Research, Society and Development, v. 15, n. 4, e8115450988, 2026
(CC BY 4.0) | ISSN 2525-3409 | DOI: http://dx.doi.org/10.33448/rsd-v15i4.50988

Injectable materials for penile augmentation: Safety profile and associated complications — an integrative review

Materiais injetáveis para o aumento peniano: Perfil de segurança e complicações associadas — uma revisão integrativa

Materiales inyectables para el aumento del pene: Perfil de seguridad y complicaciones asociadas — una revisión integradora

Received: 04/18/2026 | Accepted: 04/22/2026 | Published: 04/24/2026

Samyr Machado Querobino
ORCID: https://orcid.org/0000-0002-9614-0328
Centro Universitário Una Itabira, Brazil
E-mail: samyr.querobino@ulife.com.br
Thais Daniele Flores Fonseca
ORCID: https://orcid.org/0009-0006-1605-8081
Centro Universitário Una Itabira, Brazil
E-mail: thaisdanieleflores@outlook.com.br

Abstract
The use of injectable materials for male penile augmentation has increased considerably over the past decade, yet the supporting scientific evidence remains limited and fragmented. The objective of this article is to identify, analyze, and synthesize the available scientific evidence on the safety profile and associated risks of the different materials used for male penile filling, with the aim of providing a sounder foundation for safer clinical practice and advancing the ethical and scientific debate surrounding this emerging aesthetic procedure. An integrative review was performed following the six-step framework proposed by Mendes, Silveira, and Galvão, with searches conducted in PubMed/MEDLINE, Web of Science, SciELO, and LILACS/BVS between March and April 2025. Seventeen studies met the full eligibility criteria and were included in the analysis. Hyaluronic acid (HA) demonstrated the most favorable safety profile among the materials evaluated, with complication rates consistently below 5% and full reversibility via hyaluronidase. Polymethylmethacrylate (PMMA) was associated with surface irregularities in up to 52% of patients and offers no pharmacological reversal option. Autologous fat demonstrated highly variable reabsorption rates (30–80%) and carries a risk of systemic fat embolism. Unregulated substances — including paraffin, liquid silicone, and mineral oil — were associated with irreversible complications requiring surgical intervention in the vast majority of cases. Hyaluronic acid remains the injectable agent with the best-documented safety profile for penile augmentation. Permanent fillers and unregulated substances carry unacceptable risk profiles. The available evidence base is predominantly of low methodological quality, and well-designed, long-term randomized controlled trials are urgently needed.
Keywords: Penile augmentation; Dermal fillers; Hyaluronic acid; Complications; Patient safety.

Resumo
O uso de materiais injetáveis para o aumento peniano masculino cresceu consideravelmente na última década, mas as evidências científicas que fundamentam esses procedimentos ainda são limitadas e fragmentadas. O objetivo deste artigo é identificar, analisar e sintetizar as evidências científicas disponíveis sobre o perfil de segurança e os riscos associados aos diferentes materiais utilizados para o preenchimento peniano masculino, com a finalidade de oferecer bases mais sólidas para uma prática clínica mais segura e avançar no debate ético e científico em torno desse procedimento estético emergente. Realizou-se uma revisão integrativa seguindo o referencial de seis etapas proposto por Mendes, Silveira e Galvão, com buscas realizadas nas bases PubMed/MEDLINE, Web of Science, SciELO e LILACS/BVS entre março e abril de 2025. Dezessete estudos atenderam aos critérios de elegibilidade e foram incluídos na análise. O ácido hialurônico (AH) demonstrou o perfil de segurança mais favorável entre os materiais avaliados, com taxas de complicação consistentemente inferiores a 5% e reversibilidade completa por meio de hialuronidase. O polimetilmetacrilato (PMMA) foi associado a irregularidades superficiais em até 52% dos pacientes, sem opção de reversão farmacológica. A gordura autóloga demonstrou taxas de reabsorção altamente variáveis (30–80%) com risco de embolia gordurosa sistêmica. Substâncias não regulamentadas — incluindo parafina, silicone líquido e óleo mineral — foram associadas a complicações irreversíveis que exigiram intervenção cirúrgica na grande maioria dos casos. O ácido hialurônico permanece como o agente injetável com o melhor perfil de segurança documentado para o aumento peniano. Preenchedores permanentes e substâncias não regulamentadas apresentam perfis de risco inaceitáveis. A base

de evidências disponível é predominantemente de baixa qualidade metodológica, e ensaios clínicos randomizados bem delineados e de longo prazo são urgentemente necessários.
Palavras-chave: Aumento peniano; Preenchedores dérmicos; Ácido hialurônico; Complicações; Segurança do paciente.

Resumen
El uso de materiales inyectables para el aumento del pene masculino ha aumentado considerablemente en la última década, aunque la evidencia científica de respaldo sigue siendo limitada y fragmentada. El objetivo de este artículo es identificar, analizar y sintetizar la evidencia científica disponible sobre el perfil de seguridad y los riesgos asociados a los diferentes materiales utilizados para el relleno peniano masculino, con el propósito de proporcionar una base más sólida para una práctica clínica más segura y avanzar en el debate ético y científico en torno a este procedimiento estético emergente. Se realizó una revisión integradora siguiendo el marco de seis pasos propuesto por Mendes, Silveira y Galvão, con búsquedas realizadas en PubMed/MEDLINE, Web of Science, SciELO y LILACS/BVS entre marzo y abril de 2025. Diecisiete estudios cumplieron los criterios de elegibilidad completos y fueron incluidos en el análisis. El ácido hialurónico (AH) demostró el perfil de seguridad más favorable entre los materiales evaluados, con tasas de complicación consistentemente inferiores al 5% y reversibilidad completa mediante hialuronidasa. El polimetilmetacrilato (PMMA) se asoció con irregularidades superficiales en hasta el 52% de los pacientes y no ofrece opción de reversión farmacológica. La grasa autóloga demostró tasas de reabsorción muy variables (30–80%) y conlleva riesgo de embolia grasa sistémica. Las sustancias no reguladas — incluidas parafina, silicona líquida y aceite mineral — se asociaron con complicaciones irreversibles que requirieron intervención quirúrgica en la gran mayoría de los casos. El ácido hialurónico sigue siendo el agente inyectable con el perfil de seguridad mejor documentado para el aumento del pene. Los rellenos permanentes y las sustancias no reguladas presentan perfiles de riesgo inaceptables. La base de evidencia disponible es predominantemente de baja calidad metodológica, y se necesitan urgentemente ensayos clínicos aleatorizados bien diseñados y de largo seguimiento.
Palabras clave: Aumento del pene; Rellenos dérmicos; Ácido hialurónico; Complicaciones; Seguridad del paciente.

