NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

INTERVENTIONAL PROCEDURES PROGRAMME

Interventional procedure overview of liposuction for chronic lipoedema

In chronic lipoedema, the bottom, legs, and sometimes the arms become enlarged because of abnormal build-up of fat cells. This leads to pain, bruising, and limited mobility. Under either general or local anaesthesia, the abnormal fat is removed using suction through punctures in the skin (liposuction). Afterwards, a compression garment must be worn most of the time for several months after surgery. The procedure may need to be repeated. The aim is to reduce swelling and pain.

Contents

Abbreviations

Word or phrase	Abbreviation
Analysis of variance	ANOVA
Body mass index	BMI
British National Formulary	BNF
Interquartile range	IQR
Quality of life	QoL
Standard deviation	SD
United Kingdom	UK

Introduction

The National Institute for Health and Care Excellence (NICE) prepared this interventional procedure overview to help members of the interventional procedures advisory committee (IPAC) make recommendations about the safety and efficacy of an interventional procedure. It is based on a rapid review of the medical literature and professional opinion. It should not be regarded as a definitive assessment of the procedure.

Date prepared

This overview was prepared in June 2021.

Procedure name

- Liposuction for chronic lipoedema

Professional societies

- British Association of Plastic, Reconstructive and Aesthetic Surgeons
- British Lymphology Society
- The Vascular Society of Great Britain and Ireland
- British Association of Dermatology

Description of the procedure

Indications and current treatment

Lipoedema is characterised by an abnormal, usually symmetric, accumulation of fat in the legs, hips, buttocks, and occasionally arms. It is a different condition from lymphoedema which is secondary to obstruction to the lymphatic system. The aetiology of lipoedema is unknown, but hormonal changes, weight gain, and genetics are each thought to be involved. Lipoedema is considerably more prevalent in women and very rarely affects men. Symptoms include swollen, heavy legs that are painful to touch and bruise easily. Ankles and feet do not usually have fat accumulation. The size and shape of legs, and the resultant mobility issues and pain, can have a profound effect on QoL.

Treatment typically involves healthy lifestyle changes, conservative therapy and, in chronic cases, surgery. The fat associated with lipoedema may be resistant to diet modification and exercise. Conservative therapy, including compression and manual lymphatic drainage (a specialist type of light massage that is mainly used to reduce swelling caused by fluid) can reduce discomfort, improve mobility, and reduce oedema formation by promoting lymphatic return. The main surgical treatment for lipoedema is liposuction. Some people have bariatric surgery to reduce weight from areas of the body not affected by lipoedema, or to prevent further weight gain in those who are obese.

What the procedure involves

The aim of liposuction for lipoedema is to reduce limb bulk, reduce pain, and to improve mobility and functioning. Liposuction for chronic lipoedema can be done under general or local anaesthesia. Several small incisions are made in the limb. Modern liposuction usually involves infiltrating the limb with large volumes of fluid (tumescence) to allow the cannula to glide through the tissue with minimal damage to blood vessels and lymphatics. Tumescent liposuction needs an infiltration pump to deliver the tumescent fluid. Cannulas, connected to a vacuum pump, are then inserted into the incisions and oedematous adipose tissue is removed by vacuum aspiration. Using vibrating cannulas (power-assisted liposuction) or water-jet-assisted liposuction can help remove fat more easily. Water-jet-assisted liposuction needs less initial infiltration because fluid is simultaneously infiltrated and aspirated during liposuction. Liposuction is done around and all the way along the limb. In tumescent liposuction, both fat and tumescent fluid are suctioned out together.

The procedure can take 1 to 4 hours depending on the size of the treatment area. Immediately after liposuction, a compression bandage is applied to the limb to control any bleeding and to prevent postoperative oedema. Antibiotics are typically prescribed as prophylaxis after the operation. When the wounds are

healed after the procedure, a custom-made compression garment is worn. This garment is typically revised and refitted multiple times during the first year until the oedema volume has been reduced as much as possible.

Outcome measures

Lipoedema staging

The different stages of lipoedema can be classified as such:

- **Stage 1:**
  - Skin appears smooth.
  - On palpation, the thickened subcutaneous tissue contains small, soft nodules.
- **Stage 2:**
  - Skin has an irregular texture that resembles the skin of an orange.
  - Larger subcutaneous nodules occur that vary from the size of walnut to that of an apple.
- **Stage 3:**
  - The indurations are larger and more prominent than in Stage 2, with pronounced sclerosis.
  - Deformed lobular fat deposits form, especially around thighs and knees, and may cause considerable distortion of limb profile.
- **Stage 4:**
  - Lipoedema with lymphoedema (lipolymphoedema).

