



Safety and Efficiency of Minimally Invasive Buttock Augmentation: A Review

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Abstract

Background Volume restoration and enhancement of the gluteal region appearance has become nowadays a popular concern in particular for many women. Several options are available, none however are without complications and side effects. Volume enhancement with soft tissue fillers of the gluteal region is emerging as a highly attractive minimally invasive modality. It has led unfortunately to more unlicensed, nonmedical practitioners administering illicitly injections for buttock augmentation at relatively low costs. **Materials and Methods** To determine safety, efficacy, and cost effectiveness of mostly used soft-tissue fillers for buttock augmentation, a systematic literature search of PubMed, Medline, and Embase was conducted to identify the mostly used fillers for gluteal augmentation. It was complemented by searching for each of the identified filler material separately to retrieve any missed reports. References of clinical studies and trials, reviews, and consensus reports were reviewed as well for the same objective. **Results** In the final analysis 12, mostly strongly biased clinical reports providing a low level of evidence, were identified for inclusion in the review. Two studies involved Polymethylmethacrylate (PMMA), 5 Poly-L-lactic acid, 1 Calcium hydroxyapatite and 4 hyaluronic acid filler injection. No studies were identified involving liquid silicone or Polyacrylamide hydrogel. The little available evidence provided by this review indicates that a specific brand of PMMA in Brazil has a demonstrable relatively good safety, efficiency, and cost-effectiveness record

superior to surgical alloplastic gluteal augmentation or to lipofilling only when injected by experts.

Conclusion Gluteal augmentation with soft tissue fillers is not as simple and innocuous as advertised. Serious complications may occur. Moreover, optimal buttock contouring entails not only volume augmentation but also volume removal; thus, volume augmentation with soft tissue fillers may not be ideal. Popularizing this modality must also be approached with great care. Serious complications do occur; they become inevitable when performed illegally by non-specialized, non-authorized, and unscrupulous practitioners in non-accredited facilities. Patients must be warned that adherence to regulations is critical and that only well-trained certified experts practicing legally in accredited facilities can address safely and efficiently their concerns. **Level of Evidence III** This journal requires that authors assign a level of evidence to each article. For a full description of these Evidence-Based Medicine ratings, please refer to the Table of Contents or the online Instructions to Authors www.springer.com/00266.

Keywords Buttock augmentation · Buttock enhancement · Soft tissue filler · Polymethylmethacrylate · Injectable filler

Introduction

The buttocks have long been recognized as an important secondary sexual characteristic and are increasingly gaining importance in the perception of female beauty and physical attractiveness [1]. Fueled by Internet accessibility, strong media influence, and an increased focus on body image, volume restoration and enhancement of the buttocks' appearance has become nowadays a popular concern in particular for many women looking for pleasing youthful

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gluteal features such as rounded and lifted posterior projection, smooth inward sweep of the lumbar curvature, and short infra-gluteal folds in addition to an hourglass figure with an optimal waist-to-hip ratio [2, 3].

Most recognizable aesthetic anatomical characteristics of the buttocks include a lumbosacral depression, two sacral dimples, or supragluteal fossettes with absence of excess fat in the lumbosacral and medial thigh in addition to areas commonly referred to as “love handles, saddlebags, and banana rolls” (Fig. 1). Analysis from the lateral view incorporating the buttocks, surrounding torso, and lower extremities reveals that in aesthetically pleasing buttocks, the point of maximum projection corresponds to the level of the trochanter and the maximal mons pubis projection. Detailed aesthetic analysis of the female buttock has been recently reported by Mendieta et al. [4] and previously described aesthetic standards of the buttocks have been recently updated [5] (Figs. 2, 3). Though different preferences by gender or ethnicity have been challenged [5], the general impression is that each ethnicity presents a different standard of beauty and ethnic and gender variations in gluteal size and shape must not be overlooked [6–8]. With growing media frenzy for more voluptuous buttocks, a unique female buttock style with specific characteristics in Brazil has recently emerged as a reference standard for ideal buttocks beauty [6]. A new ideal curvier than previous standards with a more dramatic difference between the waist and hip widths has been defined, signaling an important paradigm shift in preferred aesthetic ideals of the general population in North America [5].

For determining the most appropriate procedure of buttock enhancement, three components must be evaluated: volume, shape, and skin quality/laxity in addition to

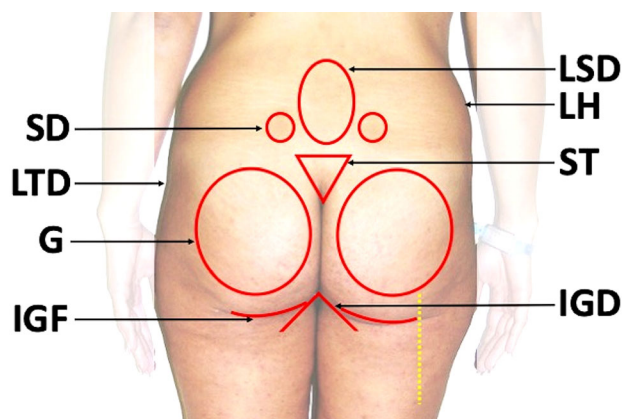


Fig. 1 Key aesthetic features of the buttock. LSD (lumbosacral depression), SD (sacral dimple), ST (sacral triangle), upper flank LH (love handle), LTD (lateral trochanteric depression), IGF (infragluteal fold) not extending beyond the medial two thirds of the posterior thigh, IGD (infragluteal diamond), G (Gluteus)

addressing the upper, middle, and lower buttock independently. Moreover, in order to achieve the best aesthetic shape, buttock contouring and gluteal augmentation need to be addressed concomitantly though contour should be considered first and augmentation second [9]. It is clear from Mendieta’s analysis [4] that when contemplating gluteal augmentation, it must be evident that achieving a harmonious profile entails not only augmentation but also volume removal depending on the patient’s preoperative shape and her desire in terms of waist-to-hip ratio. If increasing gluteal projection and improving lateral gluteal curve necessitate volume addition, accurate volume reduction of the upper flank is essential to narrow the waist. Volume removal may also be needed to define the lower gluteal curve. 80–85% of gluteal shaping is by lipoplasty; volume addition is just an ancillary factor to enhance buttock profile. More precisely, and in line with new standards of buttocks beauty and attractiveness, volume enhancement of the periphery and lateral aspects of the buttocks to aim for a waist-to-hip ratio of 0.60 adds more to buttock aesthetics than increasing projection that must not exceed the 0.70 waist- to-hip ratio on lateral view [5].