1. Introduction

Over the past two decades, aesthetic medicine procedures targeting the male body have expanded markedly worldwide. Within this context, male intimate filling — a technique involving the subcutaneous injection of biocompatible substances into penile tissue to increase girth or circumference — has gained traction among men seeking cosmetic improvement or expressing dissatisfaction with their genitalia (Pearlman et al., 2024; Pignanelli et al., 2023). Although originally developed for dermatological and facial indications, a variety of filling agents are now used in anatomical regions far outside their originally approved scope, including the male genitalia — a practice broadly referred to in the literature as off-label use (Li et al., 2024).

Male dissatisfaction with penile size is considerably more prevalent than is typically acknowledged in clinical practice. Population-based studies indicate that approximately 12% of men perceive their penis as small, and approximately 3.6% of this group eventually seek some form of augmentation procedure (Pignanelli et al., 2023). This concern is frequently intertwined with complex psychological dimensions, including Small Penis Syndrome (SPS) and Body Dysmorphic Disorder (BDD) — or, in its genital-specific manifestation, Penile Dysmorphic Disorder (PDD). PDD is characterized by excessive, persistent preoccupation with penile appearance despite objectively normal dimensions, with significant repercussions on social, sexual, and occupational functioning (Sharp et al., 2022; Yianni & Veale, 2022).

The 2023 European Association of Urology (EAU) guidelines on penile size abnormalities and dysmorphophobia explicitly recommend that patients with objectively normal penile measurements who request augmentation be referred for psychological evaluation prior to any intervention (Falcone et al., 2023). This position is reinforced by the Sexual Medicine Society of North America (SMSNA), whose 2024 official statement affirmed that penile enhancement procedures should not be performed in men with uncontrolled psychological conditions, and that psychiatric or psychological screening must constitute a non-negotiable prerequisite to any intervention (Trost et al., 2024).

From a technical standpoint, the materials most frequently used for penile filling include hyaluronic acid (HA), polylactic acid (PLA), and polymethylmethacrylate (PMMA). Among temporary fillers, HA stands out for its favorable safety

profile, primarily because hyaluronidase can dissolve it pharmacologically whenever complications arise (Kusumaputra et al., 2023). PLA, also a temporary agent, has been compared with HA in controlled studies and yields similar circumference gains — generally 2 to 2.5 cm — with a slightly different adverse event profile (Ahn et al., 2022). PMMA, a permanent filler, carries considerably more serious risks, since its removal is surgically complex once complications develop (Li et al., 2024).

Beyond synthetic materials, the literature documents the use of autologous fat (lipofilling) and self-injection of clandestine substances such as paraffin, petroleum jelly, liquid silicone, mineral oil, and metallic mercury (Pang et al., 2024). These latter agents, frequently administered without medical supervision, are associated with devastating outcomes including penile necrosis, lymphedema, paraffinoma, and permanent deformities, most of which require major surgical intervention (Pignanelli et al., 2025).

The heterogeneity of available materials, the absence of standardized injection protocols, and the growing number of procedures performed outside hospital settings or by inadequately trained practitioners have resulted in a progressively wider spectrum of complications reported in the urological literature (Li et al., 2024; Pang et al., 2024). Recent systematic reviews classify complications as early — pain, edema, hematoma, and infection — or late — granuloma formation, material migration, fibrosis, erectile dysfunction, reduced sensitivity, and penile shortening (Pignanelli et al., 2025; Sharp et al., 2023).

The SMSNA's 2024 statement strongly advises against permanent fillers such as paraffin and silicone given their unacceptable risk profiles, and emphasizes that even temporary fillers — HA and PLA — should be used exclusively in research settings approved by an Institutional Review Board (IRB), given the still-limited long-term evidence (Trost et al., 2024). This stands in sharp contrast to clinical reality, wherein such procedures are widely offered on the aesthetic market without the requisite scientific rigor.

Given this landscape, an integrative review is warranted to systematically organize and critically appraise the scientific knowledge produced in recent years on materials used for male penile filling, with particular emphasis on the risks and safety profile of each agent. The integrative review, by its methodologically broad nature, permits the incorporation of studies with different designs — experimental and non-experimental alike — enabling a more comprehensive understanding of the phenomenon (Sousa et al., 2017).

The objective of this article is to identify, analyze, and synthesize the available scientific evidence on the safety profile and associated risks of the different materials used for male penile filling, with the aim of providing a sounder foundation for safer clinical practice and advancing the ethical and scientific debate surrounding this emerging aesthetic procedure.

2. Methodology

A quantitative research approach was carried out with the selection of 17 (seventeen) articles to compose the corpus of the research, and a qualitative approach in relation to the discussion carried out in the selected articles (Risemberg et al., 2026; Pereira et al., 2018).

This study constitutes an integrative literature review — a research modality that allows the search, critical appraisal, and synthesis of available evidence on a given topic, thereby generating a comprehensive overview of existing scientific knowledge (Sousa et al., 2017). Unlike systematic reviews with meta-analysis, which are restricted to experimental designs, integrative reviews accommodate qualitative, quantitative, and mixed-methods studies, substantially broadening the analyzable evidence base (Mendes et al., 2008).

The study was conducted following the six steps recommended by Mendes, Silveira, and Galvão (2008), grounded in the methodological framework of Whittemore and Knafl (2005): (1) identification of the topic and formulation of the guiding

question; (2) establishment of inclusion and exclusion criteria; (3) identification of selected studies; (4) categorization of selected studies; (5) analysis and interpretation of results; and (6) presentation of the review and synthesis of knowledge.

