

Autologous reconstruction following nipple sparing mastectomy: a comprehensive review of the current literature

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Abstract: As surgical methods continue to evolve and patients become more educated consumers of their medical care, both oncologic breast surgeons and reconstructive plastic surgeons should understand the current options for surgical management of breast cancer. This review evaluates the current autologous breast reconstruction options following nipple sparing mastectomy (NSM). A comprehensive review of the current literature discussing autologous reconstruction after NSM was performed. Fat grafting alone has been used to reconstruct small to medium sized-breasts over multiple injection sessions. Goldilocks mastectomy-like reconstructions can be used for larger, more ptotic breasts. Pedicled latissimus dorsi (LD) flaps can be used, but usually need to be modified to ensure sufficient breast volume. While the lower abdominal tissue remains the most common donor site in free tissue transfer, other donor sites can be used if there is insufficient volume or inadequate perforators. Periareolar incisions are associated with the highest rates of overall complications and nipple areola complex necrosis. It has not been determined whether implant-based or autologous reconstructions have lower complication rates. Both prior radiation and large, ptotic breasts present unique challenges during reconstruction. Overall, there is a high rate of patient satisfaction with breast reconstruction following NSM. Autologous breast reconstruction after NSM is a safe method of breast cancer surgical management with aesthetically excellent results. Multiple techniques have been described along the reconstructive ladder. Special consideration should be given to choices of incision, previously irradiated breasts, and large, ptotic breasts.

Keywords: Mastectomy; nipples; surgical flaps

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Background

Both oncologic surgical management of breast cancer and breast reconstruction have made significant advances over time. Breast cancer was described as early as the Edwin Smith papyrus (3000 BC), in which the ancient Egyptians concluded there was no cure for breast cancer (1). Roman physicians described surgical removal of breast tumors in the first century (2). In the modern surgical era, Halsted first

performed his radical mastectomy—removal of all breast tissue, pectoralis major muscle, and associated lymphatic tissue—in 1882 (3). Now at the forefront of oncologic breast surgery is the nipple sparing mastectomy (NSM). It has been found to be oncologically safe in patients without skin involvement, nipple-areola complex (NAC) involvement, inflammatory breast cancer, or bloody nipple discharge (4).

Autologous breast reconstruction options have evolved over time as well. In 1887, Verneuil described