A recent literature review of studies published from 1969 through 2015 has identified 5 gluteal augmentation techniques in decreasing frequency: augmentation with implants, autologous fat grafting, local flaps, soft-tissue filler primarily hyaluronic acid gel injection, and local tissue rearrangement [10]. None of these modalities, however, is without complications and side effects. Surgical gluteal augmentation with silicone implants or fat transfer have been over the last decade the most rapidly progressing cosmetic procedures [11] with flaps and local tissue rearrangements indicated in cases of massive weight loss [10]. Reconstruction and buttocks contour due to malformation, asymmetry, trauma, and radiotherapy may require as well regular implants, liposculpture, and skin flaps [12]. Though highly effective, implant augmentation may be associated with an alarming high complication rate of 21.6% [2, 13, 14]. Autologous fat grafting on the other hand is not suitable for patients with insufficient donor areas. Moreover, in addition to a number of high-profile fatalities, buttock lipofilling is associated with a complication rate of 9.9% [2, 15]. Lately, there has been an increased interest for less invasive approaches [1, 2].

With mounting requests for aesthetic procedures influenced perhaps by popular culture and an unrealistic standard of beauty, in addition to world-wide expanding popularity of noninvasive rejuvenative modalities for the face, demand for nonsurgical rejuvenation options for nonfacial areas is rapidly growing and is being widely publicized. There is at present an increased emphasis on minimally invasive whole-body rejuvenation with injectable fillers rapidly challenging and complementing

Fig. 2 Most attractive waist to hip ratios from posterior and lateral views

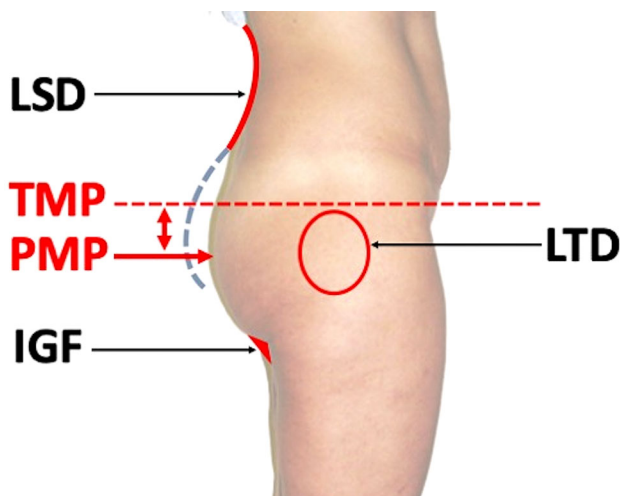
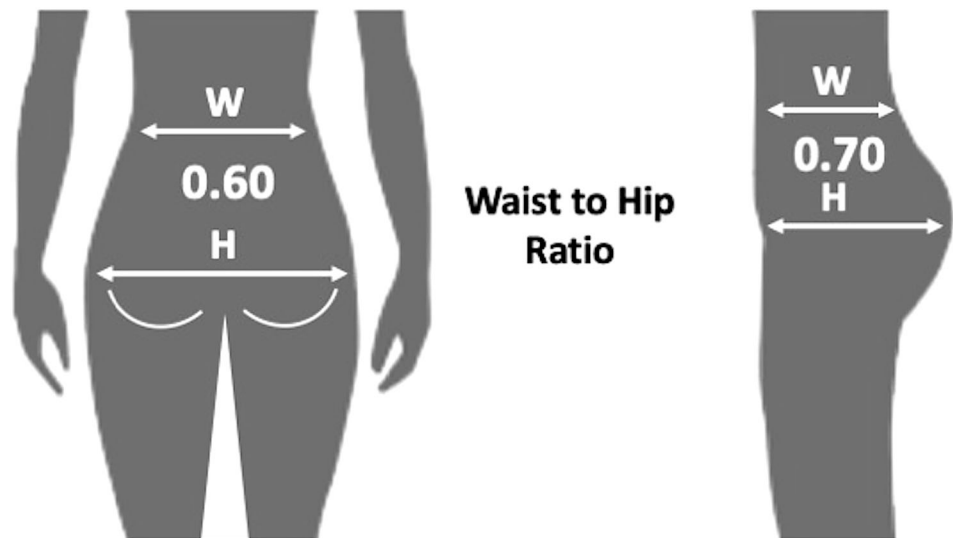


Fig. 3 Lateral variable aesthetic characteristics of the buttock depending on ethnicity. Deeper LSD (lumbosacral depression), absence of lateral thigh depressions (LTD), and higher point of maximal projection (PMP) with increased projection in relation to trochanter-mons pubis (TMP) projection are preferred by Hispanic and African Americans. Higher IGF (infragluteal fold) results in a shorter buttock preferred by Asian Americans

the market share of other surgical as well as non-surgical body contouring approaches. Popularity of injectable fillers has been due to the ease of their application by several medical and surgical practitioners, and even by dentists and non-medical providers on one hand, and their relative affordability on the other. Their popularity has been amplified by social media in addition to great efforts made by the industry to promote their benefits and presumed safety and effectiveness [2, 16–19].