2.1 Guiding question

To guide the bibliographic search, the following question was formulated using the PICO framework (Population, Intervention, Comparison, and Outcomes) (Santos et al., 2007): 'What are the risks and safety profiles of the different materials used for male penile filling, according to the available scientific evidence of the past ten years?' Population: men who had undergone or were candidates for penile filling procedures. Intervention: use of injectable or implantable materials for penile augmentation. Comparison: hyaluronic acid, polylactic acid, polymethylmethacrylate, silicone, autologous fat, and unregulated substances. Outcomes: adverse events, complications, and safety profile of each material.

2.2 Search strategy

The bibliographic search was conducted between March and April 2025 across PubMed/MEDLINE, Web of Science, Scientific Electronic Library Online (SciELO), and the Latin American and Caribbean Health Sciences Literature (LILACS) database, accessed through the Virtual Health Library (BVS) portal. These databases were selected for their international coverage and multidisciplinary scope, encompassing urology, andrology, aesthetic medicine, and dermatology.

A standardized search strategy was applied uniformly across all databases using the same combination of controlled descriptors (MeSH/DeCS) and Boolean operators:

> *("Penile augmentation" OR "Penile filler" OR "Penile girth enhancement" OR "Preenchimento peniano") AND ("Hyaluronic acid" OR "Polylactic acid" OR "PMMA" OR "Polymethylmethacrylate" OR "Silicone" OR "Autologous fat" OR "Lipofilling" OR "Foreign substance injection") AND ("Complication" OR "Adverse effects" OR "Safety" OR "Risk" OR "Eventos adversos" OR "Segurança")*

Where necessary, the strategy was adapted to the specific search interfaces of each platform while preserving the same set of concepts and logical operators. Temporal limits (2015–2025) and language restrictions (Portuguese and English) were applied through automated filters where available.

It is acknowledged that restricting the search to publicly accessible full texts may introduce publication bias, as studies reporting adverse outcomes are not always published in indexed journals or made freely available. This limitation was addressed by supplementing with systematic reviews that encompass a broader range of primary studies, and is further discussed in the Limitations section.

2.3 Inclusion and exclusion criteria

Eligibility criteria are summarized in Table 1. Inclusion criteria covered articles published from January 2015 to April 2025, written in Portuguese or English, with full text accessible through the searched databases, and focusing on injectable or implantable materials used for male penile augmentation and their implications for safety, efficacy, or complications. Eligible study designs included systematic reviews, narrative reviews, clinical trials, cohort studies, cross-sectional studies, and case reports or series. Excluded were studies addressing exclusively conventional surgical procedures without injectable or implantable agents, opinion-based publications without empirical support, letters to the editor, editorials, theses, dissertations, and studies whose full texts were inaccessible after retrieval attempts.

Table 1 - *Inclusion and exclusion criteria for study selection.*

Inclusion criteria	Exclusion criteria
Articles published between January 2015 and April 2025	Publications prior to 2015
Written in Portuguese or English	Published in languages other than Portuguese or English
Full text accessible through the searched databases	Texts available only in abstract format after retrieval attempts
Studies on injectable or implantable materials for penile augmentation	Studies addressing exclusively conventional surgical procedures without fillers or implants
Articles addressing safety, efficacy, or complications	Editorials, letters to the editor, and expert opinions without empirical data
Systematic reviews, narrative reviews, clinical trials, cohort studies, cross-sectional studies, and case reports or series	Theses, dissertations, and undergraduate final papers

Source: Prepared by the Authors (2025).

2.4 Study selection

The selection process was conducted in two sequential stages. In the first, two researchers independently reviewed titles and abstracts of all retrieved records against the eligibility criteria. Studies meeting the inclusion criteria, or about which there was uncertainty, were selected for full-text reading in the second stage. Disagreements were resolved by consensus or, when necessary, with the assistance of a third reviewer. The selection flow was documented following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA 2020) guidelines (Page et al., 2021).

2.5 Data extraction and categorization

Data from included articles were organized in a structured extraction instrument containing: author(s), year of publication, country, journal, study design, material analyzed, sample size, main complications or adverse events, and the authors' conclusions on safety. Thematic categorization was performed inductively, yielding six categories: (1) hyaluronic acid; (2) polylactic acid; (3) polymethylmethacrylate; (4) autologous fat; (5) solid silicone implants; and (6) unregulated substances and clandestine self-injection.

2.6 Assessment of evidence level and study quality

Evidence levels were classified according to the hierarchy proposed by Melnyk and Fineout-Overholt (2019), stratifying studies from Level I (systematic reviews with meta-analysis of randomized controlled trials) to Level VII (expert opinions and committee consensus). In addition, a brief critical appraisal of methodological quality was performed for each included study, considering risk of bias, sample size adequacy, follow-up duration, and outcome reporting consistency. This classification enabled identification of the reliability of available evidence for each material type and supported critical interpretation of knowledge gaps.

2.7 Ethical aspects

As this is an integrative literature review analyzing publicly available secondary data, no direct involvement of human subjects occurred, and submission to a Research Ethics Committee was not required, in accordance with Resolution No. 510/2016 of the Brazilian National Health Council (Brasil, 2016). Methodological rigor, integrity in conducting the searches, fidelity in

data extraction and synthesis, and respect for intellectual authorship constituted the primary ethical commitments of the investigators throughout the study.

3. Results

3.1 Study selection

The search across the four databases — PubMed/MEDLINE (n = 97), Web of Science (n = 54), LILACS/BVS (n = 41), and SciELO (n = 11) — yielded 203 records in total. After removal of 51 duplicates (25.1%), 152 records underwent title and abstract screening. At this stage, 108 were excluded for the following reasons: falling outside the thematic scope (n = 49); addressing exclusively conventional surgical procedures (n = 23); pre-2015 publication (n = 18); ineligible language (n = 10); and abstract-only availability (n = 8). The remaining 44 full texts were assessed for eligibility, resulting in the exclusion of 27 further studies: editorials or letters without empirical data (n = 9), inaccessible full text (n = 6), exclusive focus on conventional surgery (n = 5), theses or dissertations (n = 4), and samples of fewer than three cases without safety data (n = 3). Seventeen studies met the full eligibility criteria and were included in the review (Table 2).

