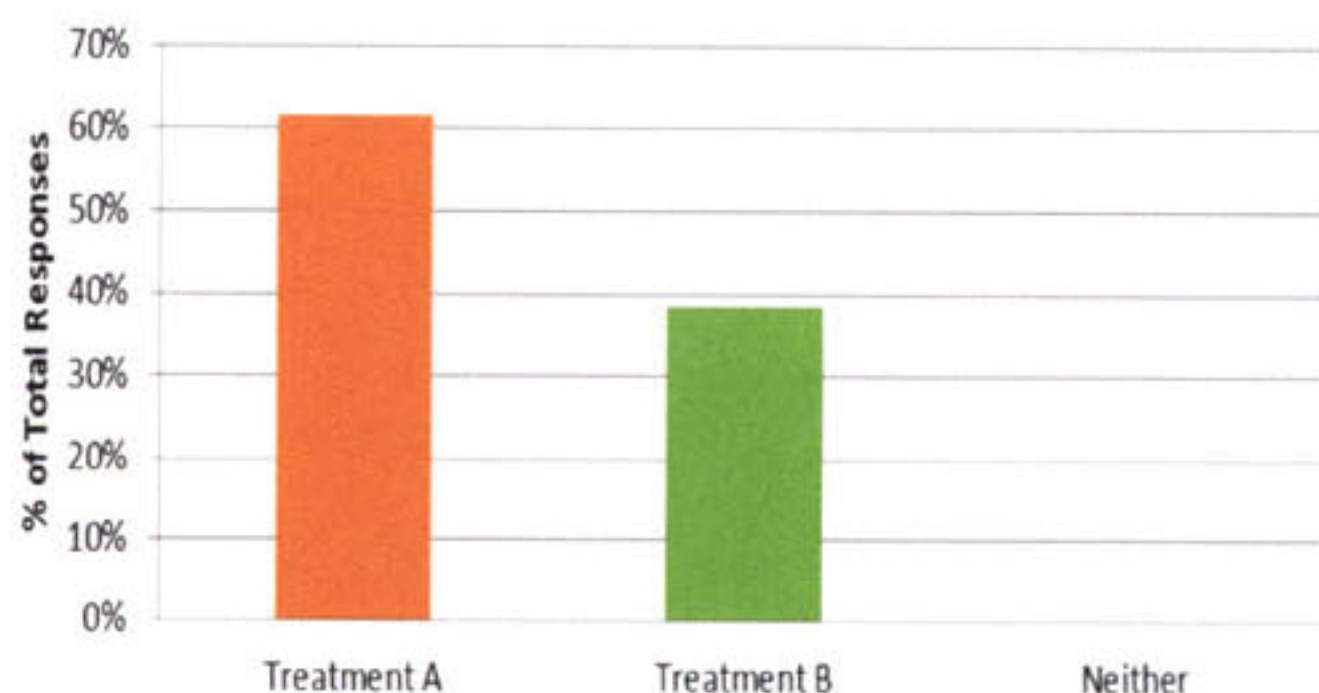
While the results trend toward showing the mass-marketed system scoring better than both professional systems with respect

