

# Insights on Skin Quality and Clinical Practice Trends in Asia Pacific and a Practical Guide to Good Skin Quality from the Inside Out

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**OBJECTIVE:** We sought to examine the current skin quality trends and gaps in clinical practice in the Asia Pacific region and develop a practical guide to improve skin quality. **METHODS:** Medical practitioners from 11 countries in the Asia Pacific region completed an online survey on current trends in skin quality treatment. A panel of 12 leading experts convened for a virtual meeting to develop a practical guide for skin quality improvement. **RESULTS:** A total of 153 practitioners completed the survey. The four most common skin quality issues were uneven skin tone, skin surface unevenness, skin laxity, and sebaceous gland hyperactivity and enlarged pores. Most practitioners reported using a combination of treatment modalities for each skin quality issue. It was also observed that each treatment modality could be used to treat several skin quality issues. A multimodal approach targeting different interrelated issues across the tissue planes was recommended for balanced results. The panel developed a practical guide for the appropriate combinations and sequence of treatments, and created treatment protocols for specific skin quality outcome goals. The guide employed an “inside-out” approach, treating the deeper tissue planes prior to the superficial layers to achieve harmonious results. **LIMITATIONS:** Future studies are needed to support the recommended treatment protocols for skin quality improvement. **CONCLUSION:** These findings provide valuable insights on current skin quality trends and gaps in clinical practice. The practical guide provides a framework for practitioners to customize their treatment plan according to each patient's needs. **KEYWORDS:** Skin quality, practical guide, consensus, survey, multimodal, “inside-out” approach

To a large extent, facial skin quality affects an individual's appearance and has a profound influence on perceived attractiveness, youthfulness, and health.<sup>1–3</sup> Poor skin quality can have negative consequences, both psychologically and socially, with significant impact on patient quality of life.<sup>4,5</sup> The overall perception of skin quality is influenced by multiple attributes or parameters, which are determined by an interplay of underlying biological processes affecting different anatomical layers of the face.<sup>6–9</sup> A multimodal approach targeting different tissue planes (as opposed to only treating the skin surface) is required for skin quality improvement.<sup>6</sup> Skin quality attributes or parameters are also interrelated and interdependent.<sup>6</sup> Likewise, individual treatment modalities can have effects on more than one attribute or

parameter. Therefore, a holistic approach selecting a combination of treatments is beneficial towards achieving balanced results. However, practical guidance on selecting and combining treatment modalities to achieve the desired outcome has not been developed so far. There is also a lack of data on clinical practice trends for skin quality improvement in the Asia Pacific region. This article examines the common skin quality issues and current clinical practice trends in the Asia Pacific region. Consensus recommendations and practical treatment algorithms for skin quality improvement are also presented.

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## METHODS

**Survey on skin quality trends and panel discussion.** An online survey was initially conducted to understand the current skin quality and clinical practice trends in Asia Pacific. Medical practitioners from 11 countries in Asia Pacific participated in this survey between January and February 2021. A panel of 12 experts convened for a virtual meeting in March 2021 to establish a consensus for skin quality attributes and practices. This panel comprised aesthetic physicians, dermatologists, and plastic surgeons from 10 countries, including Hong Kong, Indonesia, Malaysia, the Philippines, Taiwan, Thailand, Singapore, South Korea, Australia, and Germany. The expert from Germany was invited to provide a global perspective on best practices for skin quality improvement. The panel discussed the survey findings and shared their clinical experience in addressing common skin quality issues encountered by patients in the Asia Pacific region. They also voted on statements relating to skin quality attributes and trends, as well as treatment strategies and current practices for skin quality improvement. Voting results were graded as follows: strong consensus (>95% agreement); consensus (>75% to 95% agreement); majority consent (>50% to 75% agreement), and no majority consent (<50% agreement). The panel developed a practical guide with recommended treatment algorithms for achieving an improvement in overall skin quality, including suggested combinations and sequence of treatments, based on their extensive clinical experience with various treatment modalities and available evidence.

## RESULTS

**Current skin quality and clinical practice trends in Asia Pacific.** A total of 153 medical practitioners in Asia Pacific participated in the survey. Practitioners from Thailand, South Korea, the Philippines, Indonesia, Hong Kong, and Australia constituted around 80% of the participants. The remaining 20% were from Taiwan, India, Malaysia, New Zealand, and Singapore. The surveyed practitioners comprised aesthetic physicians (48%), dermatologists (45%), plastic surgeons (5%), and others (3%). The results of the survey are summarized in Figures 1 and 2, and Table 1. The practitioners recognized four concepts—skin tone evenness, skin surface evenness, skin firmness, and skin

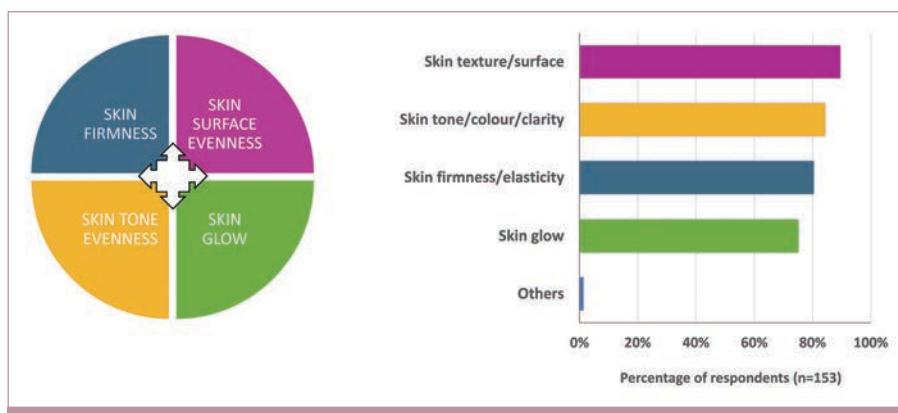


FIGURE 1. Key attributes of good skin quality selected by the surveyed practitioners