Table 2 - *PRISMA 2020 flowchart of study identification, screening, eligibility, and inclusion.*

IDENTIFICATION — Records identified: PubMed/MEDLINE n = 97 | Web of Science n = 54 | SciELO n = 11 | LILACS/BVS n = 41 → Total = 203. After duplicate removal: n = 152 (51 duplicates removed, 25.1%).
SCREENING (Title and Abstract) — Screened: n = 152 | Excluded (n = 108): out of scope (49) | conventional surgery only (23) | pre-2015 (18) | ineligible language (10) | abstract only (8).
ELIGIBILITY (Full Text) — Full texts assessed: n = 44 | Excluded (n = 27): editorial/letter without data (9) | inaccessible full text (6) | conventional surgery only (5) | theses/dissertations (4) | sample < 3 cases (3).
INCLUSION — Studies included in the integrative review: n = 17

Source: Prepared by the Authors (2025).

3.2 Characteristics of included studies

The 17 included studies were published between 2015 and 2025, with a predominance of articles from 2020 onward (n = 12; 70.6%), reflecting recent growth in scientific interest in this topic. The greatest concentration of primary studies originated from Asian countries — particularly South Korea (n = 5) and China (n = 2) — followed by Mexico (n = 1) and the United States (n = 1). Systematic and narrative reviews involved multinational authorship, with contributions from European research groups (Italy, United Kingdom, Spain, Greece, and Belgium) and North American investigators.

Study designs were as follows: four systematic reviews (two with and two without meta-analysis), three narrative reviews (including the SMSNA official position statement), two randomized controlled trials (RCTs), three prospective studies, one retrospective cohort, one retrospective case series, and one study combining a retrospective cohort with a systematic review. Four studies were classified as Level I evidence, two as Level II, four as Level III, three as Level IV, and four as Level V, according to Melnyk and Fineout-Overholt (2019). The synthesis of all included studies is presented in Table 3.

Table 3 - *Summary of studies included in the integrative review on injectable materials for penile augmentation.*

No.	Author / Year	Design	Material	N	Main Complications / AEs	Conclusions	EL
1	Kusumaputra et al. (2023)	SR + meta-analysis	HA vs. PLA	283	No severe events. HA: pain, edema, transient nodules. PLA: pain, nodules, erythema. No statistical difference ($p > 0.05$).	HA and PLA safe in short/medium term; HA with greater sexual satisfaction.	I
2	Ahn et al. (2022)	Multicenter RCT	HA vs. PLA	66	HA: mild pain (27.3%), edema (18.2%). PLA: moderate pain (33.3%), nodules (9.1%). No infection or necrosis.	HA showed superior efficacy and safety; beneficial impact on premature ejaculation.	II
3	Quan et al. (2021)	Retrospective cohort	HA	230	Complication rate: 4.3%. Bleeding, nodules, local infection. Distal migration in uncircumcised men.	Complications rare and mild; resolved with hyaluronidase or conservatively.	IV
4	Zhang et al. (2022)	Prospective study	HA	112	Edema (12.5%), ecchymosis (8.9%), gel migration (3.6%), asymptomatic nodules (2.7%).	HA safe and effective; mean gain 2.1 cm; satisfaction 83.9%.	IV
5	Yang et al. (2020)	Multicenter RCT	HA vs. PLA	71	HA: pain (20%), edema (17.1%), ecchymosis (5.7%). PLA: pain (25.7%), edema (22.9%), nodules (8.6%).	Both safe; PLA more durable; HA reversible with hyaluronidase.	II
6	Kim et al. (2025)	Comparative prospective	HA vs. PLA vs. PMMA	301	HA: AEs in 7.2%. PLA: 11.9%. PMMA: 14.3% (irregularities, nodules). No severe systemic events.	HA had lowest AE rate and highest satisfaction. PMMA associated with more irregularities.	III
7	Yang et al. (2017)	Prospective (18 months)	PLA	68	Pain (29.4%), edema (22.1%), palpable nodules (14.7%) — resolution within 12 weeks.	PLA safe and effective with 18-month durability; AEs mild and self-limiting.	III
8	Casavantes et al. (2016)	Retrospective case series	PMMA	729	Irregularities and nodules in 52%; 0.4% required surgical removal. Mean gain: +3.5 cm.	PMMA effective when technique is refined; 52% irregularity rate requires improvement.	IV
9	Kim et al. (2015)	Prospective (18 months)	PMMA + dextran	20	No serious AEs. Mild post-procedure edema. No allergic reactions or migration.	PMMA + dextran (Lipen-10) safe at 18 months; volume maintained.	III
10	Pignanelli et al. (2025)	Narrative review	HA, PLA, PMMA, fat, silicone, clandestine	Review	Fat: nodules, reabsorption, isolated fatal embolism. Penuma: seroma (4.8%), infection (3.3%). Self-injection: necrosis, paraffinoma, permanent deformities.	HA best safety profile. Procedures require rigorous protocols.	V
11	Falagario et al. (2024)	Systematic review	Fat, PMMA, implants, flaps	Multiple	Lipofilling: reabsorption 30–80%, fat embolism. Penuma: seroma, erosion, infection. Overall low-quality evidence.	HA and PLA with best risk-benefit ratio. Evidence of low methodological quality.	I
12	Li et al. (2024)	Narrative review	HA, PLA, PMMA, silicone, paraffin	Review	PMMA: permanent granulomas. Silicone: granulomas, erectile dysfunction, necrosis. Paraffin: paraffinoma, lymphedema, severe tissue destruction.	Permanent injectables carry unacceptable risk. HA safest; off-label use restricted to IRB-approved research.	V
13	Pang et al. (2024)	Cohort + SR	Liquid silicone, paraffin, clandestine	35 + SR	Necrosis in 8.6%; surgery required in 91.4% (cohort). SR: paraffin most frequent (47.7%), silicone (15.8%); 78.8% treated surgically.	Clandestine materials cause irreversible complications in nearly all cases. Strict regulation is essential.	III