**FIGURE 8.** Subject reported efficacy for ARM 1.

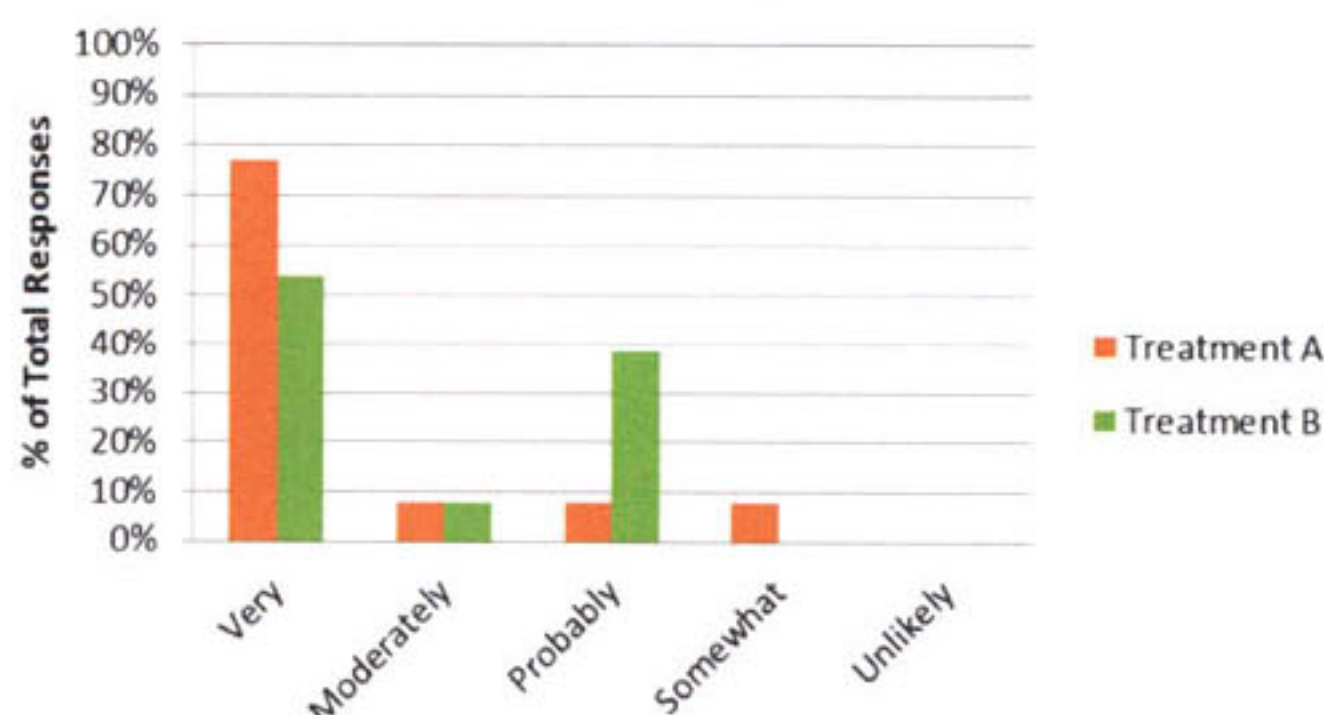
### Which treatment do you think you achieved better results with?

**FIGURE 9.** Percent of subjects reporting which product they would like to continue using for ARM 1.

### Which treatment would you like to continue using?

**FIGURE 10.** Percent of subjects reporting likelihood of recommending the two products for ARM 1.

### How likely are you to recommend the Treatment to a friend?





**FIGURE 11.** Treatment A vs Treatment C baseline on right 12-week follow up on right. Treatment A on right side of face, Treatment C to left side of face.