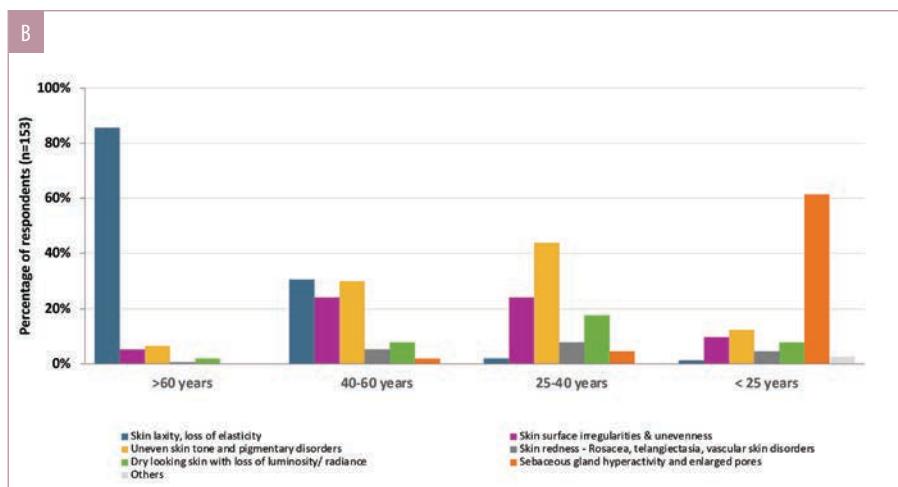
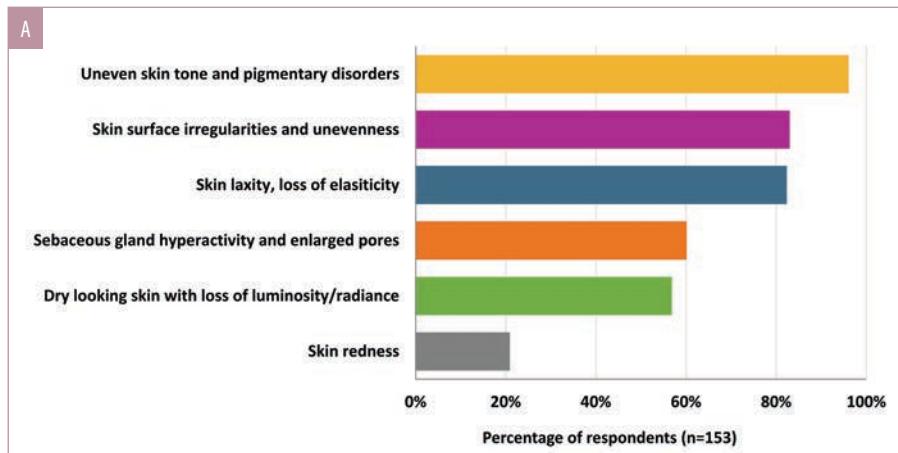


FIGURE 2. Skin quality issues encountered by the surveyed practitioners: A) All practitioners B) Stratified according to patient's age group.

glow—as key attributes of good skin quality and attractive skin (Figure 1). The same four skin quality attributes were identified in a recent consensus developed by a panel of experts mostly from the Western countries, which described these as emergent perceptual skin

quality categories (EPCs).<sup>6</sup>

When practitioners were asked about skin quality issues encountered in their clinical practice, they reported that patients were concerned with various skin quality issues. The four most common issues were uneven skin

**1. IDENTIFY patient's needs**

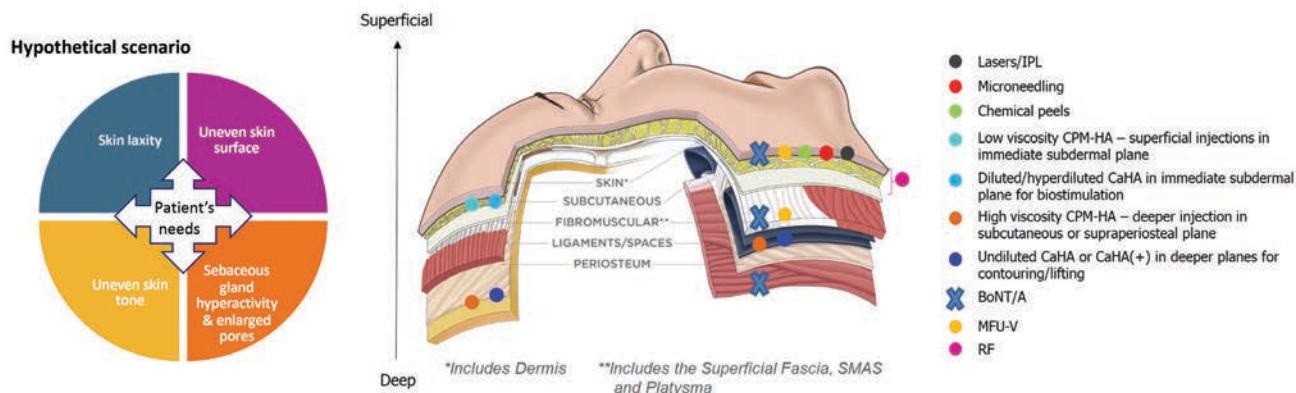
What skin quality issues are the patient concerned with?

**2. ASSESS patient**

Take note of the appearance of the skin and the affected tissue planes

**3. DESIGN treatment plan**

Address the patient's concerns and other related issues using a multimodal strategy, treating first the deeper underlying tissues prior to the superficial layers ("inside out" approach).



**FIGURE 3.** Good skin quality from the inside out: a practical guide

Skin layer photo courtesy of Ulthera, Inc.

