Appendix A: Full Guideline methodology
METHODS

The guideline was developed according to the ASPS Guideline Methodology, found here: http://tinyurl.com/ASPSgdlnmeth.

Work Group Selection Process

The 2012 guideline was revised by a 15-person multi-disciplinary work group consisting of members of the ASPS, the American Society of Breast Surgeons (ASBS), the American Physical Therapy Association (APTA), and a patient representative.

All stakeholder organizations were invited to nominate members from their respective organizations to serve on the Work Group, following their own policies and procedures for addressing content expertise, guideline experience, and potential conflicts of interest. One patient representative was included on the panel to provide insight related to patient values and preferences. An ASPS quality department staff member managed the project and provided expertise in clinical practice guideline development methodology. Four consultants from the American Academy of Orthopaedic Surgeons (AAOS) were hired to conduct the literature search and systematic review. Internal ASPS quality staff supplemented this literature review throughout this process to assure a comprehensive review of available studies.

All member workgroup applicants were required to submit a conflict of interest disclosure form for membership consideration. The co-chairs were free of all relevant conflicts of interest for the duration of the project in accordance with the ASPS Conflict of Interest policy.

Clinical Question Development

Work Group members used a consensus-based approach to select the clinical questions to be addressed in this evidence-based guideline. Work Group members reviewed the original 2012 guideline and determined whether they wanted to retain those questions, revise them, or add additional questions. At the face to face introductory meeting, clinical questions were developed and selected based on the

scope and importance to patient outcomes. The patient population for the guideline is post-menarche female patients with symptomatic breast hypertrophy; the work group felt strongly that this guideline should apply to patients under the age of 18 who meet the criteria. A review of the literature was unable to determine a specific age cut-off, as puberty begins at many different ages. Patient-related outcomes of interest were determined to be infection rate, other surgical complications (e.g., hematoma, seroma), adverse events, pain, wound healing, and patient satisfaction. The following 6 clinical questions were constructed at the introductory meeting and refined by the consultant.

1) In female patients with symptomatic breast hypertrophy, does reduction mammaplasty reduce symptoms and improve post-treatment outcomes as compared to non-operative treatment? (Corresponds to Recommendation 1)
2) In female patients with symptomatic breast hypertrophy undergoing reduction mammaplasty, which key risk factors are associated with increased complications and decreased patient satisfaction? (Corresponds to Recommendations 1-3)
3) In female patients with symptomatic breast hypertrophy, does superomedial pedicle reduction mammaplasty reduce symptoms and improve post-treatment outcomes compared to inferior pedicle reduction mammaplasty? (Corresponds to Recommendation 4)
4) In female patients with symptomatic breast hypertrophy undergoing reduction mammaplasty, do peri-operative surgical adjuncts, such as the use of drains, antibiotics, and tumescent solutions, reduce symptoms and improve post-surgical outcomes? (Corresponds to Recommendations 5, 6, 8, 10)
5) In female patients with symptomatic breast hypertrophy undergoing reduction mammaplasty, does adjunctive pain management reduce narcotic use and improve postoperative outcomes? (Corresponds with Recommendation 7)
6) In female patients with symptomatic breast hypertrophy undergoing reduction mammaplasty, are patient age or clinical history associated with increased rates of malignancy, thus mandating a tailored approach to pathological examination? (Corresponds with Recommendation 9)

Literature Search

Between 2018 and 2019, multiple literature searches were performed to identify relevant studies published from 1990 to 2019. The initial search dates were January 1, 1990 through November 16, 2018, with a subsequent updated and final search on May 8, 2019. Electronic searches of PubMed, Embase,

and Cochrane Central Register of Controlled Trials (CENTRAL) were performed using appropriate combinations of the following MEDLINE Medical Subject Headings (MeSH) terms and keywords, as permitted by the search functionalities of each database/journal:

- MeSH terms (used in PubMed only): “Mammaplasty” [MeSH], “Hypertrophy” [MeSh], “Breast” [MeSH],
- Keywords: breast hypertrophy, macromastia, gigantomastia, breast reduction, mammaplasty, mastoplasty

Initial study selection for each clinical question was performed by 2 reviewers with a multi-level screening process. Level I screening involved title and abstract review to identify potentially relevant studies for inclusion in level II screening. Level II screening involved full-text review of articles to confirm relevance given the inclusion and exclusion criteria below:

Inclusion Criteria:

- Published since 1990 (01/01/1990 – 05/08/2019)
- English language
- Reported a meta-analysis/systematic review, randomized controlled trial (RCT), prospective or retrospective cohort/comparative, case-control, or case series
- Reported outcomes of interest for clinical questions
- Included at least 20 patients per study and/or per arm of study
- Human subjects

Relevant clinical practice guidelines and systematic reviews underwent a separate bibliographic screen, as a cross-reference to ensure no relevant literature was excluded during the search process. These articles were screened as described above. Duplicate articles were eliminated. Studies meeting inclusion criteria were assessed for methodologic quality, as described below. Excluded studies and their reasons for exclusion were documented for review by the Work Group to confirm the final rejection or to reconsider the study for inclusion. See Appendix Figure 1 for details. Additional references were

included in this review if considered necessary for background or discussion; however, these references were not critically appraised or used in the development of recommendation statements.

Critical Appraisal of Evidence

A modified version of the GRADE (Grading of Recommendations Assessment, Development, and Evaluation) process was used to evaluate the methodologic quality of clinical studies and the strength of clinical evidence for the purposes of developing clinical practice guidelines and performance measures. GRADE determines the quality of evidence across outcomes rather than assessing each study individually. The quality of evidence for each outcome is initially determined by study design. The evidence from randomized controlled trials (RCTs) is assigned as high-quality evidence, while evidence from observational studies begin as low quality. From there, high quality evidence can be downgraded, and low-quality evidence can be graded up or down based on the following: risk of bias; publication bias; imprecision related to the estimate of effect; inconsistency across studies; and indirectness related to the clinical questions. The full Quality Appraisal and Evidence Tables can be found at: http://links.lww.com/PRS/E941.

Grading of Recommendations

Clinical practice recommendations were developed using BRIDGE-wiz (Building Recommendations in a Developers' Guideline Editor) software[1], with consideration of the following 4 factors: 1) level of evidence (study quality); 2) assessment of benefits versus harms; and 3) patient preferences; 4) feasibility. Work Group members jointly drafted statements for each recommendation during a face to face meeting in the Spring of 2019 and refined these during subsequent conference calls and online discussions. After each meeting, members had an opportunity to further comment and suggest revisions of the draft recommendations until unanimous consensus was achieved for each recommendation

statement. Each recommendation in this guideline is accompanied by a grade indicating the strength of the recommendation, which was determined by considering the overall level of evidence supporting the recommendation and the judgment of the guideline developers. See Figure 1 and Table 1 in the manuscript for explanations.

Peer Review and Public Comment Process

The draft guideline was peer reviewed by members and/or committees of the ASPS, the ASBS, the APTA (all groups represented on the work group), and the College of American Pathologists (invited to review for the section on pathology). Peer reviewers were invited to review and provide feedback on the validity, generalizability, and clarity of the draft guideline using the Appraisal of Guidelines for Research & Evaluation Global Rating Scale (AGREE-GRS) instrument (Brouwers 2010), as well as asked to review the clinical content and attest to either support, support with modifications, or not support individual recommendations. The draft guideline was also posted on the ASPS website for a 30-day public comment period, as well as distributed through the Council on Medical Specialty Societies (CMSS) Clinical Practice Guidelines email distribution list. Comments were reviewed by the full Workgroup and assessed for relevance. Revisions were made when the workgroup agreed that the modifications would add clarity or value to the document. Reviewer recommendations without evidentiary support are not able to be considered.

Guideline Approval Process

After the peer review and public comment process, the guideline draft was reviewed and modified by the Work Group after consideration of peer review and public comments. The final guideline was approved by the Executive Committee of the American Society of Plastic Surgeons during their August 2020 meeting.