Furthermore, given their low cost and easy access, liquid silicone, vitamin E, synthol, mineral oil, as well as several obsolete and unconventional products such as liquid

paraffin, petroleum jelly, lanolin, beeswax, castor oil, flax oil, linseed oil, olive oil, and even automobile transmission fluid have been used for volume enhancement illegally by unlicensed providers not related to the healthcare profession, often resulting in uncorrectable disfigurement or more serious complications and even death [20–24]. Daily injections of 25 mg of depot medroxyprogesterone acetate (DMPA) for 2 months, a synthetic progestin commonly used as a contraceptive, has also been reported for buttock and thigh augmentation with the conviction that this hormone has a lipogenic effect [8]. Currently, there are more than 160 different injectable cosmetic products worldwide from more than 50 companies [25]. Biocompatible fillers considered to be safe and associated with minimal down time used in routine clinical practice for cosmetic indications include collagen (bovine, porcine, or human), hyaluronic acid of animal or synthetic origin, polylactic-L-acid (PLLA), calcium hydroxyapatite (CaHA), polymethyl-methacrylate (PMMA), and polyacrylamide hydrogel (PAAG). Various injectable formulations have been reported as well, all different in their modes of action and their longevity before being absorbed [12, 26]. Collagen, hyaluronic acid and PMMA are approved by FDA for augmentation of the face and back of hand, but not for other anatomic sites, nevertheless, despite lack of regulatory approval, off-label injection of various fillers has been frequently used for cosmetic augmentation of the breasts and buttocks [21, 25]. The current literature review is aimed at analyzing the various filler materials described for gluteal enhancement and rejuvenation with a special attention to their safety, efficacy, and cost effectiveness in addition to current regulations and unlawful injections.

Materials and Methods

Injectable filler materials that have been reported for buttock rejuvenation and volume enhancement were identified by a preliminary search. A systematic literature search of PubMed, Medline, and Embase was then conducted with the terms [(filler) OR (silicone inject*) OR (polyacrylamide hydrogel) OR (polymethylmethacrylate) OR (poly-L-lactic acid) OR (hyaluronic acid)] AND [(buttock augmentation) OR (buttock enhancement) OR (buttock contouring) OR (buttock volum*)]. A second search was then conducted for each of the identified filler materials separately to identify any missed reports. References of clinical studies and trials, reviews, and consensus reports were reviewed as well for the same objective. Retrospective and prospective clinical studies about more than 5 patients reported in the English literature were included for analysis. Non-English manuscripts, case reports, comments, narrative reports and recommendations, surveys, and reviews were excluded.

Results

The search yielded 225 reports in total. After eliminating duplicates and 1 non-English report, a total of 171 publications were identified including a study about complications of fillers in Portuguese [27] but with English abstract. After screening titles and abstracts, 77 reports were not relevant; they were about non-injectable fillers gluteal augmentations and were excluded. Of the 94 records retrieved, 4 were reviews, 7 narrative reports, 3 case reports, 65 complication case reports, 5 cohort studies involving patients with gluteal fillers complications presenting for treatment, 1 survey and 1 comment; they did not meet the inclusion criteria and they were excluded. 4 additional relevant records were identified by secondary searches and were included for analysis [28–31]. Details of the conducted search are summarized in Fig. 4. In the final analysis 12 clinical trials and studies were identified for inclusion in the review. 2 studies involved Polymethylmethacrylate (PMMA), 5 Poly-L-lactic acid (PLLA), 1 Calcium hydroxyapatite (CaHA)4 about hyaluronic acid (HA) filler injection. No studies were identified involving liquid silicone or Polyacrylamide hydrogel (PAAG). Details of study analysis are summarized in Table 1.

In view of the generally high popularity of minimally invasive aesthetic procedures and the wide plethora of injectable fillers advertised and marketed aggressively for not only facial rejuvenation and volume enhancement, it is surprising that very little clinical studies about gluteal volumization with such fillers are available. The few

clinical trials and cohort studies that were identified for inclusion in this study provided a low level of evidence and were mostly strongly biased (Table 2). The large number of case reports about complications is also striking. Moreover, clinical cohort studies about patients presenting with fillers complications for treatment [27, 32–35] amounted to 50% of studies and clinical trials related to application of injectable fillers for buttocks rejuvenation and volume enhancement, in addition to a report of special interest [25] about 23 patients with cosmetic injection-associated granuloma and hypercalcemia identified from 20 articles (Table 3).

Discussion

Aesthetic body contouring procedures are elective interventions, thus minimizing if not eliminating potential risks is of paramount importance [12]. Volume enhancement with soft tissue fillers is an attractive minimally invasive modality theoretically associated with less morbidity, down time, and side effects than more invasive techniques. Despite marked improvements in the safety, efficacy, and longevity of new generation fillers, the search for the ideal filler is still ongoing [32]. An ideal filler, in addition of providing a long-term good aesthetic result, is safe, biocompatible, and stable in the implantation site with low-risk of migration or any other complication [26]. Non-permanent fillers, such as collagen and hyaluronic acid, produce short-term results and require repeated injections to maintain long-term outcome. Semi-permanent fillers tend to remain longer but are also eventually resorbed. Only permanent fillers can produce long-term results but may raise concerns about potential infection and long-term complications and side effects [26, 36].

Various Injectable Products Reported for Buttock Augmentation and Product-Dependent Complications

Permanent Fillers

Liquid Silicone Being a minimally antigenic and non-carcinogenic permanent filler. Medical-grade liquid silicone (polydimethylsiloxane) injection is an attractive option to many patients due to its relatively low cost [37–39]. It is a popular soft-tissue filler in some parts of the world [37, 40]. Industrial-grade silicone developed for the military was first injected in Japanese prostitutes in the aftermath of World War II to cater to the cultural aesthetics preferred by stationed servicemen. Similar injections were also performed in Germany and Switzerland during that same period and in the USA during the 50 s and 60 s,