BoNT: botulinum toxin; CaHA: calcium hydroxylapatite; CaHA(+): calcium hydroxylapatite with integral lidocaine; HA: hyaluronic acid; IPL: intense pulsed light; MFU-V: microfocused ultrasound with visualization; RF: radiofrequency; SMAS: superficial musculaponeurotic system

**TABLE 1.** Treatment modalities used by the surveyed practitioners to address common skin quality issues.

TREATMENT MODALITIES	UNEVEN SKIN TONE	UNEVEN SKIN SURFACE	SKIN LAXITY	SEBACEOUS GLAND HYPERACTIVITY & ENLARGED PORES
Intradermal BoNT		✓	✓	✓
Biostimulators		✓	✓	
Superficial HA injections	✓	✓	✓	✓
MFU-V			✓	
RF		✓	✓	✓
Lasers	✓	✓	✓	✓
IPL	✓		✓	✓
Microneedling	✓	✓	✓	✓
Chemical peels	✓	✓	✓	✓

A checkmark denotes use of the treatment modality by at least 5% of the surveyed practitioners

Abbreviations: BoNT: botulinum toxin; HA: hyaluronic acid; IPL: intense pulsed light; MFU-V: microfocused ultrasound with visualization; RF: radiofrequency

tone, skin surface unevenness, skin laxity, and sebaceous gland hyperactivity and enlarged pores (Figure 2A). However, it is important to note that different skin quality issues were prevalent in different age groups (Figure 2B). Patients younger than 25 years were most disturbed by sebaceous gland hyperactivity and enlarged pores, whereas those older than

60 years were most concerned with skin laxity. Patients in the 25–40 years and 40–60 years age groups were concerned with a range of issues, namely uneven skin tone, skin surface unevenness, dry skin, and/or skin laxity.

When practitioners were asked about the treatment modalities used in their practice to address common skin quality issues, they

reported that more than one treatment modality was often used to address each issue (Table 1). For instance, a combination of lasers, microneedling, chemical peels, and/or injectables were used to address skin surface unevenness in practice. It was also observed that each treatment modality could be used to treat several skin quality issues, often in combination with other modalities. For example, superficial hyaluronic acid (HA) injections alone or in combination with other modalities, were used for managing all four common skin quality issues. On the other hand, practitioners reported relatively low use of certain treatment modalities for some skin quality issues. Less than 5% of the practitioners used microfocused ultrasound with visualization (MFU-V) for improving skin tone or skin surface evenness. Similarly, only 4% used intradermal botulinum toxin (BoNT) and 1% used biostimulators for addressing uneven skin tone.

**Consensus on skin quality attributes and practices.** A summary of consensus statements relating to skin quality and treatment trends in Asia Pacific is provided in Table 2. Overall, the expert panel expressed high level ( $\geq 92\%$ ) of agreement with all statements. The panel's

**TABLE 2.** Consensus statements on skin quality and treatment trends in Asia Pacific

STATEMENTS	AGREEMENT (%)
<b>GENERAL</b>	
The key attributes contributing to overall skin quality and attractiveness are: 1) smooth texture 2), even skin tone and uniformity in skin pigmentation, 3) firmness and elasticity, and 4) luminosity and hydration ("glow")	100
The definition and perception of skin attractiveness are largely similar regardless of ethnicity, but different intrinsic and extrinsic factors determine the common skin issues encountered by Asians (vs. Caucasians)	92
The four most common skin quality issues identified are consistent with what I encounter in my practice	100
All patients have the same desire for healthy, smooth and radiant looking skin, but are facing different issues at different stages in life. E.g., skin laxity is more prevalent in the older generation vs. sebaceous gland hyperactivity in the young	100
<b>TREATMENT</b>	
<b>Skin Tone</b>	
Skin glow and skin hydration can also contribute to the overall perception of skin tone.	100
Skin surface evenness also contribute to overall skin tone, as smoother skin will have better light reflection.	100
<b>Skin Surface</b>	
In addition to lasers, a multimodality approach including (but not limited to) superficial HA injections, intradermal BoNT-A and 1.5mm MFU-V is needed for skin surface irregularities	100
<b>Skin Elasticity</b>	
There is a need to differentiate between (A) superficial loss of skin elasticity and (B) deep tissue laxity, as distinct treatment approaches are required for both conditions	100
<b>Sebaceous Glands and Pores</b>	
Given the current evidence, intradermal delivery of BoNT-A can be considered as a useful treatment option for sebaceous gland hyperactivity and enlarged pores.	100
As intradermal injections carry a higher risk of immunogenicity, it is important to choose a highly purified BoNT-A formulation containing only the active 150 kDa neurotoxin molecule free from unnecessary bacterial peptides and contaminants.	100
<b>Overall Skin Quality</b>	
The adoption of diluted CaHA and/or superficial 1.5mm MFU-V as useful tools for skin quality improvement is currently still low amongst many clinical practices in Asia Pacific.	100
Published scientific and clinical evidence support the use of diluted CaHA and/or superficial 1.5mm MFU-V for various skin quality issues e.g., skin surface irregularities, tone & laxity.	100
To enhance current practices in Asia Pacific, practitioners should consider incorporating biostimulators (e.g., diluted CaHA) and/or superficial 1.5mm MFU-V as part of their overall treatment plan for skin quality improvement.	100
As aging changes in deeper planes (e.g., bony resorption and soft tissue volume loss) have a significant impact on the appearance of superficial layers, these factors also need to be taken into consideration for overall skin quality.	100

Abbreviations: BoNT-A: botulinum toxin A; CaHA: calcium hydroxylapatite; HA: hyaluronic acid; MFU-V: microfocused ultrasound with visualization

opinions were consistent with those of the surveyed practitioners (100% agreement) in terms of key attributes of good skin quality (Figure 1), the four most common skin quality issues encountered in practice (Figure 2A), and the prevalent skin quality issues at different stages in life (Figure 2B). Although the majority of the panel members agreed that the definition and perception of attractive skin are largely similar between different ethnicities (92% agreement), they recognized that Asian patients tend to desire lighter and brighter skin tone compared with Caucasian patients. This is consistent with the survey findings that uneven skin tone and pigmentary disorders were the most common skin quality issues encountered by practitioners in the Asia Pacific region (Figure

2A). The panel also added that skin tone is regarded of greater importance to patients residing in countries with higher sunlight exposure than those living in countries of lower exposure.