Questionnaires for QoL assessment

Each study used a questionnaire to quantify patient QoL, and the severity of symptoms and complaints, before and after liposuction. Several different questionnaires were used. Questionnaires were typically scored on a 0 to 10 scale, with higher scores on each item indicative of worse QoL or more severe symptoms/complaints. Throughout the Quality of life section in the Efficacy summary, the scoring of questionnaires is described in brief for each study.

Coroner regulation 28 letter

NICE received a regulation 28 letter from a coroner in February 2020 highlighting the absence of UK guidance relating to indications for safe practice for lipoedema-related liposuction. The coroner's letter triggered the development of

IP1843 – liposuction for chronic lipoedema, and the review of IP409/2 (IP409/3) – liposuction for chronic lymphoedema.

The coroner specifically suggested guidance would be helpful in respect of:

1. the frequency of procedures on a single patient.
2. the amount of fluid to put into the patient during the procedure.
3. the amount of fluid to remove from the patient during the procedure.
4. the post-procedure patient recovery plan.

A summary of the literature relevant to these 4 points is provided in the Coroner-Regulation 28 letter findings summary in the Safety summary.

Efficacy summary

Body shape, size, and weight

Limb size

A before-and-after study of 112 people reported mean reductions in the circumference of the thighs of 8 cm (range 1 cm to 23 cm) and calves of 4 cm (range 1 cm to 11 cm) at a follow up of 2 years 11 months after the final liposuction. No test of statistical significance was reported (Schmeller, 2012).

A before-and-after study of 111 people reported a median reduction in the circumference of the thighs of 6 cm (SD 1.6 cm) at a follow up of 2 years. No test of statistical significance was reported (Wollina, 2019).

A before-and-after study of 25 people reported a mean reduction in leg volume of 18.0 litres (SD 3.8 litres) to 16.8 litres (SD 3.5 litres) at a follow up of 6 months. No test of statistical significance was reported (Rapprich, 2011).

BMI

A before-and-after study of 25 people reported a reduction in BMI from a mean of 35.3 kg/m^2 (range 24.5 kg/m^2 to 50.6 kg/m^2) before liposuction, to a mean of 33.9 kg/m^2 (range 22.7 kg/m^2 to 47.2 kg/m^2) at an unspecified follow up (either 16 or 37 months). No test of statistical significance was reported (Dadras, 2017).

A before-and-after study of 106 people reported a statistically significant reduction in mean BMI of 2.7 kg/m^2 (IQR 1.1 kg/m^2 to 5.2 kg/m^2) from preoperative assessment to a follow up of 20 months ($p<0.0001$; Ghods, 2020).

Weight

The before-and-after study of 112 people reported a mean reduction in weight from 79.3 kg (range 50 kg to 123 kg) before surgery to 75.0 kg (range 48.5 kg to 113.0 kg) at a follow up of 2 years 11 months after the final liposuction. No test of statistical significance was reported (Schmeller, 2012).

In a long-term follow up of Schmeller (2012), 60 people reported that average weight increased from 79.7 kg (range 50.0 kg to 116.0 kg) before surgery to 80.2 kg (range 40.0 kg to 130.2 kg) at a follow up of 12 years. No test of statistical significance was reported (Baumgartner, 2021).

QoL

Overall QoL

The before-and-after study of 112 people reported a statistically significant improvement in the mean score for 'reduction in QoL' from 3.36 (SD 0.86) before surgery to 0.76 (SD 0.91) after a follow up of 2 years 11 months after the final liposuction ($p<0.001$). The questionnaire was scored on a 0 to 4 scale, with 0 corresponding to 'none' and 4 corresponding to 'very strong', so higher scores indicate worse QoL (Schmeller, 2012).

In the long-term follow up of Schmeller (2012), 60 people reported a statistically significant improvement in the mean score for 'reduction in QoL' from 3.49 (SD 0.77) before surgery to 0.96 (SD 0.90) at a follow up of 12 years ($p<0.001$; Baumgartner, 2021).

The before-and-after study of 25 people reported a statistically significant decrease in the mean score on the questionnaire item 'How much does your condition affect your QoL?' from 8.7 before surgery to 3.6 at a follow up of 6 months ($p<0.001$). The questionnaire was scored on 0 to 10 scale, with higher scores indicating worse QoL (Rapprich, 2011).

A before-and-after study of 85 people reported a statistically significant decrease in the mean score on the questionnaire item 'How would you assess the reduction in your QoL?' from 8.5 before surgery to 3.3 at a follow up of 6 months ($p<0.001$). The questionnaire was scored on 0 to 10 scale, with higher scores indicating worse QoL (Rapprich, 2015).