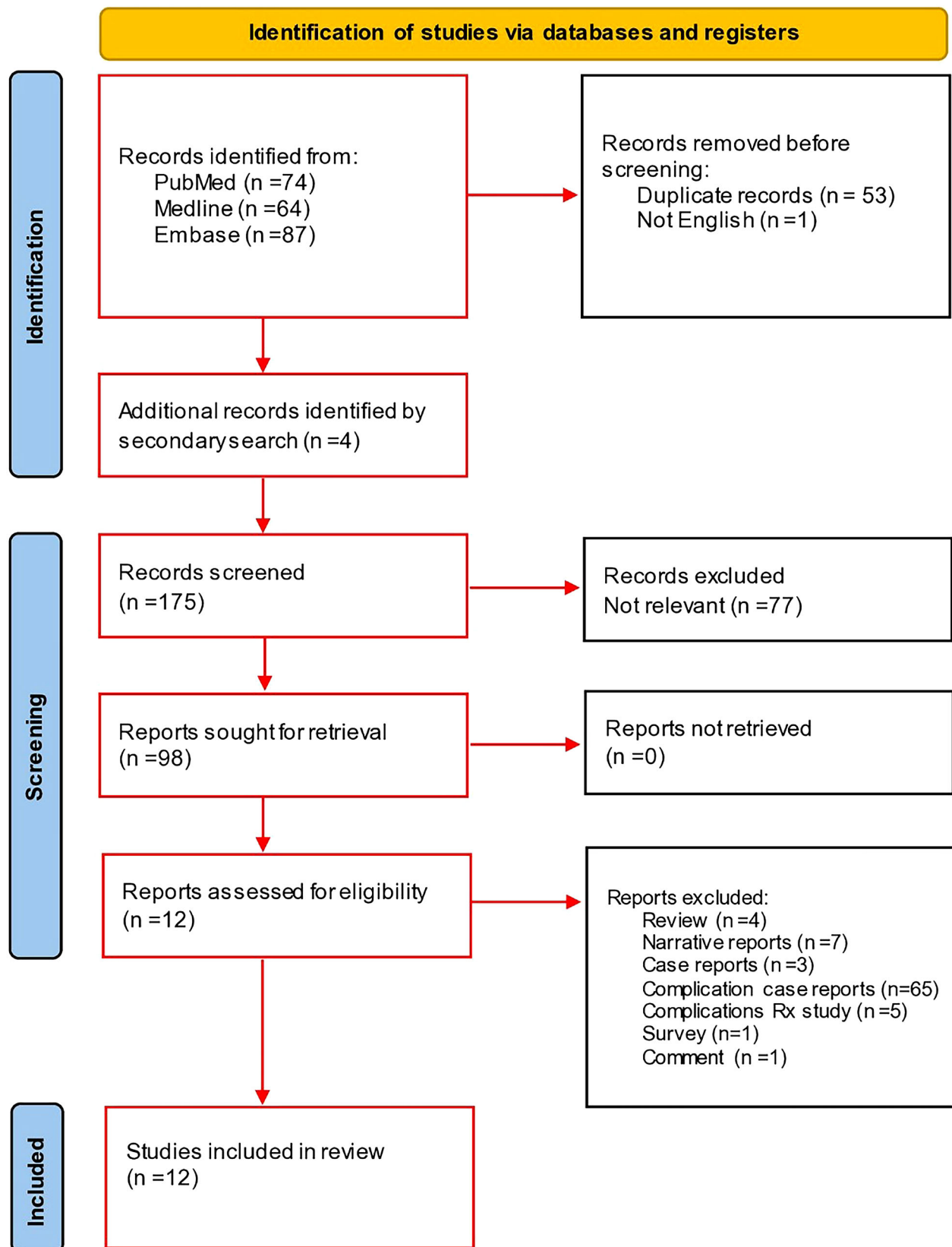


Fig. 4 PRISMA flow chart of conducted systematic literature search

Table 1 Clinical studies and trials included in the review

Authors	Type of study	# of patients	Outcome measure	Conclusion
<i>Polymethylmethacrylate (PMMA)</i>				
Serra et al. [73] 2015	Retrospective non-comparative	154 Patients with HIV buttock lipodystrophy	Patients were satisfied with this treatment and reported to be more comfortable to be seated for longer period of time	Safe and efficient for the treatment of buttock lipoatrophy associated with HIV
Chacur et al. [12] 2019	Retrospective non-comparative from 2009 to 2018	1681	Uneventful outcome in 98.12% of patients	Safe and effective buttock augmentation
<i>Poly-L-lactic acid (PLLA)</i>				
Mazzuco [28] 2020	Prospective case series treated with Subcision™ plus PLLA, in the same session for women with moderate or severe degree of cellulite	24	Before and after pictures evaluated by 3 blinded dermatologists. clinical appearance scored according to the Global Aesthetic Improvement Scale (GAIS)	Combination of Subcision™ plus PLLA, in the same session, promotes safe desirable correction of cellulite associated with flaccidity
Durairaj et al. [3] 2020	Retrospective non-comparative 20 wks study	60	Pre- and post-treatment photographs assessed by investigators in blinded and double-blinded surveys. Global Aesthetic Improvement Scale used to quantify improvements in volume, skin texture, and cellulite dimpling	Higher number of total PLLA vials yields more visible increase in buttocks volume but not significantly associated with improvement in skin texture
Mazzuco et al. [30] 2020	Prospective study non-comparative non-random with injections to buttocks, thighs, abdomen, and arms for skin laxity, cellulite, striae, and liposuction sequelae	45	Pre- and post-treatment photographs evaluated by an expert panel of 3 trained dermatologists using the Global Aesthetic Improvement Scale (GAIS)	90% of cases treated on the buttocks, abdomen, and arms improved, and 81.3% of those treated on thighs improved. Patients must be informed about gradual onset of results
Shridharani et al. [59] 2021	Prospective non-comparative non-random injection for buttock volumization or for cellulite, skin quality, and postsurgical deformities Rx	20	Reconstitution, injection volume and dosage documented. Treatment response assessed by patients and provider. Adverse events recorded	Injection is well tolerated and can achieve good aesthetic outcomes
Swearingen et al. [29] 2021	Prospective trial with Subcision™ plus PLLA, in the same session for women with moderate or severe degree of cellulite of thighs and buttocks	31	Assessments included live ratings, rating of standardized pictures by a blinded evaluator, patient questionnaires, safety, and tolerability ratings. Follow-up at 1, 3, and 6 months	Repeated PLLA treatments combined with subcision are effective and safe in improving the appearance of cellulite
<i>Calcium hydroxyapatite (CaHA)</i>				
Casabona et al. [60] 2017	Retrospective non-comparative	20 Women with skin laxity and moderate-to-severe cellulite on buttocks and thighs	Photographs at baseline and 90 days assessed by 2 independent, blinded evaluators using 5-item cellulite severity scale	Combination treatment with MFU-V and diluted CaHA is effective for improving skin laxity and appearance of cellulite on buttocks and upper thighs
<i>Hyaluronic acid (HA)</i>				
Lazzari et al. [66] 2010	Prospective, non-comparative one session of body thermage® associated with NASHA™ gel injection	10 Patients with loss of volume and skin laxity in arms (2), buttocks (6) and inside thigh (2)	Subjective evaluation. Results evaluated at 6, 12 and 24 weeks	NASHA™ gel is a promising and well tolerated for body volume restoration. Use in association with Thermage® opens new horizons in body contouring