The panel recognized that the overall perception of good skin quality is influenced by multiple attributes, which are interrelated and can affect each other.<sup>6</sup> For example, skin glow can affect the overall perception of skin tone, and skin surface evenness can give better light reflection, which can influence the overall skin tone as well. Hence, there was a strong consensus to adopt a holistic approach considering related skin quality issues in the treatment plan to achieve harmonious results (100% agreement). This is in line with the

guidance provided in a recent skin quality consensus, which recommended achieving a balance of skin quality attributes for youthful and attractive skin.<sup>6</sup> In addition, the panel acknowledged that morphological and structural deficits in deeper tissue planes also affect the appearance of the skin surface.<sup>6-9</sup> Hence, it is agreed that practitioners should consider the different tissue layers that might be involved and distinguish treatments between the deep and superficial layers (100% agreement). For example, it is important to differentiate between skin surface unevenness due to alterations in the superficial layer and deeper planes (e.g. bony resorption, soft tissue volume loss, etc.), and between superficial loss of skin elasticity and deep tissue laxity.



**FIGURE 4.** Intradermal incobotulinumtoxin A injection protocol. Injection doses can be adjusted according to individual patient's concerns and the severity of their conditions. Practitioners might consider treating the forehead region with 0.2U per injection point.

Distinct treatment approaches are required for addressing age-related changes in different tissue planes. To achieve harmonious and balanced outcomes, the panel recommended a multimodal strategy to address interrelated issues across different tissue planes, and adopting an “inside-out” approach, treating the deeper tissue planes prior to the superficial layers.

Published evidence supports the use of MFU-V, biostimulators (e.g. diluted or hyperdiluted calcium hydroxylapatite [CaHA]), superficial HA injections, and intradermal BoNT as part of treatment plans to address various skin quality issues.<sup>10–18</sup> However, the adoption of these modalities, particularly MFU-V and biostimulators for managing certain skin quality issues was noted to be low in clinical practices in Asia Pacific (Tables 1 and 2) despite the published evidence. This could be due to low awareness of these modalities or lack of knowledge and expertise to use or combine them in Asian patients. It could also be related to the fact that the proposed “inside-out” treatment approach has not been frequently used in daily practice as most patients, or even practitioners, commonly view and tackle each issue in isolation without considering the possible interplay of underlying causes. The panel acknowledged that although some of these treatment modalities may not be the first-line treatment for addressing certain skin quality issues, they are complementary and supplementary to current treatment for enhancing aesthetic outcomes. For instance,

topical lightening agents and lasers are the first-line treatment options for skin tone/pigmentary disorders, but there is emerging evidence on the use of superficial HA injections and intradermal BoNT for improving skin tone.<sup>11,19</sup> Hence, there was strong consensus to include these treatment modalities as part of the overall treatment plan to enhance the current practices for skin quality improvement (100% agreement). The panel recognized the need to provide more specific guidance on appropriate combination and sequence of these treatment modalities in patients with varying skin quality issues, and to create treatment protocols as a guide for practitioners to properly administer each treatment modality to meet specific treatment goals.

## DISCUSSION

**Good skin quality from the inside out: a practical guide.** This practical guide integrates current evidence, as well as the panel's collective clinical experience with various treatment modalities to help practitioners tailor their treatment plans to meet the needs of each patient. Besides including recommendations on the use of treatment modalities for approved indications, the guide also provides practical advice for off-label applications based on published guidelines/consensus, emerging evidence, and clinical expertise of the panel. The recommendations represent a holistic and multimodal approach that uses a combination of MFU-V, diluted/hyperdiluted CaHA, undiluted CaHA, HA fillers, and BoNT, as part of the

treatment plan (including other modalities such as lasers, radiofrequency [RF], intense pulsed light [IPL], chemical peels, microneedling, etc.) for enhancing facial skin quality (Figure 3). Treatment protocols detailing how MFU-V, diluted/hyperdiluted CaHA, HA fillers, and/or intradermal BoNT can be administered to meet specific treatment goals are presented in Table 3. As with any treatment, practitioners should be familiar with the complete local product information, including approved indications, precautions, contraindications, and adverse events before administering the treatment.

The guide entails a three-step approach—Identify, Assess, and Design (Figure 3). The first step is to identify skin quality issues that concern the patient and to understand his/her preferences and treatment goals. A detailed assessment of the face then follows, taking note of the degree of age-related changes and the affected tissue planes (bone, ligaments, fibromuscular/superficial musculopaponeurotic system [SMAS], subcutaneous [deep and superficial fat compartments], or skin surface [dermis and epidermis]), as well as the appearance of the skin (such as uneven tone, surface unevenness, skin laxity, oily skin, enlarged pores, dry skin, etc.). Facial assessment forms the basis for designing an individualized treatment plan. The overall perception of skin quality is influenced by multiple interrelated attributes, and these attributes can in turn affect one another.<sup>6</sup> Hence, when designing a treatment plan to address the patient's concerns, other related skin quality issues should also be considered for overall skin quality improvement. Skin quality can also be affected by biological processes in multiple tissue planes.<sup>6–9</sup> It is therefore important to consider not only the skin surface but also other tissue planes that may be involved, and distinguish treatments between the deep and superficial layers. The panel recommended a strategy that combines treatment modalities targeting different manifestations across the involved tissue planes, and employing an “inside out” approach, treating first the deeper underlying tissues followed by superficial layers (Figure 3 and Table 3). Depending on the patient's availability and preferences, individual modalities can be administered sequentially on the same day or on separate visits. For stepwise treatment over several sessions, visits should be spaced 1 to 4 weeks apart for resolution of local adverse

effects and to assess the treatment response. (20) The sequence of modalities administered depends on several factors such as the patient's main presenting complaint and skin condition. For instance, some experts prefer to perform MFU-V to strengthen the soft tissue envelope before injecting fillers in patients with severe skin laxity, while some prefer to "prime" the skin and fibroblasts by injecting diluted/hyperdiluted CaHA before MFU-V. However, if patients are unable to commit to multiple treatment visits due to their schedules or preferences, combined treatments on the same day may be performed. Published review on combined same-day treatments with energy-based interventions and injectable treatments (BoNT and fillers) reported no increase in adverse effects, such as spread of neurotoxin, displacement of filler material, or other untoward effects.<sup>21</sup> For same-day treatment, MFU-V is recommended before injectable treatments; BoNT and fillers can be administered in either sequence.<sup>20</sup>