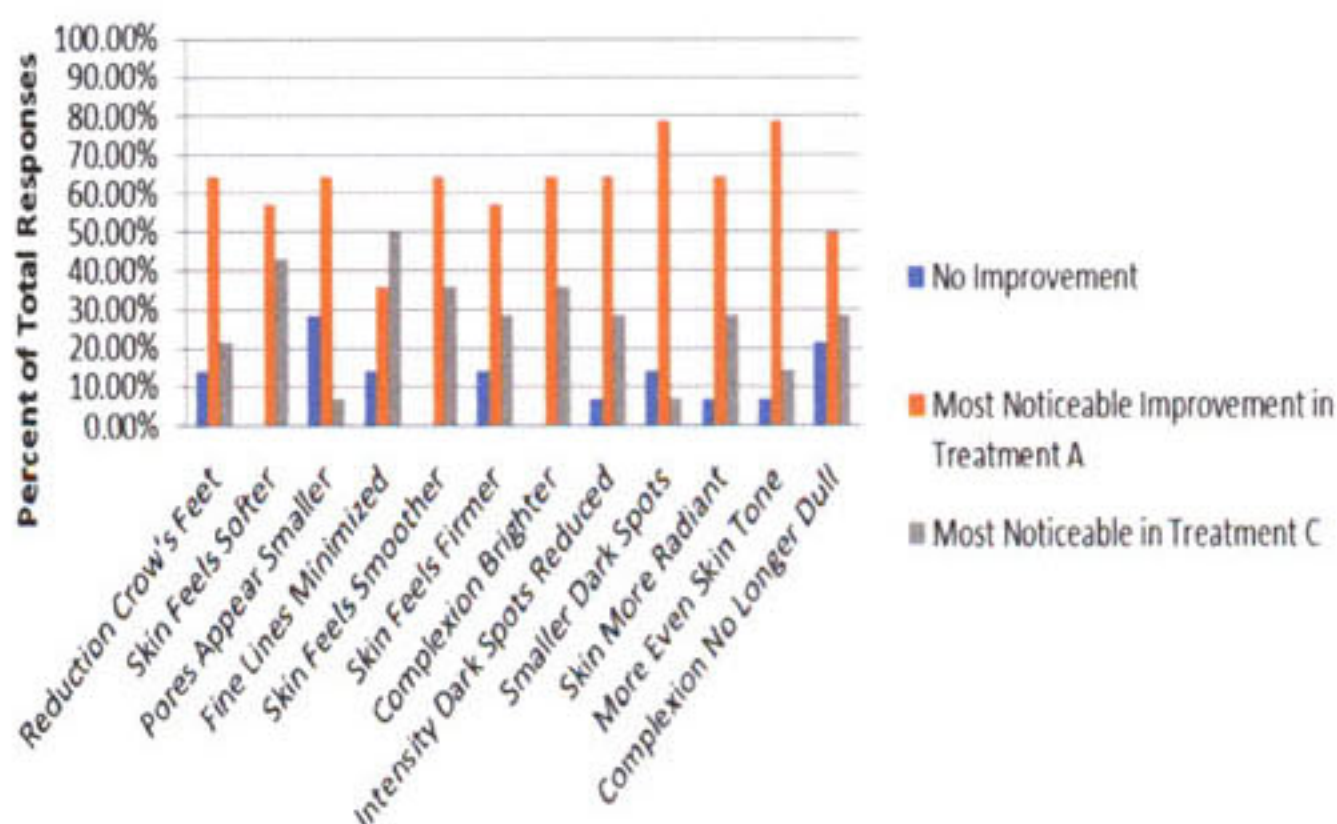


to fine lines and wrinkles as assessed by three blinded physician evaluators, there was no statistical significance between the three systems tested. Additionally, the physician global aesthetic improvement scale (PGAIS) scores were comparable between all three treatment regimens.

Overall, participant's surveys rated the mass-marketed system higher than both of the professional systems for a number of attributes including visible skin changes, ease of use, and likelihood to recommend to a friend. Furthermore, 12 of 27 subjects preferred the mass-marketed system for overall improvement while 12 thought each system gave the same improvement and 2 of 27 subjects preferred the professional system without the prescription tretinoin and 1 preferred the professional system with the prescription tretinoin.

Besides these cosmetic improvements, participants spent, on average, less time with the application of mass-market system

**FIGURE 12.** ARM 2 subject survey responses regarding product efficacy for a number of attributes.



as compared to both professional systems. Despite the perceived benefits of the mass-market system, subjects did note that this system was slightly more irritating than the professional system without tretinoin, while the professional system with the prescription tretinoin correlated to a higher degree of subject reported irritation than the other two systems. However, the degree of irritation was not statistically significant between the three systems. The majority of subjects wished to continued use with the mass-market system when asked at the conclusion of the study.