Table 1 continued

Authors	Type of study	# of patients	Outcome measure	Conclusion
Camenisch et al. [1] 2013	Prospective open-label noncomparative	8	Gluteal augmentation evaluated by MRI and photographic documentation at set intervals till 24m after injection; subjects and investigators independently assessed improvement of the buttocks using the five-point Global Esthetic Improvement Scale; Safety assessed by adverse event reporting	HA gel degraded with minimal displacement. 36% of the gel remained at 12m. It was well tolerated. Subjects' and investigators' perceptions remained high, even if only small volumes of the gel remained
De Meyere et al. [74] 2014	Prospective noncomparative multicenter	61	Safety and efficacy assessments (24-month follow-up evaluation) included adverse event reporting, aesthetic improvement (Global Aesthetic Improvement Scale [GAIS]), and subject satisfaction	Stabilized HA gel is safe and effective for temporary aesthetic augmentation of the buttocks
Claude et al. [31] 2015	Prospective pilot study Macrolane VRF30 injected for buttock lipoatrophy in HIV patients	10	Primary outcome assessment was to compare 6-month pain score with baseline. Aesthetic improvement assessed using standardized photographs and the 5-point Global Esthetic Improvement Scale	Macrolane treatment of buttock lipoatrophy is a promising, well-tolerated method that reduces pain at sitting and improves buttock appearance

specifically in Las Vegas, till the practice was outlawed in 1975. Liquid silicone injections for cosmetic volume enhancement remains highly controversial due to potentially devastating short, intermediate, and long-term adverse effect [18].

Silicone is neither as inert nor innocuous as initially presumed. Silicone injection for cosmetic augmentation carries one of the highest complication rates. Many side effects are caused by injecting large volumes or injecting too superficially. Complications may be particularly frequent and severe when intentionally adulterated silicone with additives such as olive oil, peanut oil, and cobra venom is injected in an attempt to incite an inflammatory fibrous response and enhance sequestration of the injected material. Even in its pure medical-grade form, granuloma formation may develop in up to 20% of patients [11, 35, 37, 38, 41–43]. These granulomas can lead in rare instances several years after initial injection to calcitriol-mediated hypercalcemia that can be severe enough to cause renal failure and death [25, 32]. Though recent studies using newer preparations of medical grade liquid silicone injected with the microdroplet technique have demonstrated an increased safety profile [11], liquid silicone is not approved by the U.S. Food and Drug Administration (FDA) for any cosmetic soft tissue volume augmentation. Today, free-silicone injection is approved only for the treatment of retinal detachment [38]. Unfortunately, black-market injections of silicone are on the rise for the last few years and are illegally performed at dramatically reduced

prices for medically underserved or marginalized transgender individuals [11, 21, 25, 37, 38, 44].

Polyacrylamide Hydrogel (PAAG) Polyacrylamide hydrogel (PAAG), is a synthetic soft-tissue permanent filler currently approved in various countries for breast augmentation, facial contouring, and correction of HIV-associated facial lipoatrophy. It has also been reported to be injected for buttock augmentation [41]. Though not approved by FDA and not recommended in formal medical institutions, illegal injections of PAAG are being performed in many clinics and beauty parlors across the United States due to its low cost and rapid long-lasting results [41]. A study published about patients injected with PAAG for breast augmentation with a wide range of complications hinted to the fact that the hydrogel may not be as safe and as biocompatible as it was initially claimed [19]. Similar to other permanent fillers, side effects and complications of PAAG comprise injection-related pain, erythema, ecchymoses, hematomas and edema, in addition to overcorrection, hypersensitivity reactions, inflammatory and non-inflammatory nodules, foreign body granulomas, infection, asymmetry, irregularity at the injection site, gel migration, post-inflammatory dyschromia and hyperpigmentation, and even skin necrosis. In some studies, PAAG has also been associated with neurotoxicity, genotoxicity, carcinogenicity, mutagenicity, and reproductive toxicity [41].

Table 2 Level of evidence and conflict of interest of reviewed clinical studies

Authors	Level of evidence	Conflict of interest
Serra et al. [73]	IV	None
Chacur et al. [12]	IV	None
Mazzuco [28]	III	The author is an Advisory Board member and speaker for Galderma Inc.
Durairaj et al. [3]	IV	Durairaj KK and Devgan L are consultants for Galderma, Merz, and Allergan, and Evolus
Mazzuco et al. [30]	IV	Not mentioned
Shridharani et al. [59]	IV	Shridharani SM is an advisory board member, speaker and investigator for Galderma. Edwartz C is employed by Galderma Aesthetics
Swearingen et al. [29]	III	<i>Sadick N is a consultant for Allergan Aesthetics, an AbbVie Company, Almirall, Venus Concept, Cynosure, Endo, Eternogen, Gerson Lehrman Group, Merz Aesthetics, and Valeant; an investigator for Amgen, Cassiopea SpA, Celgene Corporation, Cutera, Inc., Cynosure, Inc., DS Laboratories, Eli Lilly and Company, Endo, Foamix, Galderma, Hydropeptide, Kadmon Corp, LEO Laboratories Ltd, Neostrata, Novartis, Nutratceutical Wellness, Pfizer, Ralexar Therapeutics, Regeneron, Roche, Valeant, Vanda Pharma, Venus Concept</i>
Casabona et al. [60]	III	Article Processing Charge was paid for by Merz Pharmaceuticals GmbH
Lazzari et al. [66]	IV	Not available*
Camenisch et al. [1]	IV	Study supported by Q-Med, a Galderma Division, Uppsala, Sweden. Medical writing assistance with development of the article was carried out by Dr. Elizabeth Hutchinson on behalf of Fishawack Communications Ltd., supported by Q-Med
De Meyere et al. [74]	IV	Per Hedén is a consultant for Galderma (paid for lectures and travel). De Meyere B has given presentations and workshops on the use of Macrolane, paid for by Galderma. Study supported by Galderma, Uppsala, Sweden
Claude et al. [31]	IV	Lantieri received honoraria from Galderma, who also funded the study and provided the study product and medical writing assistance. The Article Processing Charge was paid for by Galderma