The panel provided suggestions on how MFU-V, diluted/hyperdiluted CaHA, HA fillers, and/or intradermal BoNT can be administered to meet specific treatment goals (Table 3). The following modalities were used to construct examples for the treatment protocols: MFU-V (Ultherapy®; Merz North America, Inc. Raleigh, N.C.), diluted or hyperdiluted CaHA (Radiesse®; Merz North America, Inc), Cohesive Polydensified Matrix® (CPM®)-HA fillers (Belotero Revive®, Belotero Soft®, Belotero Balance®, Belotero Intense®, and Belotero Volume®; Anteis S.A., Geneva, Switzerland), and a BoNT formulation without complexing proteins (incobotulinumtoxin A [INCO]) (Xeomin®; Merz Pharmaceuticals GmbH, Hessen, Germany). Treatment protocols included detailed information on the target tissue planes, doses, injection techniques, injection protocol and treatment intervals. Properties and mechanisms of action for each of these treatment modalities are provided in Supplementary Table 1.

*Treatment protocol for using MFU-V.* MFU-V is regarded as the gold standard treatment for nonsurgical lifting and tightening of lax skin.<sup>16,22</sup> It has been reported to be effective for superficial skin rejuvenation and lifting tissues, as well as reducing skin laxity, fine lines and pore size.<sup>23–32</sup> MFU-V provides real-time visualization of distinct tissue layers beneath the skin surface, including the dermal and

subdermal layers (superficial fascia, SMAS, and platysma), which allows precise delivery of microfocused ultrasound energy to the intended collagen-rich tissue planes (Supplementary Table 1).<sup>16,22,33,34</sup> MFU-V induces the creation of thermal coagulation points in the targeted tissue planes and stimulates the natural wound healing process to trigger the production of new collagen and elastin.<sup>33–35</sup> This results in tissue remodeling, increased viscoelasticity, tissue lifting, as well as thickening and tightening of the skin.<sup>16,22,33,34</sup>

A group of experts recently developed a consensus on the use of MFU-V treatment in Asian patients, that provides recommendations for tailoring MFU-V treatment for optimal aesthetic outcomes.<sup>22</sup> The following protocol was established based on the recommendations of the Asian consensus.<sup>22</sup> The panel recognized that skin thickness can vary between patients and treatment area, and that the choice of MFU-V transducer is dependent on the patient's concerns and his/her individual skin anatomy. Practitioners should perform real-time visualization to determine the exact depths of dermal and superficial fascia layers, and select the appropriate transducers to ensure precise delivery of ultrasound energy to the target tissues. To address fine lines, enlarged pore size, and superficial unevenness and laxity, the panel suggested using either a 1.5mm or 3.0mm transducer to target the dermis, delivering 20 to 30 treatment lines per 2.5cm x 2.5cm square. To improve tissue laxity and firmness, the panel suggested using a 1.5mm, 3.0mm, or 4.5 mm transducer to target the superficial fascia or SMAS layer, delivering 600 to 1000 lines for full face and submental treatment. Depending on patient's concerns, more than one transducer depth can be used per treatment session. For instance, MFU-V can also improve skin texture indirectly through tightening of the deeper underlying tissues. The exact treatment depths and the number of lines depend on the patient's concerns and condition; practitioners should tailor their treatment protocol according to the individual patient's needs. The panel recommended assessing the results within 3 to 6 months of the initial treatment, followed by maintenance treatment every 12 to 18 months.

*Treatment protocol for using diluted or hyperdiluted CaHA.* CaHA comprises microspheres of CaHA suspended in an aqueous carboxymethylcellulose gel matrix.<sup>36</sup>

In recent years, diluted or hyperdiluted CaHA injections have been used to induce dermal regeneration without creating unnecessary volume gain.<sup>10,13,14,37–44</sup> Superficial injections of diluted or hyperdiluted CaHA, as monotherapy or part of a combination approach, have been shown to address a number of skin quality issues leading to improvements in skin quality in the face and body.<sup>13,37–44</sup> After injection, the CaHA microspheres act as a scaffold for new tissue formation by stimulating neocollagenesis, neocolagenesis, dermal cell proliferation, and angiogenesis for long-lasting aesthetic improvements (Supplementary Table 1).<sup>37,45,46</sup> CaHA has also been found to restore fibroblast contractility *in vitro* and induce production of proteoglycans in human skin, indicating its unique beneficial effects on fibroblast activity and extracellular matrix (ECM) remodeling.<sup>47,48</sup> Consensus guidelines on the use of diluted or hyperdiluted CaHA for biostimulation in the face and body have been published. They provide detailed recommendations for improvements of a range of skin quality issues, including laxity, superficial wrinkles, roughness, and acne scars.<sup>10,14</sup> The following protocol was established in accordance with these recommendations.<sup>10,14</sup> The panel recommended administering diluted or hyperdiluted CaHA to the immediate subdermal plane for treating skin laxity, acne scars, superficial wrinkles and pore size, and increasing skin firmness and thickness (Table 3). As in published guidelines,<sup>10,14</sup> the preferred dilution for effective biostimulation is 1:1; hyperdilution up to ratios of 1:3 may be used in areas of thin skin. The panel members recommended using the retrograde linear fanning technique, gently scraping the underside of the dermis with a 22–25G cannula for more precise delivery of a thin, uniform coating of diluted product to the treatment area. Similar to published guidelines,<sup>10,14</sup> the panel recommended assessing response within 3 to 4 months after treatment and reinject as necessary. One to three sessions are usually required at treatment initiation, followed by maintenance treatment every 12 to 18 months.