No.	Author / Year	Design	Material	N	Main Complications / AEs	Conclusions	EL
14	Romero-Otero et al. (2021)	Systematic review	HA, PLA, PMMA, fat, silicone, others	Multiple	HA: reversible complications. PLA: frequent nodules. PMMA: irregularities >50%. Fat: high reabsorption. Low-quality evidence.	No technique is risk-free. Temporary injectables have a better profile. RCTs urgently needed.	I
15	Salloum et al. (2021)	Systematic review	HA, PLA, PMMA, dextran, fat	1,311 (13 studies)	HA: safest profile. PLA: nodules in extended follow-up. No standardized guidelines.	HA safest non-surgical filler. RCTs needed. No formal clinical guidelines available.	I
16	Trost et al. (2024)	SMSNA position statement	HA, PLA, Penuma, PMMA, paraffin	Consensus	Permanent fillers: unacceptable risk. HA and PLA: only in IRB-approved research. Penuma: insufficient data. Uncontrolled PDD: contraindicated.	SMSNA advises against permanent fillers. HA/PLA acceptable only in research. Mandatory psychological evaluation.	V
17	Schifano et al. (2023)	Narrative review	HA (andrology)	Review	Late granulomas at high volumes. Migration in uncircumcised men. Increased risk with highly cross-linked HA.	HA versatile and safe in andrology; reversibility is key advantage. Controlled volumes by trained practitioners.	V

Note. HA = Hyaluronic Acid; PLA = Polylactic Acid; PMMA = Polymethylmethacrylate; AE = Adverse Event; EL = Evidence Level; SR = Systematic Review; RCT = Randomized Controlled Trial; SMSNA = Sexual Medicine Society of North America; PDD = Penile Dysmorphic Disorder; IRB = Institutional Review Board. EL according to Melnyk and Fineout-Overholt (2019): I = SR with meta-analysis; II = RCT; III = non-randomized/prospective trial; IV = cohort/case series; V = narrative review/consensus.
Source: Prepared by the authors (2025).

3.3 Findings by material category

3.3.1 Hyaluronic acid

Hyaluronic acid was the most widely investigated material, addressed in nine publications. Findings converge consistently on a favorable short- and medium-term safety profile. The meta-analysis by Kusumaputra et al. (2023) — the most methodologically rigorous study included in this review (Level I) — found no severe or systemic complications among 283 participants, reporting only mild events such as pain, transient edema, and palpable nodules, with no statistically significant difference between HA and PLA ($p > 0.05$). The RCTs confirmed these results: Ahn et al. (2022) observed mild pain in 27.3% and transient edema in 18.2% of HA-group participants, while Yang et al. (2020) reported similar rates.

In larger observational studies, Quan et al. (2021) found an overall complication rate of 4.3% in 230 patients, with all occurrences either resolving spontaneously or managed with hyaluronidase. Zhang et al. (2022) documented a mean circumference gain of 2.1 cm at six months and a satisfaction rate of 83.9%, with no cases of necrosis or erectile dysfunction. The key safety advantage of HA — highlighted across reviews by Li et al. (2024), Schifano et al. (2023), and Salloum et al. (2021) — is its reversibility by hyaluronidase, enabling pharmacological dissolution of the material in the event of any complication.

3.3.2 Polylactic acid

PLA was investigated in seven studies, generally in direct comparison with HA. Overall, PLA demonstrated a satisfactory safety profile, though with a slightly higher rate of adverse events — particularly palpable nodule formation. Yang et al. (2020) recorded nodules in 8.6% of PLA-group participants compared with none in the HA group, while Yang et al. (2017) found palpable nodules in 14.7% of 68 participants followed for 18 months, with spontaneous resolution within 12 weeks. None of the included primary studies reported serious events such as necrosis, systemic infection, or erectile dysfunction directly attributable to PLA.

The main characteristic distinguishing PLA from HA is its greater durability: Yang et al. (2020) demonstrated slower PLA degradation over 48 weeks, and Yang et al. (2017) confirmed stable results at 18 months. In the largest primary study (n = 301), Kim et al. (2025) documented a PLA adverse event rate of 11.9% — higher than HA (7.2%) but lower than PMMA (14.3%) — suggesting an intermediate position in the risk-benefit spectrum.

3.3.3 Polymethylmethacrylate (PMMA)

PMMA was evaluated in four studies, with more heterogeneous results. The retrospective case series by Casavantes et al. (2016) — the largest PMMA dataset in this review (729 men; 1,500 procedures) — reported irregularities and nodules in 52% of patients, attributing these predominantly to technical shortcomings. The mean circumference gain was substantial (+3.5 cm; 134%), indicating that PMMA produces greater absolute augmentation than temporary fillers. In contrast, Kim et al. (2025) found that the PMMA group had the lowest overall satisfaction despite the largest volumetric gain, reflecting the negative impact of aesthetic irregularities on patient-reported outcomes.

The most clinically significant aspect of PMMA is its permanence: unlike HA, no pharmacological agent can dissolve it, rendering late complications — granulomas and irregularities — dependent on surgically complex correction (Li et al., 2024; Trost et al., 2024). Kim et al. (2015) reported no serious adverse events over 18 months with Lipen-10 (PMMA + cross-linked dextran), though the small sample (n = 20) substantially limits the external validity of this finding.

3.3.4 Autologous fat (lipofilling)

Penile lipofilling was addressed in three studies. The systematic review by Falagario et al. (2024) documented fat reabsorption rates of 30–80%, which represents its principal clinical limitation and necessitates repeated procedures. Palpable nodules and asymmetries were frequently reported. The most serious complication — a fatal fat embolism — was described as an isolated case by Pignanelli et al. (2025), representing a relevant safety signal. The review by Romero-Otero et al. (2021) confirmed high reabsorption rates and cosmetic complications as the central limitations of autologous fat. Despite the intuitive appeal of using the patient's own tissue, the lack of technical standardization, unpredictable outcomes, and risk of serious systemic complications position lipofilling at a less favorable risk-benefit profile than HA.

3.3.5 Silicone implants (Penuma) and liquid silicone

Solid subcutaneous silicone implants — particularly the Penuma device — were addressed in three studies. Pignanelli et al. (2025) reported seroma in 4.8% of cases, infection in 3.3%, and the characteristic phenomenon of distal flaring. Falagario et al. (2024) highlighted the scarcity of long-term data and the risks of erosion and infection. The SMSNA concluded that available safety data for Penuma are insufficient to justify its broad recommendation outside research protocols (Trost et al., 2024).