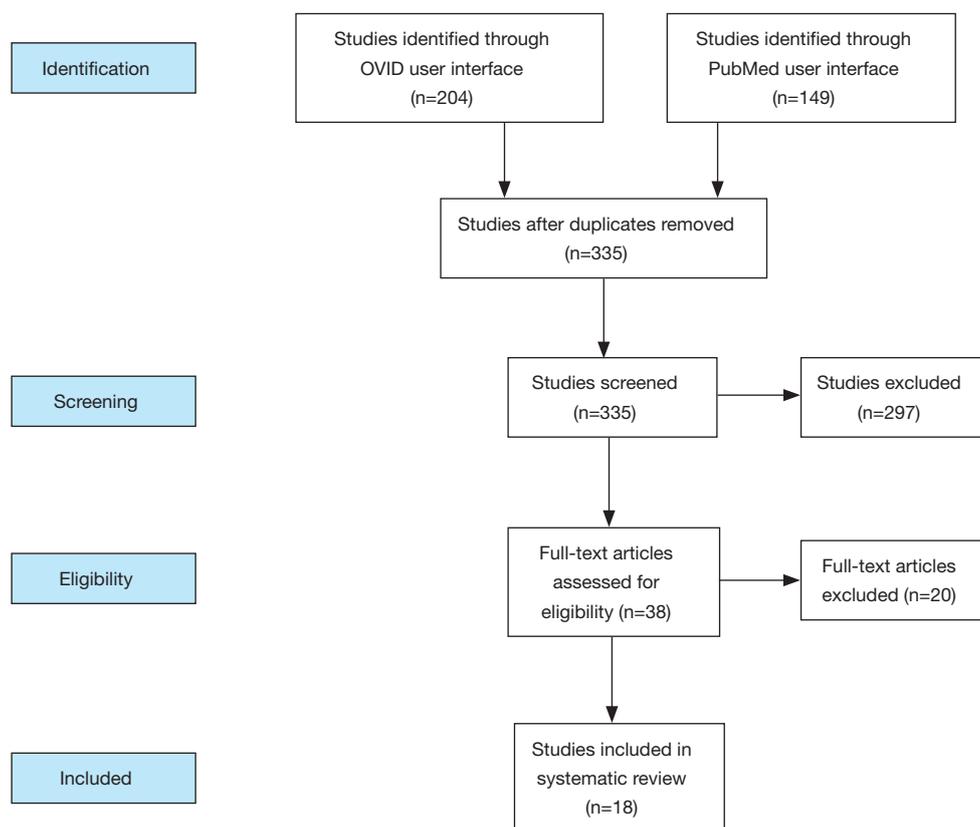


Figure 1 Selection process of peer-reviewed articles.

reconstructing a breast with a superiorly based pedicle of breast tissue from the contralateral breast (5). In 1982, Hartrampf *et al.* first described the pedicled transverse rectus abdominis musculocutaneous (TRAM) flap for breast reconstruction (6). In 1979, Holmstrom first described abdominally-based free tissue transfer in breast reconstruction (7). And in 1989, the deep inferior epigastric artery perforator (DIEP) flap was described by Koshima and Soeda (8).

As surgical methods continue to evolve, and as patients become more educated consumers of their medical care, both breast surgeons and reconstructive plastic surgeons should understand the current options for both surgical resection and reconstruction in the treatment of breast cancer. This review will evaluate the current autologous breast reconstruction techniques following NSM.

Methods

The MEDLINE database was queried using both the OVID and PubMed user interfaces. Within OVID, the Medical

Subject Headings (MeSH) “mastectomy”, “nipples”, and “surgical flaps” were exploded and combined with “and” modifiers, yielding 204 articles. Within PubMed, the search phrase “nipple sparing mastectomy autologous” yielded 149 results.

Potentially relevant abstracts were reviewed. Exclusion criteria were papers not in English, unavailable full texts, duplicates, or those that did not discuss autologous reconstruction after NSM. The remaining articles were thoroughly reviewed. Works cited within these papers, as well as supporting literature, were included within our review if deemed relevant.

Results

A total of 38 studies were included in the present review (*Figure 1* and *Table 1*). Various rungs of the reconstructive ladder (27) have been used for autologous breast reconstruction following NSM. This results section will work its way up the ladder, with the majority of the review dedicated to free tissue transfer.

Table 1 Articles included in this review

Type of reconstruction	Reference	Study design	No. of patients [No. of breasts]	Mean age (year)	Mean follow up (months)	Pre-reconstruction radiation (%)	Total complication rate (%)
Autologous fat grafting	Longo <i>et al.</i> , 2014 (9)	Prospective, cohort	21 [29]	37.6	26.4	47.60	0
Local tissue rearrangement	Vrekoussis <i>et al.</i> , 2013 (10)	Retrospective,	1 [2]	55	1.3	0	0
Pedicled flap	Denewer and Farouk, 2007 (11)	Retrospective, case series	41 [41]	41.5	7.9	N/A	43.80
Pedicled flap + autologous fat grafting	Santaneli di Pompeo <i>et al.</i> , 2014 (12)	Retrospective, case series	23 [25]	52.3	18.3	N/A	21.70
	Niddam <i>et al.</i> , 2016 (13)	Retrospective, case series	20 [20]	55.2	12.8	N/A	15
	Zhu <i>et al.</i> , 2016 (14)	Retrospective, case series	10 [14]	55	14.3	N/A	30%
Free tissue transfer	Fujimoto <i>et al.</i> , 2016 (15)	Retrospective, case series	100 [100]	N/A	N/A	N/A	N/A
	Satake <i>et al.</i> , 2016 (16)	Retrospective, case study	1 [1]	46	N/A	0	0
	Colwell <i>et al.</i> , 2014 (17)	Retrospective, cohort	N/A [11]	N/A	N/A	N/A	N/A
	Frey <i>et al.</i> , 2017 (18)	Retrospective, cohort	N/A [263]	47.7	43.3	6.80	31.80
	Levine <i>et al.</i> , 2013 (19)	Retrospective, case series	84 [134]	N/A	N/A	N/A	32.50
	Lee <i>et al.</i> , 2013 (20)	Prospective, cohort	70 [70]	41.5	N/A	0	N/A
	Andree <i>et al.</i> , 2012 (21)	Retrospective, case series	N/A	N/A	N/A	N/A	N/A
	Alperovich <i>et al.</i> , 2014 (22)	Retrospective, case series	N/A [8]	N/A	N/A	100	N/A
	Schneider <i>et al.</i> , 2012 (23)	Retrospective, case series	19 [34]	47.4	N/A	5	10
	DellaCroce <i>et al.</i> , 2015 (24)	Retrospective, case series	70 [116]	49.6	N/A	4.30	15.10
	Cho <i>et al.</i> , 2015 (25)	Retrospective, case series	85 [89]	44.3	N/A	8.20	N/A
	Raghavan <i>et al.</i> , 2015 (26)	Prospective, cohort	31 [48]	48.2	N/A	20.80	22.90