*Treatment protocol for using HA fillers.* HA fillers have been shown to be safe and effective for improving skin hydration, elasticity, tone and glow, as well as decreasing surface roughness, sebum production, and enlarged pore size.<sup>11,17,18,32,49,50</sup> Upon superficial injection of HA filler with low viscoelasticity, a condensed

**TABLE 3.** Treatment protocols for improving overall skin quality with the Merz Aesthetics portfolio\*

TYPE	MFU-V		DILUTED/HYPERDILUTED CAHA FILLER	HA FILLERS		BONT
Treatment goals	Superficial skin rejuvenation, improve fine lines, and reduce superficial unevenness and pore size	Improve tissue laxity and firmness	Improve skin laxity, increase skin firmness and thickness, reduce superficial wrinkles and pore size, and improve acne scars	Increase skin hydration and elasticity, improve skin tone and glow, as well as decrease surface roughness, sebum production and pore size	Volume restoration and structural support	Reduce sebum production, pore size, and erythema, and facial skin lifting
Target tissue plane	Dermis	Superficial fascia/ SMAS layer	Immediate subdermal layer	Dermis to immediate subdermal layer	Suprperiosteal and/or subcutaneous (superficial and deep fat compartments) layer	Dermis
Dose/ Dilution	<ul style="list-style-type: none"> <li>MFU-V (Ultherapy®)</li> <li>Transducer depth: 1.5 mm or 3.0mm (depending on the thickness of deep reticular dermis as determined by real-time visualization)</li> <li>Total no. of lines: 20–30 lines per 2.5 x 2.5 cm square</li> </ul>	<ul style="list-style-type: none"> <li>MFU-V (Ultherapy®)</li> <li>Transducer depth: 1.5 mm, 3.0 mm or 4.5mm (depending on the thickness of superficial fascia/SMAS as determined by real-time visualization)</li> <li>Total no. of lines: 600–1000 lines for full face and submental treatment</li> </ul>	Dilute 1.5 mL of CaHA (Radiesse®) 1:1 (preferred) to up to 1:3 (for thinner skin) with 2% lidocaine or saline per 100 cm <sup>2</sup> area	Low-viscosity and elasticity HA filler (Belotero Revive®/ CPM®-HA 20Gt; or Belotero Soft®/ CPM®-HA 20 mg/mL) at 0.01–0.02 mL per point spaced 1–2cm apart into the treatment area (total: 1mL per cheek)	<ul style="list-style-type: none"> <li>Moderate viscosity and elasticity HA filler (Belotero Balance®/ CPM®-HA 22.5 mg/mL) for correction of moderate lines and highly mobile/ dynamic areas (e.g. periorbital and perioral)</li> <li>High viscosity and elasticity HA filler (Belotero Intense®/ CPM®-HA 25.5 mg/mL or Belotero Volume®/ CPM®-HA 26.5 mg/mL) for correction of deep lines, facial contouring (e.g. jawline) and deep volume replacement (e.g. cheeks and temples)</li> <li>Choice of filler and dose are dependent on skin thickness, the area being treated and severity of volume loss.</li> </ul>	<ul style="list-style-type: none"> <li>Reconstitute each vial (100-U) of INCO (Xeomin®) with 5 mL of saline</li> <li>Refer to Figure 4 for injection protocol</li> </ul>
Injection technique	NA	NA	<ul style="list-style-type: none"> <li>Retrograde linear fanning technique using a 22–25G cannula for more precise and uniform placement (preferred)</li> <li>Short linear threading technique using a 27–30G needle</li> </ul>	Superficial injections using micropuncture technique with a 4-mm 31–33G needle	<ul style="list-style-type: none"> <li>Depending on the targeted treatment area and treatment goals, fillers are injected slowly using: <ul style="list-style-type: none"> <li>Bolus or vertical depot technique with a 27–30G needle and/or Retrograde linear fanning technique with 25G or larger cannula</li> </ul> </li> </ul>	Microdroplet technique using a 31–34G needle
Treatment intervals	<ul style="list-style-type: none"> <li>Assess response at 3–6 months</li> <li>Maintenance treatment every 12–18 months</li> </ul>	<ul style="list-style-type: none"> <li>Assess response at 3–4 months; reinject as necessary</li> <li>1–3 sessions are usually required at treatment initiation, with maintenance treatment every 12–18 months thereafter</li> </ul>	<ul style="list-style-type: none"> <li>Initial treatment: 2–3 sessions spaced 1 month apart are usually required</li> <li>Assess response at 1–3 months after last injection session</li> <li>Maintenance treatment every 6–9 months</li> </ul>	<ul style="list-style-type: none"> <li>Assess response at 2–4 weeks (touch up if required)</li> <li>Depending on HA filler used, maintenance treatment: every 6–9 months for Belotero Balance®, 9–12 months for Belotero Intense®, and 12–18 months for Belotero Volume®</li> </ul>	<ul style="list-style-type: none"> <li>Assess response at 2–4 weeks</li> <li>Maintenance treatment every 3–4 months</li> </ul>	
Remarks	-	-	-	-	Undiluted CaHA or CaHA(+) can be considered for volume restoration and structural support depending on practitioner's preference and product availability	Intramuscular BoNT-A injections to relax hyperactive facial muscles and reduce the appearance of dynamic wrinkles are recommended to complement the effects of intradermal BoNT-A injections.

\*The treatment protocols are developed based on available evidence<sup>10,12,14,22,59–61</sup> and the panel's collective clinical experience with the treatment modalities.

<sup>1</sup>CPM-HA 20mg/mL with glycerol. Abbreviations: BoNT-A: botulinum toxin A; CaHA: calcium hydroxylapatite; CaHA(+): calcium hydroxylapatite with integral lidocaine; CPM-HA: cohesive polydensified matrix-hyaluronic acid; G: gauge; INCO: incobotulinumtoxin A; MFU-V: microfocused ultrasound with visualization; SMAS: superficial musculoaponeurotic system; NA: Not applicable