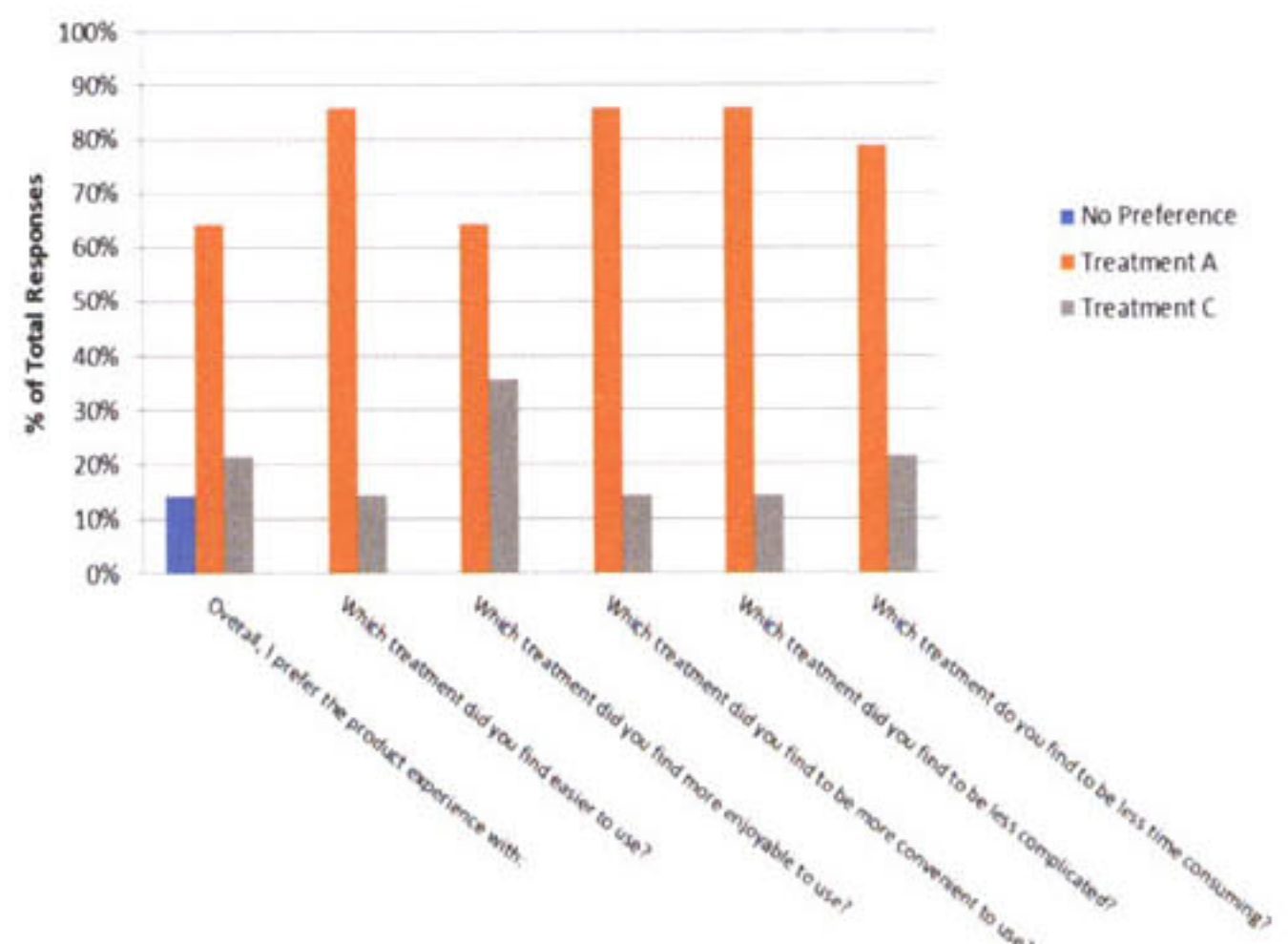
The limitations of this evaluation include the fact that it is a single site study with only 27 subjects. As with most clinical studies on medications, this study was funded by a company that has ownership of one of the tested products. And while the reviewing physicians were blinded and have no financial ties to either product tested, the principal investigator has an equity position in MD Professional.