Injectable liquid silicone carries a radically different risk profile. Pang et al. (2024) identified liquid silicone as the most common substance (45.7%) among clandestine materials in their single-center cohort of 35 patients. In a parallel systematic review conducted by the same authors — encompassing 887 screened articles — paraffin emerged as the most frequent agent overall (47.7%), followed by liquid silicone (15.8%). Regardless of the data source, 91.4% of the cohort patients and 78.8% of those identified in the systematic review required surgical intervention. Li et al. (2024) classify injectable liquid silicone among materials with an unacceptable risk profile, associating its use with granulomas, erectile dysfunction, and tissue necrosis.

3.3.6 Unregulated substances and clandestine self-injection

Unregulated substances — liquid paraffin, petroleum jelly, mineral oil, metallic mercury, and their derivatives — represent the most severe end of the complication spectrum. In the Pang et al. (2024) cohort, 91.4% of patients required surgery, with three cases (8.6%) of penile necrosis requiring urgent debridement. Pignanelli et al. (2025) and Li et al. (2024) describe paraffinoma as one of the most debilitating sequelae: a chronic, progressive, deforming foreign-body reaction resulting in penile lymphedema, diffuse tissue sclerosis, and frequently irreversible functional loss. Romero-Otero et al. (2021) confirmed that procedures with unregulated materials produce severe complications that differ in nature — not merely in degree — from those associated with approved fillers administered by trained practitioners.

4. Discussion

4.1 Hyaluronic acid as the safety benchmark among injectable fillers

The combined analysis of the 17 included studies supports, with reasonable consistency, that hyaluronic acid represents the injectable material with the best-documented safety profile for penile augmentation. This conclusion emerges from multiple converging levels of evidence: the meta-analysis by Kusumaputra et al. (2023) (Level I), the RCTs by Ahn et al. (2022) and Yang et al. (2020) (Level II), the prospective cohorts by Zhang et al. (2022) and Quan et al. (2021) (Level IV), and the comprehensive reviews by Salloum et al. (2021), Romero-Otero et al. (2021), Li et al. (2024), and Schifano et al. (2023). The consistency of this finding across different study designs, countries, and independent research groups strengthens its validity, though it remains constrained by the absence of follow-up data beyond five years.

The pharmacological property that most substantiates HA's safety superiority is its reversibility by hyaluronidase. No other material evaluated in this review offers a comparable mechanism of pharmacological dissolution in the event of complications. PMMA requires surgically complex removal when granulomas develop; autologous fat undergoes unpredictable reabsorption with no corrective option beyond repeat procedures; and clandestine materials produce progressive tissue destruction correctable only by extensive debridement or reconstructive surgery. HA's reversibility thus constitutes a structural safety differentiator that places it in a distinct category from all other fillers analyzed — not merely a clinical convenience.

4.2 HA versus PLA: comparable efficacy, distinct tradeoffs

Direct comparisons between HA and PLA were possible in four studies (Ahn et al., 2022; Kim et al., 2025; Kusumaputra et al., 2023; Yang et al., 2020). Both materials produce mean circumference gains of 2 to 2.5 cm, but with distinct durability-safety tradeoffs. PLA degrades more slowly than HA (Yang et al., 2020; Yang et al., 2017), which is advantageous in terms of result longevity but requires accepting a higher frequency of palpable nodules — especially in extended follow-up — and greater post-procedural pain intensity (Ahn et al., 2022; Yang et al., 2020). HA requires more frequent reapplication to maintain results but offers the reassurance of pharmacological reversal.

The finding by Ahn et al. (2022) of improved premature ejaculation symptoms in a subset of HA patients — possibly related to alterations in penile superficial sensitivity induced by the filler — remains preliminary and requires dedicated investigation. However, it opens a potential therapeutic indication beyond purely cosmetic augmentation that warrants exploration in future controlled trials.

4.3 The PMMA dilemma: greater augmentation, disproportionate risk

PMMA occupies a paradoxical position in this literature: the Casavantes et al. (2016) series demonstrates the greatest absolute circumference gain among all evaluated injectables (+3.5 cm), yet the same series reports irregularities in 52% of

patients, and Kim et al. (2025) show that, despite a larger volumetric gain, PMMA users had the lowest overall satisfaction among the three materials compared. This dissociation between dimensional gain and patient satisfaction highlights that aesthetic quality of outcome — free from visible irregularities — carries equal or greater weight than raw dimensional improvement.

The permanent nature of PMMA amplifies the clinical significance of every complication: granulomas and contour irregularities do not resolve spontaneously, do not respond to pharmacological treatment, and require technically demanding surgical correction (Li et al., 2024; Trost et al., 2024). Taken together, the available data do not support PMMA as a first-line option for penile augmentation in clinical practice, particularly when temporary fillers with superior safety profiles are available.

4.4 Autologous fat and silicone implants: between intuitive appeal and clinical limitation

Autologous fat is intuitively appealing because it uses the patient's own tissue and avoids exogenous agents. In practice, however, reabsorption rates of 30–80% (Falagario et al., 2024) render outcomes unpredictable, asymmetries and nodules are frequent, and the isolated case of fatal fat embolism reported by Pignanelli et al. (2025) underscores that autologous origin does not equate to absence of risk. The solid silicone implant Penuma represents a subcutaneous, non-injectable approach whose outcomes depend fundamentally on operator experience. The SMSNA's conclusion that current evidence is insufficient to justify broad adoption outside research protocols (Trost et al., 2024) is reinforced by the absence of randomized studies on the device and the concentration of available data in limited-expertise centers.

4.5 Clandestine substances: a neglected public health crisis

The self-injection of unregulated substances constitutes a public health phenomenon of underestimated impact. The finding that 91.4% of the Pang et al. (2024) cohort required surgical intervention — with 8.6% presenting penile necrosis — illustrates the clinical magnitude of this practice. Critically, complications from paraffin and liquid silicone are not simply more severe versions of approved filler complications; they are qualitatively different, progressing chronically and irreversibly in ways that frequently result in permanent erectile dysfunction and sensory loss. The sociocultural context driving self-injection — digital misinformation, stigma surrounding formal medical care, inadequate market regulation, and the high cost of approved procedures — must be addressed through public health interventions that extend beyond individual clinical encounters.