Autologous fat grafting

In 2014, Longo *et al.* published a 21-patient cohort study using fat grafting alone to reconstruct the breast following NSM (9). Their indications included: patient refusal of implant reconstruction, patients' breasts were small or medium-sized, and there was a contraindication to free tissue transfer (e.g., insufficient donor site volume or previous surgeries precluding the use of common donor sites). Their surgical algorithm consisted of multiple fat grafting sessions, with a 3-month interval between each round of fat transfer. In non-irradiated patients, the first session was within 6 months of the oncologic resection. In irradiated patients, the group waited a minimum of 6 months after the completion of radiation before proceeding with fat grafting. Fat was harvested using a dry method, processed using centrifugation, and then was injected in small aliquots in the subcutaneous and submuscular planes. Intraoperative overcorrection was performed after the initial session, as the authors expected a 20–30% resorption rate. All non-irradiated patients had three rounds of fat grafting, while the irradiated patients required four to six sessions. As can be expected, the authors reported that the tight retracted skin in irradiated breasts limited the volume of fat able to be injected per session. No complications were reported from the fat grafting. Blinded, independent plastic surgeons rated results of the irradiated and non-irradiated breasts as 3.50 and 3.82, respectively, on the global aesthetic scale by Harris *et al.*, in which 3 is good and 4 is excellent (28).

There has been concern that autologous fat grafting may increase patients' risk of cancer recurrence. *In vitro* studies have shown that adipocytes can stimulate breast cancer cells via various mechanisms (29); however, no increased clinical risk has been demonstrated in recent literature. Myckatyn *et al.* published a multicenter, case-control study in the US in 2017 comparing 225 patients with recurrence following immediate breast reconstruction with 972 random controls (30). The subset of patients reconstructed with fat grafting had an equivalent risk of recurrence compared to other patients, even after controlling for other variables. Petit *et al.* performed a cohort study in 2017 with 322 patients who had fat grafting reconstruction following oncologic surgery for invasive breast cancer (31). These were compared to a group of individually matched patients who did not receive fat grafting. No difference was seen between these two groups for local recurrence or distant metastases.

Local tissue rearrangement

In 2012, Richardson and Ma first described the Goldilocks mastectomy (32). This surgery begins with a skin sparing mastectomy performed via circumareolar or elliptical skin incisions. The redundant mastectomy skin within the markings of a standard Wise skin-reduction pattern (33) is deepithelialized and then used to create the new breast mound. In 2013, Vrekoussis *et al.* published a case report of a patient treated with bilateral NSM and reconstructed in a fashion similar to the Goldilocks mastectomy, except with preservation of the NAC (10). The patient had large, severely ptotic breasts. The breast tissue resection was accessed through the superior aspect of the markings, with the NAC maintained on an inferiorly-based dermal-subcutaneous pedicle. Due to a significant amount of fat remaining on the mastectomy skin flaps, the dermal-subcutaneous pedicles were able to reconstruct the breast mounds with a reasonable amount of volume. The only postoperative complication reported was transient bruising.

In 2016, Schwartz and Skowronski described a case of a patient with large ptotic breasts on whom they performed bilateral Goldilocks mastectomies with free NAC grafting (34). As these procedures rely solely on the volume of the mastectomy skin flaps, patients with small breasts and/or minimal ptosis are poor candidates for this type of reconstruction. In 2017, Schwartz and Skowronski suggested adding a second stage to their Goldilocks mastectomy with free NAC grafting in patients with moderate breast size (35). After the initial procedure, triangles of skin along the vertical limbs were deepithelialized and involuted, and fat grafting to the upper pole and retroareolar regions was performed to increase volume and improve shape.