This study shows the availability of a clinically effective mass-market anti-aging skin care system in which the consumer benefits both in time and expense. According to the manufacturers, the mass-market system available for retail costs less than one third of the current professional prescription anti-aging skin care system. The reduction in cost, superiority of subject approval, along with the availability of the product, gives consumers an effective and affordable option with the tested mass-market system.

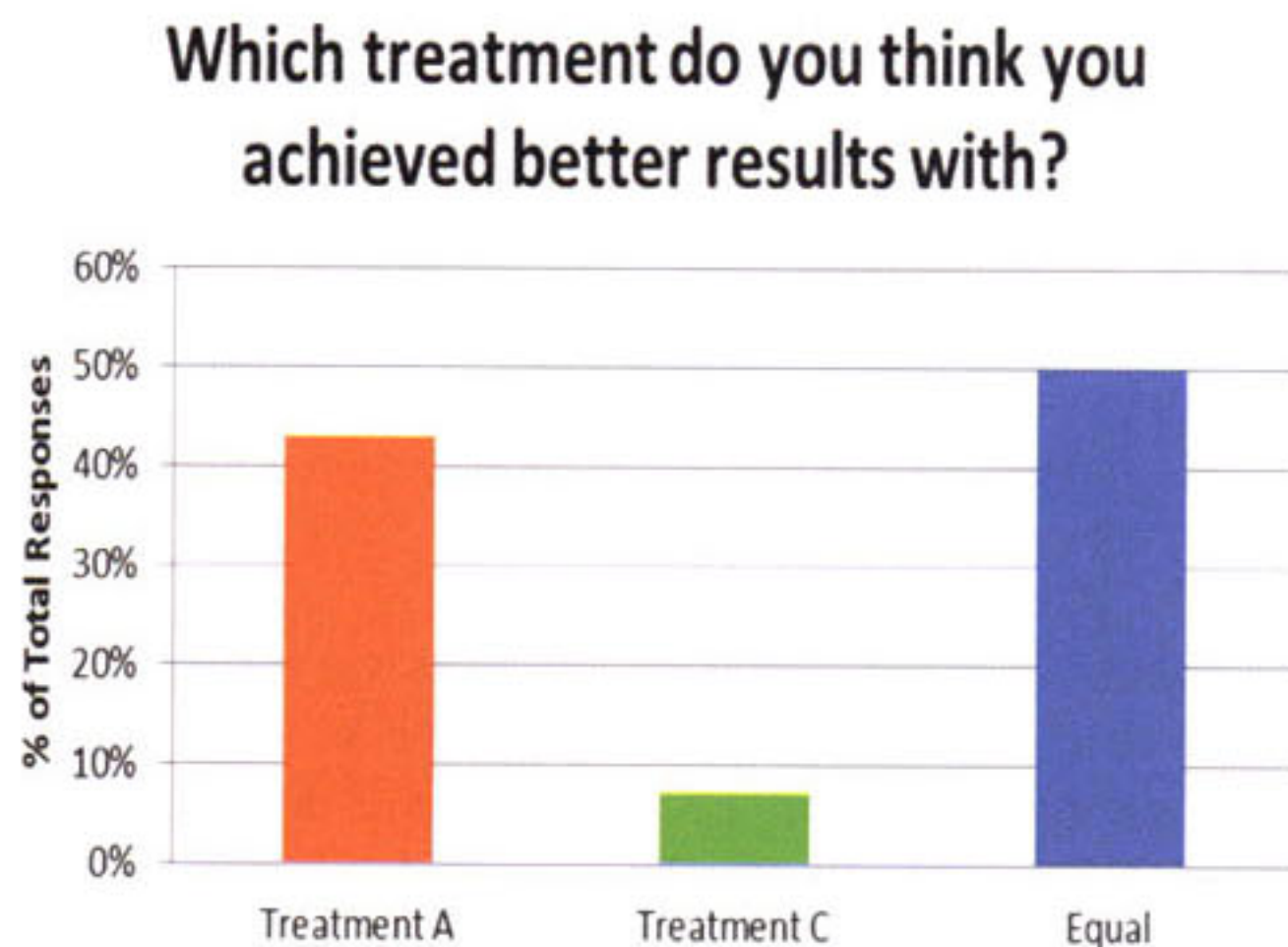
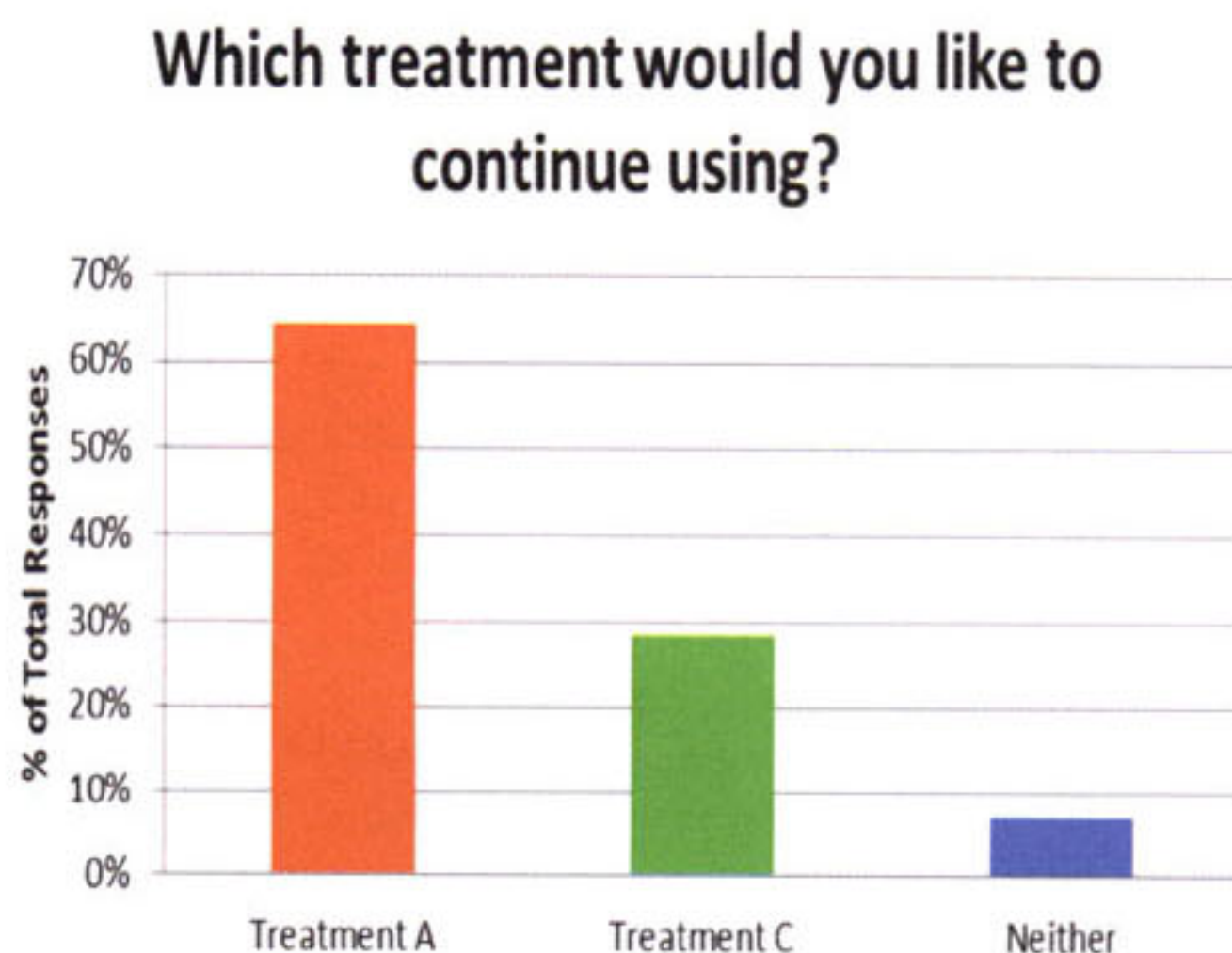
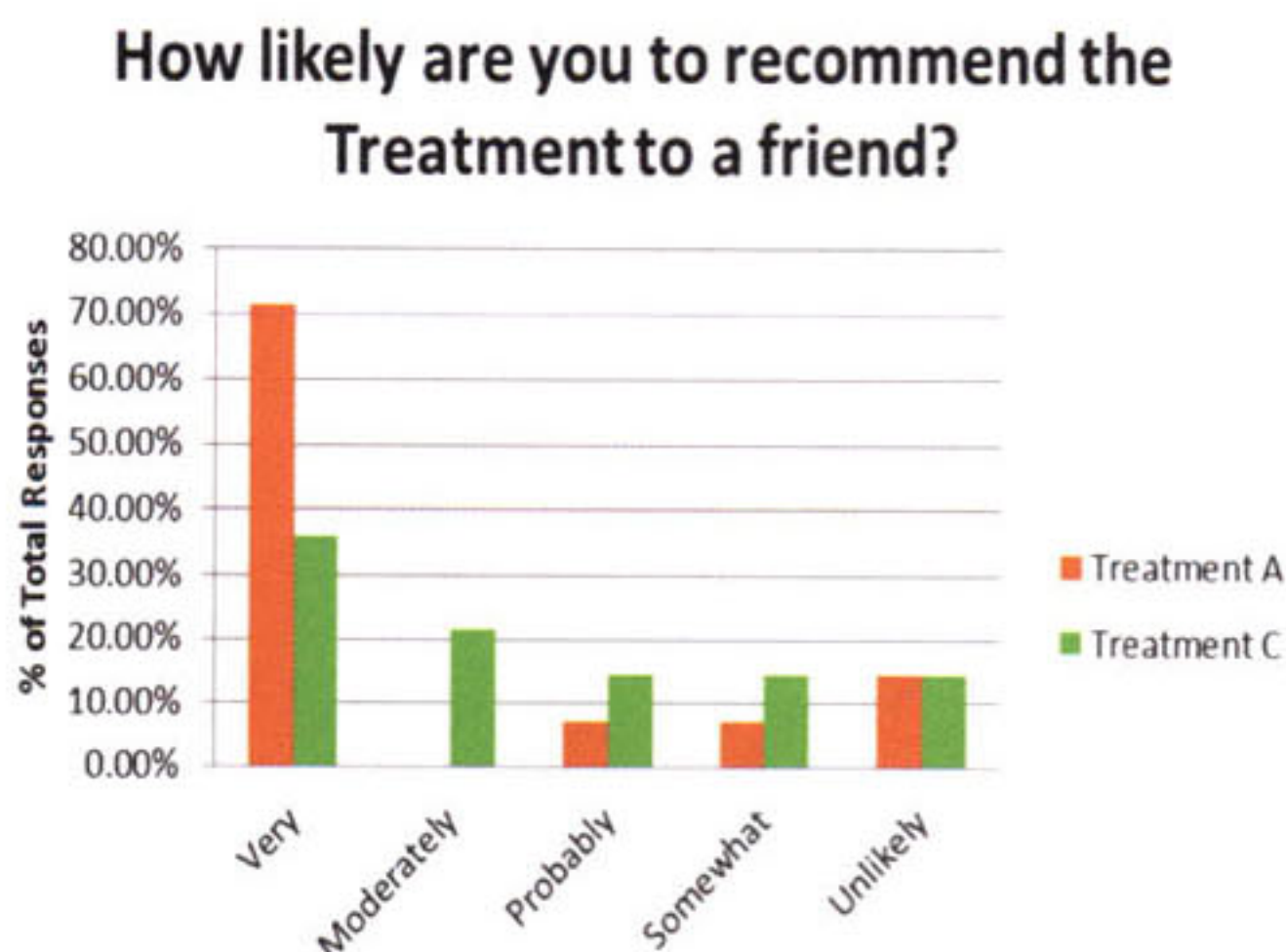
## DISCLOSURES