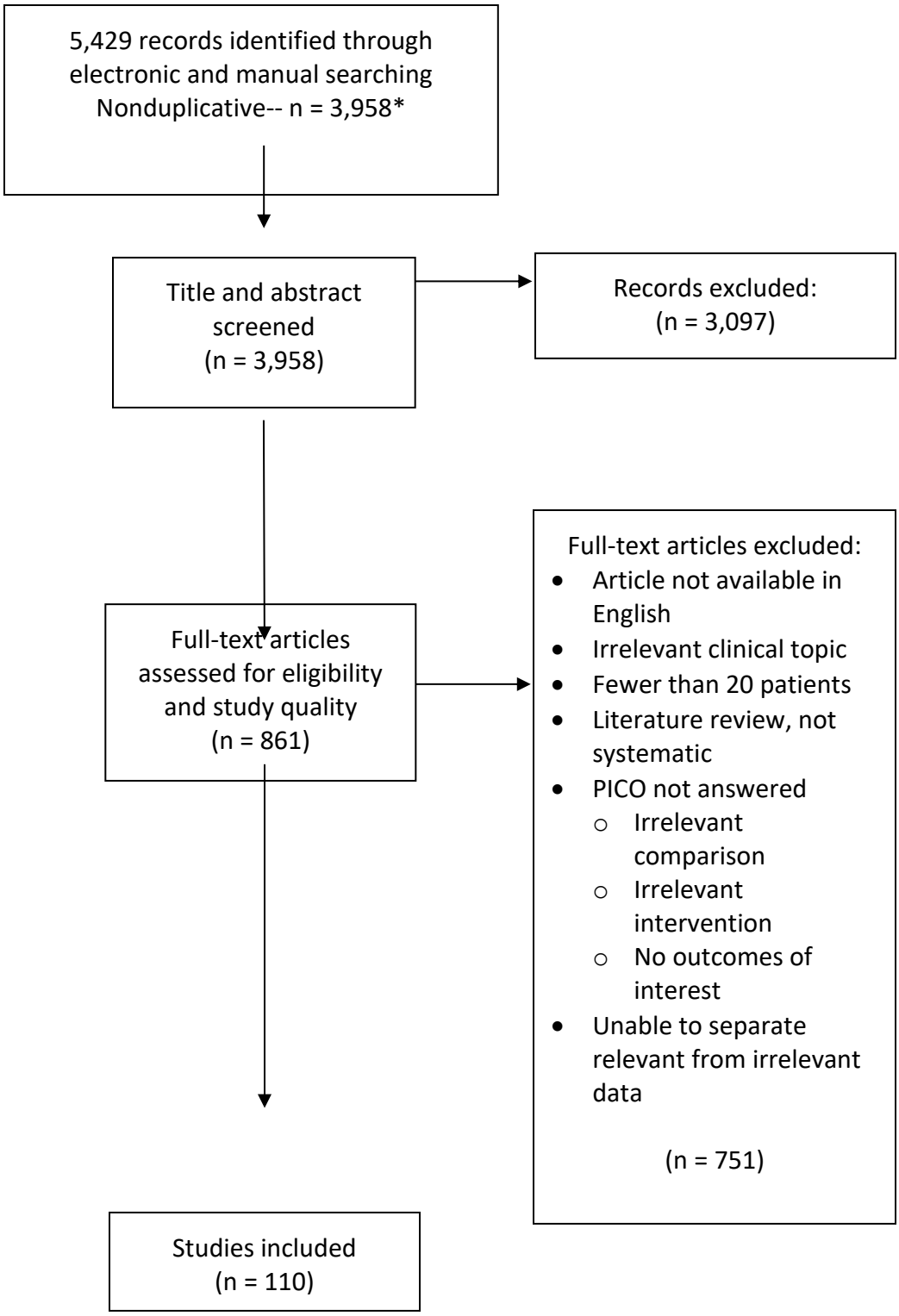
Plan for Updating Guideline

In accordance with the inclusion criteria of the ECRI Guidelines Trust, this guideline will be updated within 5 years or when newly published evidence may result in a change to current recommendations. ASPS uses a digital platform (P.E.E.R.) to store literature and data, thereby facilitating an efficient updating process.

RESULTS

A total of 5,429 studies were identified from databases during the literature search and 3,958 were screened after excluding duplicate records. After both levels of screening and quality critical appraisal were performed, 114 studies were selected for final data analysis within the systematic review and were used as the evidence base for this guideline (Figure 2). The recommendations listed below were based on low, moderate, and high-quality evidence.

Appendix Figure 1. Literature Search Attrition Diagram



* Includes 3 studies that were not initially captured by the search and were identified by manually searching the bibliographies of relevant systematic reviews.

[1] Shiffman RN, Michel G, Rosenfeld RM, Davidson C. Building better guidelines with BRIDGE-Wiz: development and evaluation of a software assistant to promote clarity, transparency, and implementability. J Am Med Inform Assoc. 2012;19(1):94-101.