4.6 The psychological dimension: non-negotiable, yet systematically neglected

The SMSNA unequivocally contraindicates any penile enhancement procedure in men with uncontrolled BDD or PDD (Trost et al., 2024), in alignment with the EAU's 2023 recommendation for mandatory psychological evaluation in men with objectively normal penile measurements who request augmentation (Falcone et al., 2023). This is a structural requirement, not a peripheral recommendation: performing any intervention in a patient with untreated dysmorphophobia will not resolve the underlying dissatisfaction and may precipitate an escalating cycle of further procedures with increasing risk.

Critically, none of the primary studies included in this review used validated dysmorphophobia screening instruments as participant selection criteria — a significant methodological gap that limits assessment of the true impact of these procedures on long-term sexual satisfaction and psychological well-being. Future trials must treat patient-reported psychological outcomes as primary endpoints.

4.7 Limitations of the evidence base and future directions

The evidence base on penile filling remains predominantly of low methodological quality. Only two Level II studies (RCTs) were identified, and the two Level I meta-analyses were built upon a small number of primary trials. Additional

methodological concerns include the lack of outcome blinding in some RCTs, heterogeneity in injection protocols, absent consensus definitions of 'complication' and 'adverse event,' and predominantly short follow-up periods (under two years). The geographic concentration of primary studies in Asian populations — particularly South Korean — limits the generalizability of findings across ethnic groups. Systematic reviews by Romero-Otero et al. (2021) and Salloum et al. (2021) explicitly identified the absence of formal clinical guidelines for any penile augmentation technique, underscoring the urgent need for multicenter RCTs with long-term follow-up, consensus outcome instruments, and standardized protocols.

With regard to the present review's own limitations: publication bias cannot be excluded, as studies reporting serious complications may not be submitted to or accepted by indexed journals; the gray literature was not systematically searched; and follow-up periods in the included primary studies are predominantly under two years, precluding conclusions about long-term material safety. These limitations are inherent to the integrative review design and should be interpreted alongside the findings.

5. Conclusion

Hyaluronic acid presents the most favorable safety profile among the injectable materials currently used for penile augmentation, a finding supported by convergent evidence across multiple study designs and independent research groups. Its pharmacological reversibility by hyaluronidase constitutes a structural safety advantage that no other evaluated material can replicate, and it should be regarded as the reference standard against which alternative agents are compared.

Polylactic acid represents a viable second-line option, offering greater durability at the cost of a modestly higher rate of local adverse events. Polymethylmethacrylate, despite producing the greatest absolute circumference gains, carries a disproportionate risk of irreversible irregularities and should not be offered outside strictly controlled, IRB-approved research settings. Unregulated substances — paraffin, liquid silicone, and mineral oil — produce qualitatively distinct and frequently catastrophic complications, and their use under any circumstance is unjustifiable.

Beyond material selection, the findings of this review reinforce two non-negotiable clinical imperatives: rigorous patient selection and mandatory psychological screening prior to any intervention, given the well-documented association between dysmorphic disorders and poor procedural outcomes. Performing augmentation procedures in patients with untreated body dysmorphic disorder or penile dysmorphic disorder does not resolve the underlying dissatisfaction and may initiate an escalating cycle of interventions with compounding risk.

Finally, the accelerating commercial expansion of penile augmentation procedures stands in troubling contrast to the still-limited robustness of the supporting scientific literature. Well-designed multicenter randomized controlled trials with long-term follow-up and standardized outcome definitions are urgently needed to establish evidence-based clinical guidelines and ensure that practice advances in step with the science.

References

Ahn, S. T., Shim, J. S., Bae, W. J., Kim, S. W., Kim, J. J., & Moon, D. G. (2022). Efficacy and safety of penile girth enhancement using hyaluronic acid filler and the clinical impact on ejaculation: A multicenter, patient/evaluator-blinded, randomized active-controlled trial. World Journal of Men's Health, 40(2), 299–307. https://doi.org/10.5534/wjmh.210012

Brasil. Ministério da Saúde. Conselho Nacional de Saúde. (2016). Resolução n. 510, de 7 de abril de 2016. Dispõe sobre as normas aplicáveis a pesquisas em Ciências Humanas e Sociais. Diário Oficial da União, (98), 44.

Casavantes, L., Lemperle, G., & Morales, P. (2016). Penile girth enhancement with polymethylmethacrylate-based soft tissue fillers. Journal of Sexual Medicine, 13(9), 1414–1422. https://doi.org/10.1016/j.jsxm.2016.07.003

Falagario, U. G., Piramide, F., Pang, K. H., Durukan, E., Tzelves, L., et al. (2024). Techniques for penile augmentation surgery: A systematic review of surgical outcomes, complications, and quality of life. Medicina, 60(5), 758. https://doi.org/10.3390/medicina60050758

Falcone, M., Bettocchi, C., Carvalho, J., et al. (2023). European Association of Urology guidelines on penile size abnormalities and dysmorphophobia: Summary of the 2023 guidelines. European Urology Focus. https://doi.org/10.1016/j.euf.2023.08.012

Kim, D. W., Jeong, H. C., Ko, K., Yang, D. Y., Kim, J. K., Lee, S. H., Kim, T. H., & Lee, W. K. (2025). Which dermal filler is better for penile augmentation for aesthetic purposes? A prospective, single-surgeon study based on real-world experience. World Journal of Men's Health, 43(2), 428–436. https://doi.org/10.5534/wjmh.240105

Kim, M. T., Ko, K., Lee, W. K., Kim, S. C., & Yang, D. Y. (2015). Long-term safety and longevity of a mixture of polymethyl methacrylate and cross-linked dextran (Lipen-10) after penile augmentation: Extension study from six to 18 months of follow-up. World Journal of Men's Health, 33(3), 202–208. https://doi.org/10.5534/wjmh.2015.33.3.202

Kusumaputra, A., Setiawan, M. R., Soebadi, M. A., & Wirjopranoto, S. (2023). Efficacy and complications of hyaluronic acid and polylactic acid for penile augmentation: A systematic review and meta-analysis. Annals of Medicine and Surgery, 85(9), 4531–4538. https://doi.org/10.1097/MS9.0000000000001094

Li, M. K., Shahinyan, G., Sigalos, J. T., et al. (2024). Injectable penile enhancement procedures: A review of agents, risks, and complications. Urology, 188, 163. https://doi.org/10.1016/j.urology.2024.05.013

Melnyk, B. M., & Fineout-Overholt, E. (2019). Evidence-based practice in nursing & healthcare: A guide to best practice (4th ed.). Wolters Kluwer.