Dr. Zelickson has an equity ownership in MD Professional and has received education and research grants from Allergan. MD Professional supplied a research grant to help support this study. Irmina Wallander owns stock in MD Professional. The other authors have no conflicts to disclose.

**FIGURE 13.** Subject responses various product attributes for ARM 2.





**FIGURE 14.** Subject reported efficacy for ARM 2.**FIGURE 15.** Percent of subjects reporting which product they would like to continue using for ARM 2.**FIGURE 16.** Percent of subjects reporting likelihood of recommending the two products for ARM 2.**REFERENCES**

1. Bruce S. Cosmeceuticals for the attenuation of extrinsic and intrinsic dermal aging. *J Drugs Dermatol*. 2008;7(2 Suppl):s17-22.
2. Kligman AM. Current status of topical tretinoin in the treatment of photoaged skin. *Drugs Aging*. 1992;2(1):7-13.
3. Stefanaki C, Stratigos A, Katsambas A. Topical retinoids in the treatment of photoaging. *J Cosmet Dermatol*. 2005;4(2):130-4.
4. Baldwin HE, Nighland M, Kendall C, Mays DA, Grossman R, Newburger J. 40 years of topical tretinoin use in review. *J Drugs Dermatol*. 2013;12(6):638-42.
5. Ladizinski B, Mistry N, Kundu RV. Widespread use of toxic skin lightening compounds: medical and psychosocial aspects. *Dermatol Clin*. 2011 Jan;29(1):111-23. doi: 10.1016/j.det.2010.08.010. Epub 2010 Oct 13.
6. Monteiro RC, Kishore BN, Bhat RM, Sukumar D, Martis J, Ganesh HK. A Comparative Study of the Efficacy of 4% Hydroquinone vs 0.75% Kojic Acid Cream in the Treatment of Facial Melasma. *Indian J Dermatol*. 2013 Mar;58(2):157. doi: 10.4103/0019-5154.108070.
7. Draelos ZD. Skin lightening preparations and the hydroquinone controversy. *Dermatol Ther*. 2007;20:308-313.
8. Fluhr JW, Vienne MP, Lauze C, Dupuy P, Gehring W, Gloor M. Tolerance profile of retinol, retinaldehyde and retinoic acid under maximized and long-term clinical conditions. *Dermatology*. 1999;199 Suppl 1:57-60.
9. Canfield Imaging Systems internet homepage. Fairfield, New Jersey. Available from: <http://www.canfieldsci.com/FileLibrary/RBX%20tech%20overview-LoRz1.pdf>. Accessed May 28, 2015.
10. Miravex. Antera 3D®, analysis of your skin [Internet homepage]. Dublin, Ireland: Miravex Limited; 2013. Available from: [http://miravex.com/english/antera\\_3d/antera\\_3d\\_analysis\\_of\\_your\\_skin-4.html](http://miravex.com/english/antera_3d/antera_3d_analysis_of_your_skin-4.html). Accessed May 28, 2015.

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