*ePoster Presented at American Society for Laser Medicine and Surgery 30th Annual Conference; Phoenix, Arizona; 2010

Aquafilling filler (Biomedica, Prague, Czech Republic) a biocompatible hydrophilic gel equivalent to PAAG composed of 98% sodium chloride solution (0.9%) and 2% cation copolyamide was developed in 2005 and is being used as a soft tissue filler for facial volumizing and for soft tissue augmentation in several countries where it has become a popular option for breast and buttock augmentation. It is claimed to offer stable results for approximately 8–10 years [32, 45]. A recent report has described however serious complications related to this filler material several years after injection of large volumes. Patients with Aquafilling filler complications often exhibit irreversible deformities, requiring complex reconstructions.

Polymethylmethacrylate (PMMA) Polymethylmethacrylate (PMMA), a highly biocompatible agent, has been used for more than 7 decades as bone cement, contact and intraocular lenses, bone screw fixation, filling of bone cavities and defects of the skull, and stabilization of vertebrae in patients with osteoporosis or fractures [12].

Approved only for minimally invasive procedures in facial tissue, highly uniform in size PMMA microspheres suspended in bovine collagen are being used also as a permanent volume enhancing agent to provide immediate and long-term results [46]. Acting as a matrix, the microspheres stimulate fibroblasts to produce collagen that results in their encapsulation [12, 26]. Early reports about PMMA injections have confirmed that once injected, microspheres trigger a granulomatous inflammatory reaction typical of a foreign body reaction that may generate both acute and late complications with tissue necrosis. Despite overall satisfactory early results, capsules around microspheres remodel and may eventually contract forming hard nodules several years later and trigger nonspecific inflammatory mechanisms that may evolve to abscesses formation and extrusion of the implanted material [47]. Other more serious potential side effects must not be underestimated as well. A case of non-infectious shock syndrome was reported in a trans-gender patient few days after PMMA injection for buttock augmentation [48]. Another rare case

Table 3 Studies and review involving patients presenting after buttocks augmentation with injectable fillers complications for treatment

Authors	# of patients	Study details
<i>Clinical cohort studies</i>		
Carrillo et al. [33] 2009	10	Medical records and imaging examinations of patients with respiratory distress after illicit injection of fluid silicone were reviewed. Most common injection sites were gluteal and trochanteric areas. Injection of large volumes is associated with pulmonary embolism and acute alveolar hemorrhage and is associated with a significant mortality
Mello et al. [34] 2013	12	Retrospective study to analyze a series of patients who underwent illicit injection of industrial liquid silicone by unauthorized providers. The most often injected sites were the thighs and buttocks. Use of industrial liquid silicone should be completely contraindicated; it may have serious complications, even death
Salgado et al. [35] 2014	8	Evaluate liposuction as a treatment for patients experiencing complications from silicone injections to the gluteal region. Liposuction with immediate intramuscular fat transfer for buttock augmentation appears to be a safe surgical option that preserves aesthetic appearance
Namgoong et al. [32] 2020	399	Retrospective study of complications after breast augmentation and buttock augmentation using Aquafilling filler treated between 2015 and 2019. 146 underwent surgery to remove Aquafilling filler from the breast or buttock. 136 had received Aquafilling injection in their breast, six in the buttock, and four in the breast and face simultaneously
Castro et al. [27] 2021	1322	Retrospective review describing the epidemiological characteristics and adverse effects arising from the injection of modeling substances mostly performed by non-qualified personnel in a group of patients from Cali, Colombia. The most infiltrated anatomical site showing adverse effects was the buttock
<i>Review</i>		
Tachamo et al. [25] 2018	23 Eligible patients from 20 articles	Search of relevant articles on hypercalcemia associated with various cosmetic injections. The buttock was the most common of injection. Silicone was most commonly used, followed by polymethylmethacrylate and paraffin oil. Cosmetic injection-associated granuloma should be considered a cause of hypercalcemia that can be severe and life threatening and can present years after the initial procedure

of paracentral acute middle maculopathy and loss of vision after PMMA injections into the buttocks in Mexico was also reported [49].

PMMA attractive lower cost compared to other filler materials, allows injection of large volumes with less concern about expense [12]. In a retrospective study of a total of 1681 patients who underwent gluteal augmentation with PMMA between 2009 and 2018 in Brazil, Chacur et al. [12] described uneventful outcome in 98.12% of patients. Complications occurred in only 52 cases (1.88%). Less than 1% complications rate was reported by a recently conducted survey in Brazil [26]. Compared to augmentation with silicone implants, Chacur et al. [12] strongly recommended PMMA filler as a standard modality for gluteal augmentation despite expressed major objections due to several reported cases with extrusion or displacement of the product. For their part, the authors with a 10 y follow up did not observe any cases of migration, product displacement or late rejection claiming that the product does not migrate or change position after implantation [12].

Palpable nodules, not visible even with movement, are however possible and predictable, but Chacur et al. [12] advise their patients to ignore them. With purified third PMMA generation product, granuloma formation has

become relatively rare [12]. Nevertheless, these granulomas triggered by a foreign body reaction, can lead in very rare instances to calcitriol-mediated hypercalcemia months or even years after injection similar to what has been observed following liquid silicone injection [25, 50]. Furthermore, in patients with HIV, inflammatory cells surrounding globules of PMMA can strongly express locally high levels of CYP27B1 even without frank granulomas and lead to severe hypercalcemia several years after injection [51]. It has been suggested that injection of a large volume of PMMA may lead to the development of severe hypercalcemia and chronic kidney damage in a probably underestimated frequency [46].