Pedicled tissue

Pedicled flaps based on the thoracodorsal artery—either the latissimus dorsi (LD) muscle flap (with or without a skin paddle) or the thoracodorsal artery perforator (TDAP) flap—are commonly used to augment soft tissue coverage in implant-based breast reconstruction. With modifications to increase flap volume, these pedicled flaps have also been described in the setting of NSM (36), and may be used for total autologous breast reconstruction.

In 2007, Denewer and Farouk published their results from a case series of 41 patients reconstructed with unilateral, extended LD muscle flaps immediately following NSM (11). The incision for the NSM, described as “claw-

like” along the lateral half of the areola, with a lateral radial extension towards the axilla, allowed access to the thoracodorsal vessels. The pedicle was dissected along its origin at the subscapular artery towards its bifurcation. Both the dorsal branch supplying the LD muscle and the thoracic branch supplying the serratus anterior were included, and some of the subcutaneous fat was maintained on the muscle bellies in order to maximize volume. To ensure full mobilization, the LD was disinserted from the humerus, transposed to the anterior chest and the subcutaneous fat layer laid over the pectoralis major muscle. The LD muscle was then folded on itself before redraping the mastectomy skin flaps. No additional incisions were required on the back. Of the 41 patients, 90.2% had reconstructions independently rated as good or excellent at the 6-week postoperative mark. The most common complication in 14.6% of patients was donor site seroma formation, a well-known occurrence after the harvest of LD flaps.

In light of the potential for inadequate long-term reconstructed breast volume after atrophy of the LD flap, concurrent fat grafting can be performed. In 2014, Santanelli di Pompeo *et al.* described their technique of immediate fat grafting into the LD fascia and overlying adipose layers (12). In 23 patients (25 breasts), they injected an average of 101 mL of fat and reported no complications. In 2016, Niddam *et al.* reported fat injections into the pectoralis major muscle at the time of a pedicled LD flap in 20 patients undergoing unilateral breast reconstruction (13). Their mean volume of fat injected was 228 mL. Two patients required a secondary fat grafting procedure to correct asymmetry due to inadequate breast reconstruction volume. Zhu *et al.* reported using a multisite fat grafting technique at the time of a pedicled LD reconstruction (14). In 14 breasts (10 patients), an average of 176 mL of fat was distributed into the LD muscle, the adipose tissue overlying the LD, the mastectomy skin flaps, the pectoralis major muscle, and the serratus anterior muscle. Three patients required additional fat grafting.

Free tissue transfer

Free tissue transfer is the most common method of autologous reconstruction following NSM. Donor sites typically include the lower abdomen, buttocks, or thighs (posterior and medial), and the internal mammary or thoracodorsal systems most commonly serve as adequate recipient vessels. Fujimoto *et al.* described their donor site selection algorithm after NSM and skin sparing

mastectomies (15). Abdominally based flaps were avoided in patients desiring future pregnancies. In this cohort, posteromedial thigh flaps were used if the breast size was B cup or smaller. Superior and inferior gluteal artery perforator flaps were used if the tissue volume at the posterior thigh donor site was insufficient.

Satake *et al.*, in 2016, reported a unique case of reconstruction following NSM in a patient with inadequate abdominal, thigh, or buttock donor sites. An adipofascial flap based on a lumbar artery perforator (which was visualized on preoperative imaging) was harvested and anastomosed to the lateral thoracic vessels. A vein graft was required during the arterial anastomosis due to lack of pedicle length and a size mismatch (16).

Discussion

Type of incision

The type of incision used for NSM followed by autologous reconstruction needs to satisfy multiple criteria. It should preserve perfusion to the NAC, provide sufficient access to the recipient vessels for microvascular anastomosis, and allow for good cosmesis.

The perfusion of the NAC has been shown to depend on the type of incision used. In 2014, Colwell *et al.* analyzed their outcomes after reconstruction of 500 NSM based on incision type (17). Periareolar incisions were associated with the highest rate of total complications (21.1%) and NAC necrosis (10.5%). Inferolateral inframammary fold incisions were associated with the lowest total complications (8.5%) and NAC necrosis (0.8%).