**SUPPLEMENTAL TABLE 1.** Properties and mechanisms of action of treatment modalities used in the treatment protocols

TYPE	MFU-V	DILUTED/ HYPERDILUTED CAHA FILLER	HA FILLERS	INTRADERMAL BONT
Properties	MFU-V (Ultherapy®) provides real-time visualization of distinct tissue layers beneath the skin surface, including the dermal, and subdermal layers (superficial fascia, SMAS, and platysma), which allows precise delivery of microfocused ultrasound energy to the intended collagen-rich tissue layers. <sup>16,22,33,34</sup>	CaHA (Radiesse®) comprises microspheres of CaHA suspended in an aqueous carboxymethylcellulose gel matrix. <sup>36</sup> CaHA has the versatility of inducing dermal regeneration without creating unnecessary volume gain by using it in its diluted form. <sup>10,13,14,37-44</sup>	<ul style="list-style-type: none"> <li>CPM-HA fillers (Belotero Revive®, Belotero Soft®, Belotero Balance®, Belotero Intense®, and Belotero Volume®) are monophasic polydensed non-particulate gels manufactured using a patented dynamic two-stage cross-linking technology,<sup>54</sup> which results in gels with variable densities of crosslinked HA. This allows for homogeneous tissue integration, resulting in favorable aesthetic outcomes.<sup>11,18,56-58</sup></li> <li>CPM-HA fillers are available in different HA concentrations and cross-linking ratios, with different viscoelasticity and projection capacity for use in a wide range of aesthetic applications.<sup>18,55,59</sup> Products with low viscoelasticity (Belotero Soft®, Belotero Revive®) are suited for superficial injections for skin hydration and rejuvenation, whereas those with moderate (Belotero Balance®) or high viscoelasticity (Belotero Intense®, Belotero Volume®) and good projection capacity are useful for soft-tissue augmentation.<sup>18,55,59</sup> By combining CPM-HA fillers with different rheological properties in different tissue planes, a more harmonized and effective treatment outcome could be achieved with minimum quantity of fillers.<sup>59</sup></li> </ul>	INCO (Xeomin®) is a highly purified BoNT-A formulation, which contains only the pure 150 kDa active neurotoxin, free of unnecessary bacterial peptides and impurities. <sup>78,79</sup> It is known to have a low potential for immunogenicity, <sup>79,80</sup> making it a rational choice for intradermal injections, which are regarded as more immunogenic than intramuscular injections. <sup>76,77</sup>
Mechanisms of action	MFU-V induces the creation of thermal coagulation points in the targeted tissue layers and stimulates the natural wound healing process to trigger the production of new collagen and elastin, resulting in tissue remodeling, increased viscoelasticity, tissue lifting, as well as thickening and tightening of the skin. <sup>16,22,33-35</sup>	<p>After injection of diluted or hyperdiluted CaHA, the CaHA microspheres act as a scaffold for new tissue formation by stimulating neocollagenesis, neolastogenesis, dermal cell proliferation, and angiogenesis for long-lasting aesthetic improvements.<sup>37,45,46</sup></p> <p>CaHA has also been found to restore fibroblast contractility in vitro and induce production of proteoglycans in human skin, indicating its unique beneficial effects on fibroblast activity and ECM remodeling.<sup>47,48</sup></p>	<p>Upon superficial injection of HA filler with low viscoelasticity, a condensed network with the ECM is established to increase hydration and stimulate fibroblast activation. This in turn triggers the production of collagen, elastin and hyaluronic acid, and promote the release of stromal-derived factor 1 (which plays a role in inhibiting cutaneous pigmentation), resulting in increased skin hydration and elasticity, decreased surface roughness, and improved skin tone.<sup>51,52</sup></p>	<ul style="list-style-type: none"> <li>The mechanism of action of BoNT on sebum production is not entirely clear yet. Intradermal BoNT reduces sebum production possibly by blocking acetylcholine release, thereby disrupting sebocyte differentiation and decreasing sebum production.<sup>64,67</sup></li> <li>The effects of intradermal BoNT on pore size reduction could possibly be mediated directly by paralysis of arrector pili muscles or indirectly by reduced sebum production.<sup>68,69,73</sup></li> <li>Intradermal BoNT relieves erythema by inhibiting acetylcholine release from autonomic peripheral nerves of the cutaneous vasodilatory system.<sup>70</sup> It also blocks the release of inflammatory mediators, thereby promoting an anti-inflammatory effect that may reduce erythema.<sup>71</sup> Other proposed mechanism of action includes the inhibition of neuropeptides such as vasoactive intestinal peptide.<sup>74</sup> Intradermal BoNT exerts its lifting effects on the face by correcting the imbalance between the activity of the facial muscles through relaxing the depressor muscles, thereby allowing the levator muscles to contract, resulting in facial lifting.<sup>72</sup> In addition, stimulation of fibroblast contraction has been proposed as a potential mechanism underlying facial skin lifting.<sup>75</sup></li> </ul>

Abbreviations: BoNT-A: botulinum toxin A; CaHA: calcium hydroxylapatite; CPM-HA: cohesive polydensed matrix-hyaluronic acid; ECM: extracellular matrix; INCO: incobotulinumtoxin A; MFU-V: microfocused ultrasound with visualization

network with the ECM is established to increase hydration and stimulate fibroblast activation. This in turn triggers production of collagen, elastin and hyaluronic acid, and promote the release of stromal-derived factor 1 (which plays a role in inhibiting cutaneous pigmentation), resulting in increased skin hydration and elasticity, decreased surface roughness, and improved skin tone.<sup>51,52</sup> In addition, HA fillers play an important role inhibiting sebum production via CD44/RhoA signaling.<sup>17</sup>

Numerous formulations of HA fillers have been developed over the years, which are manufactured with different cross-linking technologies resulting in HA fillers with specific characteristics and rheological properties.<sup>53–55</sup> CPM-HA fillers are monophasic polydensified non-particulate gels manufactured using a patented dynamic two-stage cross-linking technology, which results in gels with variable densities of crosslinked HA.<sup>54</sup> This allows for homogeneous tissue integration, resulting in favorable aesthetic outcomes.<sup>11,18,56–58</sup> CPM-HA fillers are available in different HA concentrations and cross-linking ratios, with different viscoelasticity and projection capacity for use in a wide range of aesthetic applications.<sup>18,55,59</sup> Products with low viscoelasticity are suited for superficial injections for skin hydration and rejuvenation, whereas those with moderate or high viscoelasticity and good projection capacity are useful for soft-tissue augmentation (Supplementary Table 1).<sup>18,55,59</sup> By combining CPM-HA fillers with different rheological properties in different tissue planes, a more harmonized and effective treatment outcome could be achieved with minimum quantity of fillers.<sup>59</sup>