Many commercial PMMA products are presently available. A study conducted several years ago comparing PMMA soft tissue fillers from different countries at various time intervals demonstrated that these products are likely not equivalent exhibiting marked differences in particle morphology and related characteristics [52]. Products combining PMMA with other injectable components are marketed as well. A case of acute hemorrhagic pneumonitis from illegal Anicoll (PMMA suspended in purified collagen and silicone) injection has also been reported [22]. It must be noted though that quality of PMMA products has

gradually improved over time, thus the complications reported some years ago do not necessarily reflect what may be expected with materials of improved quality and perfected injection techniques [26]. ArteFill® (Suneva Medical, San Diego, CA), an improved PMMA filler, has been approved by the FDA in 2006, as the first and only permanent dermal filler; it is approved for augmentation of the face and correction of nasolabial folds [53] but not for other anatomic sites [25].

Semi-permanent Filler

Poly-L-lactic Acid (PLLA) Several peer-reviewed clinical studies about minimally invasive volumetric structural rejuvenation in patients with facial fat volume loss have demonstrated the efficacy of poly-L-lactic acid (PLLA), a semi-permanent biocompatible biodegradable and immunologically inert synthetic polymer derived from a group of alpha hydroxy acids. It is FDA approved for correction of antiretroviral therapy-induced facial lipoatrophy in HIV patients and of nasolabial fold in immunocompetent patients. Although the use of PLLA for non-facial cosmetic indications to improve skin laxity and body contour is approved in Brazil, it is used off label in the USA [30]. It has been used to enhance various sites, including the hands, neck/décolleté, arms, abdomen, acne scars, pectus excavatum or post-surgical thoracic deformities, medial ankles, thighs and buttocks as well as for an increasing range of indications [37, 54–58]. Unlike other temporary, space-occupying replacement fillers, PLLA semi-permanent microspheres have been shown to exert a biostimulatory activity believed to be responsible for the observed durability of volume enhancement. PLLA injection results in temporary immediate volume enhancement due to tissue edema and fluid from the reconstitution of the product that resolves within 2–3 days. Subsequently, PLLA microspheres induce an inflammatory response through phagocytosis by tissue macrophages over a period of several weeks and induce local dermal remodeling through upregulation of fibroblast activity and neocollagenesis. Approximately half of the product is digested within 6 months. Observed clinical effects and newly generated collagen have been reported to last for 24–36 months in the face, nevertheless, multiple treatments are likely to be required for optimal biostimulation [30, 37, 54, 58]. PLLA has been presented as a safe effective, and relatively long-lasting filler for patients who are not surgical candidates or do not want the downtime or risk associated with surgical gluteal augmentation [37, 54]. The ideal candidate for PLLA injection is a fit and active woman with a body mass index of less than 20 kg/m² and minimal excess fat who has also realistic expectations regarding extent and duration of the volume enhancement [37]. However, cost of this

product and the number of vials used per session are not to be neglected as the procedure may be prohibitively expensive. 20 vials or more of PLLA may be required to achieve the desired outcome [5, 59]. Two recent studies about correction of cellulite associated with flaccidity of the buttocks and thighs have claimed favorable results by injecting smaller volumes of diluted PLLA (Sculptra™ Aesthetic; Galderma Pharma SA/Galderma SA, Lausanne, Switzerland) solutions combined with Subcision™, a minimally-invasive modality performed to sever fibrous septa of deep depressions [28, 29]. Currently, there is considerable variation in PLLA reconstitution and use with lack of guidelines and expert recommendations; the safest, most effective ways to use this product still have not been clearly determined [55, 56].

Non-permanent Fillers

Calcium Hydroxyapatite (CaHA) Calcium hydroxyapatite (CaHA) (Radiesse—Merz North America, Raleigh, N.C.) is a biocompatible, long-lasting biodegradable, and completely resorbable biostimulatory filler 2.5 years after injection. Synthetically produced smooth, uniform CaHA microspheres (diameter of 25–45 µm) suspended in a sodium carboxymethylcellulose gel have been described to stimulate the endogenous production of collagen. CaHA has been reported for the correction of a wide range of conditions including generalized lipohypertrophy or lipohypotrophy, gluteal sagging, and cellulite skin-surface irregularities [16, 60, 61]. Combination treatment of microfocused ultrasound with visualization (MFU-V) and CaHA injection have been described to be effective in improving skin laxity and appearance of cellulite on buttocks and upper thighs with statistically significant improvements 90 days after treatment [16, 60]. Another more recent limited clinical trial of the combined therapy in 2 patients with buttocks laxity and 2 additional patients with chest laxity documented improved wrinkling assessment scale by 2 grade points after two or three treatment sessions [62]. It is not clear though whether the observed improvement was due primarily to MFU-V or to CaHA injections, hence the efficacy of CaHA in inducing skin tightening of the gluteal area cannot be ascertained. In a recent global consensus report about improving laxity and skin quality in the mid- and lower face, neck, décolletage, upper arms, abdomen, upper legs, and buttocks, CaHA injections were recommended as an adjunct to volume augmentation or in combination with additional modalities for optimal outcome [63].

Non-animal Stabilized Hyaluronic Acid (NASHA) Gel Body contouring with non-animal stabilized hyaluronic acid (NASHA) gel (Macrolane®—Q-Med AB, Uppsala,

Sweden) has also attracted a lot of interest and was first reported in 2013 [6, 64]. hyaluronic acid (HA) injection has been applied for breast augmentation, buttock augmentation, and for correction of pectus excavatum. It has also been used for calf augmentation and male chest enhancement [64]. Prospective studies have demonstrated that this is a safe and effective modality for temporary aesthetic augmentation of the buttocks. Although HA degrades over time, several patients still rated their buttocks as improved and expressed satisfaction 24 months after treatment [10]. It is claimed that HA stimulates procollagen, growth factors, and induces stem mesenchymal cells migration in the extracellular matrix [6]. A recently published prospective comparative study about single injection of cross-linked hyaluronic acid (CL-HA) and saline as vehicle control in separate adjacent skin on photodamaged forearm or sun-protected buttock skin demonstrated that CL-HA acts by both filling space and inducing production of collagen by dermal fibroblasts. It was postulated that deposition of mature collagen likely confers long-term benefits [65]. In spite of reported good results and high patient satisfaction, use of HA for body contouring has not become an established and common aesthetic procedure due to low cost-benefit effectiveness and the limited duration of results. Volume needed to achieve noticeable changes is relatively large making the cost of the required product a major obstacle [6, 10, 64]. NASHA combined with Thermage® was also investigated in a limited clinical trial for volume restoration and skin tightening of the arms, inner thighs and buttocks [66]. Despite being well tolerated by patients and reported promising results, this combined modality did not gain acceptance.