In a 2017 study, Frey *et al.* analyzed the outcomes of 1,028 NSM reconstructions—both autologous and implant-based (18). While the most common incision utilized for implant-based reconstruction was along the inframammary fold, the vertical incision was most commonly used during autologous reconstruction. This vertical, infra-areolar incision was preferred by reconstructive surgeons, as it allowed for easier access to the internal mammary vessels while maintaining good cosmesis, especially after subsequent excision of the skin paddle.

In 2013, Levine *et al.* described their experience with NSM incision-types when reconstructing breasts with completely buried free flaps (19). While the lateral incision was easiest for the oncologic surgeons, the reconstructive team preferred an inframammary incision for small breasts with minimal ptosis and a vertical incision for larger, more

ptotic breasts. Secondary reductions and mastopexies allowed incorporation of this vertical scar.

Autologous versus prosthetic based reconstruction

Rates of autologous versus prosthetic reconstruction following NSM are highly variable, with institutional rates of autologous reconstruction as low as 2% (17), and as high as 54% (20). Findings have been mixed regarding the comparative complication rates of the two reconstructive modalities. In 2017 Frey *et al.* analyzed 1,028 NSM (18). A total of 51.8% (n=533) were reconstructed using tissue expanders, 25.6% (n=263) autologous-based, and 22.6% (n=232) direct-to-implant. Both the tissue expander and direct-to-implant groups had higher rates of minor cellulitis (P=0.0002 and 0.0051, respectively). The tissue expander group had less complete nipple necrosis and major mastectomy flap necrosis than the autologous-based group (P=0.0126 and <0.0001, respectively). The direct-to-implant group had higher rates of minor mastectomy flap necrosis and partial nipple necrosis compared to the autologous-based group (P=0.0425 and 0.0437, respectively).

In 2013 Lee *et al.* reviewed 130 NSM, 70 reconstructed using autologous tissue and 60 utilizing tissue expander-based reconstructions (20). The mastectomy skin flap necrosis rate was significantly lower in the autologous-based group in both univariate and multivariate analyses (P=0.034 and 0.024, respectively).

Prior irradiation

Special consideration should be given during autologous reconstruction following NSM in previously irradiated breasts. In a 2012 study by Andree *et al.*, 64 immediate free flap reconstructions following both skin- and nipple-sparing mastectomies were performed in patients who had undergone prior breast conservation therapy (BCT) (21). Either DIEP or muscle sparing-2 TRAM flaps were used. Due to radiation-induced fibrotic skin changes, they externalized a skin island, even in the setting of an NSM, to expand the skin envelope. The total flap loss rate was higher in the previous BCT group (1.6% compared to 0.8%), as was the partial flap loss rate (3.1% compared to 1.3%).

In 2014, Alperovich *et al.* published their outcomes of both implant-based and autologous reconstruction following NSM in 26 previously irradiated breasts (24 patients) (22). Nine of these breasts were reconstructed

using autologous flaps and the remainder using tissue expander/immediate implant reconstruction (16/26) and LD flap with an implant (1/26). The rate of mastectomy skin flap necrosis that required reoperation was 11.5% (3/26), with one of these a free tissue transfer reconstruction requiring debridement and split thickness skin grafting. The other two cases were implant based reconstructions that required explantation. They compared these complication rates to 330 non-irradiated NSM breast reconstructions and found no statistically significant differences; however, the rate of implant or tissue expander explantation in the cohort with previous irradiation (2/26, 7.7%) was trending towards significance (P=0.06), and the true rate of explantation was underestimated as the nine autologous reconstructions were included in the denominator.

NSM in the large, ptotic breast

In 2006, Sacchini *et al.* reported that they counseled patients with large, ptotic breasts against NSM—citing risks of nipple necrosis and asymmetry (37). Since then, multiple techniques have been cited in the literature for optimizing outcomes of NSM in this breast type: pre-mastectomy delay procedures, pre- or post-mastectomy mastopexies, free NAC graft, and post-mastectomy hyperbaric oxygen therapy (38-43).