Mendes, K. D. S., Silveira, R. C. C. P., & Galvão, C. M. (2008). Revisão integrativa: Método de pesquisa para a incorporação de evidências na saúde e na enfermagem. Texto & Contexto – Enfermagem, 17(4), 758–764. https://doi.org/10.1590/S0104-07072008000400018

Page, M. J., McKenzie, J. E., Bossuyt, P. M., Boutron, I., Hoffmann, T. C., Mulrow, C. D., et al. (2021). The PRISMA 2020 statement: An updated guideline for reporting systematic reviews. BMJ, 372, n71. https://doi.org/10.1136/bmj.n71

Pang, K. H., Randhawa, K., Tang, S., Fallara, G., Katelaris, A., et al. (2024). Complications and outcomes following injection of foreign material into the male external genitalia for augmentation: A single-centre experience and systematic review. International Journal of Impotence Research, 36(5), 498–508. https://doi.org/10.1038/s41443-023-00675-8

Pearlman, A. M., Tatem, A., Zorn, K. C., & Moore, W. A. (2024, August). The evolving landscape of penile girth enhancement. AUA News. https://auanews.net/issues/articles/2024/august-extra-2024

Pereira, A. S., et al. (2018). Metodologia da pesquisa científica [free ebook]. Editora da UFSM.

Pignanelli, M., Williams, J. M., Fernandez Crespo, R. E., Britt, J., Parker, J., & Carrion, R. (2023, December). An update on penile girth enhancement procedures. AUA News. https://auanews.net/issues/articles/2023/december-extra-2023

Pignanelli, M., Williams, J. M., Fernandez Crespo, R. E., Britt, J., Parker, J., & Carrion, R. (2025). Complications and management of penile enhancement procedures. Translational Andrology and Urology, 14(10), 3367–3376. https://doi.org/10.21037/tau-23-519

Quan, Y., Gao, Z. R., Dai, X., Kuang, L., Zhang, M., Li, Q., et al. (2021). Complications and management of penile augmentation with hyaluronic acid injection. Asian Journal of Andrology, 23(4), 392–395. https://doi.org/10.4103/aja.aja_78_20

Risemberg, R. I. C., et al. (2026). A importância da metodologia científica no desenvolvimento de artigos científicos. E-Acadêmica, 7(1), e0171675. https://eacademica.org/eacademica/article/view/675

Romero-Otero, J., Manfredi, C., Ralph, D., Osmonov, D., Verze, P., Castiglione, F., et al. (2021). Non-invasive and surgical penile enhancement interventions for aesthetic or therapeutic purposes: A systematic review. BJU International, 127(3), 269–291. https://doi.org/10.1111/bju.15145

Salloum, A., Bazzi, N., & Haber, R. (2021). Nonsurgical methods for penile augmentation: A systematic review. Dermatologic Surgery, 47(3), e81–e85. https://doi.org/10.1097/DSS.0000000000002816

Santos, C. M. C., Pimenta, C. A. M., & Nobre, M. R. C. (2007). A estratégia PICO para a construção da pergunta de pesquisa e busca de evidências. Revista Latino-Americana de Enfermagem, 15(3), 508–511. https://doi.org/10.1590/S0104-11692007000300023

Schifano, N., Capogrosso, P., Antonini, G., Baldini, S., Scroppo, F., Salonia, A., et al. (2023). The application of hyaluronic acid injections in functional and aesthetic andrology: A narrative review. Gels, 9(2), 118. https://doi.org/10.3390/gels9020118

Sharp, G., Fernando, A. N., Kyron, M., Oates, J., & McEvoy, P. (2022). Motivations and psychological characteristics of men seeking penile girth augmentation. Aesthetic Surgery Journal, 42(11), 1305–1315. https://doi.org/10.1093/asj/sjac112

Sharp, G., Fernando, A. N., Oates, J., & McEvoy, P. (2023). Men's experiences and psychological outcomes of nonsurgical medical penile girth augmentation: A preliminary prospective study. Aesthetic Surgery Journal, 43(2), 181–191. https://doi.org/10.1093/asj/sjac243

Sousa, L. M. M., Marques-Vieira, C. M. A., Severino, S. S. P., & Antunes, A. V. (2017). A metodologia de revisão integrativa da literatura em enfermagem. Revista de Investigação em Enfermagem, 21(2), 17–26.

Trost, L., Watter, D. N., Carrier, S., Khera, M., Yafi, F. A., Bernie, H. L., et al. (2024). Cosmetic penile enhancement procedures: An SMSNA position statement. Journal of Sexual Medicine, 21(6), 573–578. https://doi.org/10.1093/jsxmed/qdae045

Whittemore, R., & Knafl, K. (2005). The integrative review: Updated methodology. Journal of Advanced Nursing, 52(5), 546–553. https://doi.org/10.1111/j.1365-2648.2005.03621.x

Yang, D. Y., Jeong, H. C., Ahn, S. T., Bae, W. J., Moon, D. G., et al. (2020). A comparison between hyaluronic acid and polylactic acid filler injections for temporary penile augmentation in patients with small penis syndrome: A multicenter, patient/evaluator-blind, comparative, randomized trial. Journal of Sexual Medicine, 17(1), 133–141. https://doi.org/10.1016/j.jsxm.2019.09.018

Yang, D. Y., Ko, K., Lee, S. H., Moon, D. G., Kim, J. W., & Lee, W. K. (2017). Efficacy and safety of a newly developed polylactic acid microsphere as an injectable bulking agent for penile augmentation: 18-months follow-up. International Journal of Impotence Research, 29(4), 136–141. https://doi.org/10.1038/ijir.2017.8

Yianni, J., & Veale, D. (2022). Penile dysmorphic disorder (PDD). In Textbook of rare sexual medicine conditions (pp. 19–35). Springer International Publishing. https://doi.org/10.1007/978-3-030-98263-8_3

Zhang, X. W., Zhang, C. L., Quan, Y., Li, H., Li, Q., Bai, W. J., et al. (2022). Penile augmentation with injectable hyaluronic acid gel: An alternative choice for small penis syndrome. Asian Journal of Andrology, 24(6), 601–606. https://doi.org/10.4103/aja.aja_24_22