Legalized in Europe in 1998 as an implantable medical device (IMD), Macrolane® did not fulfill the criteria for scientific validation of a drug; its marketing has never been approved by the FDA or the Public Health Agency of Canada [67]. With withdrawal of its indication for breast enhancement that had the largest demand after it was found to interfere with breast imaging and screening for breast cancer, the product has been taken completely off the market in 2017 [64, 67]. Since then, very few other HA products for body contouring are available in the market and have not been thoroughly scientifically investigated [64]. Undoubtedly, the introduction and refinement of fat grafting techniques for body contouring is a major reason for the lack of acceptance of HA enhancement as a valid modality. Nevertheless, new HA products under development may lead to reintroduction of HA for body shaping and volume restoration in the future. Favorable outcome with one such product (Sofiderm Subskin Aeskins—Hangzhou, China) that has a large (1800 nm) and stable molecule of HA gel, with a high G prime has been very recently reported [6]. Another new product, Genefill

(BioScience GmbH), is an advanced line of cross-linked hyaluronic acid of non-animal origin; it has been marketed for gluteal augmentation with an effect claimed to last 18–24 months; nothing has been reported yet in the literature about its safety and efficacy.

Complications Secondary to Buttock Improper Injection Technique

Compared to other gluteal augmentation techniques, volume enhancement by injection is technically easy; it is not however without serious implications and potential risks. The current review has demonstrated that adverse events are not uncommon with injectable soft-tissue fillers. However, many reported prohibitive complication rates are material-independent related to incorrect injection techniques [26]. Such complications have been widely reported and investigated in conjunction with buttock augmentation with fat injection focusing on life-threatening complications associated with fat emboli. Regardless of the material injected, complications, both major and minor, occur more frequently with intramuscular injections. Risks also increase with greater volumes injected [68]. Direct injury to gluteal vessels, with either direct intravascular injection or with emboli pulled intravascularly by the negative-pressure venous system, is one likely pathophysiology [68]. Understanding the location and trajectory of the main trunks of the superior and inferior gluteal veins is essential to avoid inadvertent injection. The danger zone in which the deep gluteal structures are found is on average within 3.3cm radius located one third the distance from the midsacral border to the greater trochanter [69]. Another theory suggests deep intramuscular migration where higher pressure of the gluteal compartment could force even superficially placed products down the path of least resistance causing traction-induced venous tears and consequently emboli. Thus, any breach of gluteus muscle fascia with injection into the muscle cannot be considered safe [68]. In one report, 2 of 9 fatal complications associated with gluteal augmentation by injection were due to injection of soft tissue fillers while the others were secondary to lipofilling. Medical grade silicone was confirmed in one case, and in the second it was a clear viscous product. One patient died of septic shock following intramuscular gluteal injection while the other patient had obvious transection of the deep vessels with systemic embolization of foreign material [70]. Nonthrombotic pulmonary embolism (NTPE) secondary to PAAG injection, though rare, may also occur secondary to high-pressure injection, large volume injection, and massage or trauma at the injection site, or due to direct injection into a vein [71]. Furthermore, with PMMA gluteal augmentation, increased risk of major complications is associated with the recommendation of

deeper planes (intramuscular or submuscular) injection of preferably higher concentration products for effective contouring and volumetric enhancement [26]. Thus, popularizing buttock augmentation with fillers must be approached with great care. Serious complications become inevitable when performed illegally by non-specialized, non-authorized, and unscrupulous practitioners in non-accredited facilities [25, 34], a fact exacerbated by the rise of cosmetic medical tourism allowing patients to obtain illicitly restricted products locally at the expense of inherent lack of after-care [11, 72].

Unfortunately, injection of soft tissue fillers for body contouring continues illegally throughout the world and is still very common in Latin America [24]. Off-label use of injectable substances for aesthetic purposes in low-and-middle income countries (LMIC) is nowadays a real worrying practice [8]. Complications become inevitable when the chosen filler agent concentration and quantity injected as well as the depth of injection are inadequate. A review of patients from Cali, Colombia, which consulted for complications arising from soft tissue fillers during a 6-year period, revealed that the buttocks were the most infiltrated anatomical site developing adverse effects [27]. Appreciation of the gluteal region anatomy particularly of the danger triangle, is critical when performing volume enhancement with fillers. Other important safety points are the use of smaller volumes, reduced pressures, blunt canulas, and retrograde injection. Strict sterile technique is also mandatory to avoid contamination and serious infections [34, 37, 68, 69].

Conclusion

Despite wide popularity of soft tissue fillers, well conducted studies about their use for cosmetic buttock augmentation are largely missing. The little available evidence provided by this review, indicates that a specific brand of PMMA (Linnea Safe 30% or Meta Crill 30%) in Brazil, only when injected by experts, has a demonstrable relatively good safety, efficiency, and cost-effectiveness record superior to surgical alloplastic gluteal augmentation or to lipofilling. Regardless of the efficacy and safety of the injected material, buttock contouring and gluteal augmentation need to be addressed concomitantly; contour should be considered first and augmentation second. Harmonious shapes and profiles rather than mere volume, are key for an attractive and aesthetic outcome. Thus, the public must be made aware that buttock rejuvenation and volume enhancement must not be regraded just a simple filling of a deflated or hypoplastic body part. Optimal buttock contouring entails not only volume augmentation but also volume removal; thus, simple volume augmentation with

soft tissue fillers may not be ideal. Ultimately, any intended procedure must target the most desirable outcome by patients. However, they must be warned against deceitful claims and potential serious complications particularly when the procedure is performed by none licensed practitioners with non-approved or sometimes prohibited products. Patients must be made also aware that, to date, gluteal augmentation with soft tissue fillers remains mostly an off-label indication and that only well-trained certified experts practicing legally in accredited facilities can address safely and efficiently their concerns.

Declarations

Conflict of interest The authors declare that they have no conflict of interest.

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