The following protocol was established by the panel. To increase skin hydration and elasticity, improve skin tone and glow, as well as decrease surface roughness, sebum production and pore size, the panel recommended using the micropuncture technique<sup>11</sup> to deliver CPM-HA filler with low viscoelasticity to the dermis to immediate subdermal plane (Table 3). The product can be administered in aliquots of 0.01–0.02 mL per puncture, spaced 1 to 2 cm apart using a 4-mm 31–33G needle. A total of 1 mL of the product can be injected per cheek. Two to three sessions spaced one month apart are usually required at treatment initiation. The panel recommended assessing patient's

response within 1 to 3 months after the last injection, followed by retreatment every 6 to 9 months thereafter. To address volume loss and structural deficits in deeper tissue planes, which can in turn improve skin appearance, the panel recommended injecting CPM-HA filler with moderate or high viscoelasticity into the suprperiosteal and/or subcutaneous (superficial and deep fat compartments) plane in accordance with published consensus and published literature on safe and effective augmentation with CPM-HA fillers (Table 3).<sup>59–61</sup> The choice of filler and the dose are dependent on the skin thickness, the area being treated, and the severity of volume loss and structural deficits. Depending on the target treatment area and treatment goals, the product can be administered slowly using the bolus or vertical depot technique with a 27–30G needle and/or the retrograde linear fanning technique with a 25G or larger cannula. The panel recommended assessing patient's response within 2 to 4 weeks of initial treatment and touch up if required. Repeat treatment is usually required every 6 to 18 months, depending on the type of filler injected.

*Treatment protocol using BoNT.* Encouraging results have been reported with intradermal BoNT for treating a variety of skin quality issues, including excess sebum production, enlarged pores, erythema, and facial skin laxity.<sup>12,62–66</sup> These positive effects could possibly be mediated via acetylcholine inhibition, leading to the paralysis of arrector pili muscles and depressor muscles, and reduction in exocrine gland activity (details in Supplementary Table 1).<sup>64,67–73</sup> Additional mechanisms of action proposed include the inhibition of other neuropeptides, such as vasoactive intestinal peptide, and stimulation of fibroblast contraction.<sup>74,75</sup> However, intradermal injections are regarded as more immunogenic than intramuscular injections because the dermis contains large numbers of dendritic cells, which play a pivotal role in inducing immune responses through antigen capture and presentation to T-lymphocytes.<sup>76</sup> This physiological concept is applied in immunology, where intradermal vaccination has been used for certain populations that do not respond well to intramuscular vaccination e.g. hepatitis B vaccine in hemodialysis patients.<sup>77</sup> As such, the panel agreed that it is advisable to choose a BoNT formulation containing only the active 150

kDa neurotoxin molecule to reduce the risk of immunogenicity.<sup>12</sup> INCO is a highly purified and precisely manufactured BoNT-A formulation, which contains only the active neurotoxin, free of unnecessary bacterial peptides and impurities.<sup>78,79</sup> Given its low immunogenic potential<sup>79,80</sup> and positive clinical experience in improving sebum control and facial skin laxity, and reducing pore size and erythema,<sup>12,62,74</sup> INCO can be considered a rational choice for intradermal injections to address these skin quality issues. The panel recommended reconstituting 100-U of INCO with 5mL of saline and administering the product using the microdroplet injection technique<sup>12</sup> with a 31–34G needle into the dermis (Table 3). The suggested injection protocol was described in a recent publication<sup>12</sup> and is provided in Figure 4. Practitioners may consider including injections of 0.2-U per point in the forehead region, as well as intramuscular injections into the glabella, mentalis, and masseter to complement the full face intradermal injection protocol. As the exact doses vary according to individual patient's concerns and the severity of their conditions, practitioners should tailor treatment to meet the needs of their individual patients. The panel recommended assessing response within 2 to 4 weeks after treatment, followed by retreatment every 3 to 4 months thereafter.

## CONCLUSION

To our knowledge, this is the first report describing the current skin quality and clinical practice trends in the Asia Pacific region and the first practical guide for skin quality improvement. Improving facial skin quality can have a positive impact on overall attractiveness, which can favorably affect one's self-confidence, wellbeing, and overall health. The survey findings showed that uneven skin tone, skin surface unevenness, skin laxity, as well as sebaceous gland hyperactivity and enlarged pores were the most common skin quality issues encountered by patients in the Asia Pacific region. Practitioners recognized four concepts—skin tone evenness, skin surface evenness, skin firmness, and skin glow—as key attributes of good skin quality and attractive skin. The same four skin quality attributes were identified in a recent global consensus on skin quality and were described as EPCs. Although clinical evidence supports the use of MFU-V, biostimulators, superficial HA injections,

intradermal BoNT as part of treatment plans to enhance facial skin quality, the survey revealed low adoption of MFU-V and biostimulators for managing certain skin quality issues in Asia Pacific, suggesting low awareness of these modalities, or lack of knowledge and expertise on how to use or combine these modalities among practitioners in the region. These findings provide valuable insights on the current skin quality trends and gaps in clinical practice, which can aid in improving existing practices for skin quality improvement.

The overall perception of skin quality is influenced by multiple attributes or parameters, which are interrelated and can affect each other. Morphological and structural deficits in deeper tissue planes can also affect the appearance of the skin surface. Therefore, the panel recommended a multimodal approach targeting different interrelated issues across the tissue planes involved (as opposed to only treating one issue and only the skin surface) for achieving balanced results. The practical guide relied on available evidence and the panel's collective clinical experience with various treatment modalities to provide specific guidance on the appropriate combination and sequence of treatment. Treatment protocols were created to assist practitioners in tailoring their treatment plans to the needs of their patients. The guide focuses on an "inside-out" approach, treating first the deeper underlying tissues prior to the superficial layers, to achieve harmonious and balanced outcomes. Future studies are needed to generate clinical evidence to support recommended treatment protocols for skin quality improvement, specifically in Asian patients.

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