A 2012 study by Schneider *et al.* reported their experience with autologous reconstruction in patients with large and ptotic breasts who had not undergone any pre-mastectomy delay (23). Nineteen patients (34 breasts) met inclusion criteria: cup size C or greater, sternal notch to nipple distance >24 cm, and Regnault grade II or III breast ptosis (44). There was 1 case (5%) of nipple necrosis in a breast that was previously irradiated, 1 (5%) hematoma, and no partial or complete flap loss. Five patients (26%) underwent secondary mastopexies at an average of 6.6 months after their initial surgery without any complications. The blood supply to the NAC was bolstered due to neovascularization from the underlying flap, compared to the relatively tenuous blood supply to the NAC at the time of the NSM. And, in contrast to pre-mastectomy mastopexies, the oncologic surgical management wasn't delayed in these patients. The authors believe that their success with the large, ptotic breast was attributable to oncologic surgeon dependent factors (not dissecting beyond the borders of the breast and preserving subcutaneous fat and the blood supply from the second intercostal perforator) as well as favorable patient

demographics (no smokers or diabetics).

A 2015 study by DellaCroce *et al.* corroborated the finding that secondary mastopexies can be performed safely after NSM with autologous reconstruction (24). Seventy patients with 116 NSM followed by perforator flap reconstruction had secondary mastopexy procedures for grade II or III ptosis. They used full-thickness periareolar incisions and undermining of the surrounding breast skin flaps. There were no cases of postoperative NAC necrosis. The most common complications were partial incisional dehiscence (n=9, 7.8%) and partial mastectomy flap necrosis (n=4, 3.4%).

NAC necrosis management

NAC necrosis is one of the potential complications in NSM. An advantage of autologous tissue reconstruction is the option of banking the flap skin paddle to be used to resurface necrotic NAC or mastectomy flaps (25). In 2015, Cho *et al.* described their method of preserving a circle of flap skin paddle, approximately 5 cm in diameter, underneath the NAC (45). When NAC necrosis was observed postoperatively, the NAC was debrided and the flap skin paddle externalized. In cases in which the NAC survived, the team went back to the operating room 2 weeks after the initial reconstruction and de-epithelialized the skin paddle. The authors recommend using this method if intraoperative signs of NAC ischemia are noted or if patients have at least two of four preoperative risk factors they found to be significant for NAC necrosis: BMI ≥ 25 , smoking, preoperative radiation, and large breast size.

Single stage reconstruction

A 2013 study by Levine *et al.* described their experience with immediate breast reconstruction using buried free flaps following NSM with the goal of a single stage reconstruction (19). Risk factors for mastectomy flap necrosis—smoking, prior radiation, and connective tissue disorders—were relative contraindications. Additionally, buried flaps were only used when the oncologic surgeon was known to leave healthy mastectomy flaps. Eighty-four patients and 134 buried flaps were reported in the series—all monitored with Cook implantable dopplers. A total of 3.0% of flaps (n=4) were re-explored for venous obstruction, and 2.2% of flaps (n=3) ultimately failed. Delayed mastectomy flap healing occurred in 3.7% of breasts (n=5) which were managed with local wound care. At the time of publication,

58.2% (n=78) of their breasts had secondary surgeries for cosmesis, while 41.8% (n=56) had no revisions.

While this study reports low complication rates, a 2015 study by Raghavan *et al.* supports a two-staged reconstruction (26). In their experience, immediate autologous free flap reconstruction after NSM was associated with ischemic complications of the mastectomy skin flap and NAC. Therefore, in 2013, the authors started using a two-stage technique with insertion of a tissue expander at the time of the NSM, followed by tissue expander removal and autologous free flap reconstruction at an average of 11.5 months later. Their NAC necrosis rate dropped from 29% to 0%. Additionally, NAC overall appearance and color in the delayed cohort were rated as significantly better by blinded surgeons and residents using a five-point Likert scale.

Conclusions

Autologous breast reconstruction after NSM is a safe and aesthetic method of breast cancer surgical management. Autologous reconstruction can be effectively performed using multiple rungs of the reconstructive ladder: autologous fat grafting, local tissue rearrangement, pedicled flaps, and free tissue transfer. Superiority of autologous versus prosthetic reconstruction has yet to be conclusively shown. Special consideration should be given to previously irradiated breasts, as well as large, ptotic breasts. Outcomes-based research is critical to continue to improve surgical care for this deserving patient population.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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