The before-and-after study of 25 people reported a statistically significant decrease in the mean score on the questionnaire item 'General QoL impairment' from 8.38 (SD 1.06) before surgery to 5.16 (SD 1.60) at a follow up of 37 months ($p<0.001$). The questionnaire was scored on a 0 to 10 scale, with higher scores indicating worse QoL (Dadras, 2017).

A before-and-after study of 63 people reported a statistically significant decrease in the mean score on the questionnaire item 'General impairment' from 7.79 (SD 2.11) before surgery to 0.95 (SD 1.40) at a follow up of 21.5 months ($p<0.001$). The questionnaire was scored on an 11-point scale, with higher scores indicating worse QoL (Witte, 2020).

Complaints or symptoms

The before-and-after study of 112 people reported statistically significant decreases in scores on the questionnaire items 'spontaneous pain', 'pain because of pressure', 'oedema', 'bruising', 'restriction of movement', and 'cosmetic impairment' from preoperative assessment to a follow up of 2 years 11 months after the final liposuction (all $p<0.001$). The questionnaire was scored on a 0 to 4 scale, with higher scores indicating worse impairment (Schmeller, 2012).

In the long-term follow up of Schmeller (2012), 60 people reported statistically significant decreases in scores on the questionnaire items 'spontaneous pain', 'sensitivity to pressure', 'oedema', 'bruising', 'restriction of movement', and 'cosmetic impairment' from preoperative assessment to a mean follow up of 12 years ($p<0.001$). The questionnaire was scored on a 0 to 4 scale, with higher scores indicating worse impairment (Baumgartner, 2021).

The before-and-after study of 111 people reported a statistically significant decrease in the mean score on the questionnaire item on 'pain' ($p<0.3$) from preoperative assessment to a follow up of 2 years. Pain was assessed by a 10-point visual analogue scale, with higher scores indicative of worse pain. This study also reported a statistically significant decrease in the proportion of people reporting 'bruising after minor trauma' ($p<0.5$). All people additionally reported an improvement in mobility, but no significance test was reported (Wollina, 2019).

The before-and-after study of 25 people reported statistically significant decreases in scores on the questionnaire items 'pain', 'sensitivity to touch', 'bruising', 'tension in legs', 'excessive warmth in legs', 'muscle cramps', 'legs feel heavy', 'legs feel tired', 'swelling', 'skin involvement', 'itching', 'difficulty walking', and 'appearance of legs' from preoperative assessment to a follow up of 6 months. All p values were $p<0.001$ except excessive warmth ($p<0.008$) and muscle cramps ($p<0.043$). The questionnaire was scored on a 0 to 10 scale, with higher scores indicating worse impairment (Rapprich, 2011).

The before-and-after study of 85 people reported statistically significant decreases in scores on the questionnaire items 'pain', 'sensitivity to touch', 'bruising', 'legs feel tight, 'legs feel hot', 'legs feel cold', 'muscle cramps', 'legs feel heavy', 'legs feel tired', 'swelling', 'skin complications, 'itching', 'difficulty walking', and 'appearance of legs' from preoperative assessment to a follow up of

6 months (all p<0.001). The questionnaire was scored on a 0 to 10 scale, with higher scores indicating worse impairment (Rapprich, 2015).

The before-and-after study of 25 people reported statistically significant decreases in scores on the questionnaire items 'spontaneous pain', 'sensitivity to pressure', 'feeling of tension', 'bruising', and 'cosmetic impairment' from preoperative assessment to a follow up of 37 months (all p≤0.001). The questionnaire was scored on a 0 to 10 scale, with higher scores indicating worse impairment (Dadras, 2017).

The before-and-after study of 106 people reported statistically significant decreases in scores on the questionnaire items 'pain perception' and 'quality of sex life' from before surgery to a follow up of 20 months (both p<0.0001). The questionnaire was scored on a 0 to 100 scale, with higher scores indicating worse impairment. Also, in the subset of people reporting migraines before surgery, there was a statistically significant decrease in the frequency of migraine attacks per month at 20-month follow up (p=0.0002). In the subsets of people reporting abnormal menstrual bleeding and skin disorders before surgery, there were numerical decreases in the number of people reporting these comorbidities at 20-month follow up, though a test of statistical significance was not reported (Ghods, 2020).

The before-and-after study of 63 people reported statistically significant decreases in scores on the questionnaire items 'pain', 'sensitivity to touch', 'bruising', 'feeling of tension', 'feeling of heavy legs', 'swelling', 'itching', 'running impairment', 'occupational impairment', and 'aesthetic impairment' from preoperative assessment to a follow up of 21.5 months (all p<0.001). The questionnaire was scored on an 11-point scale, with higher scores indicating worse QoL (Witte, 2020).

Relapse

The before-and-after study of 111 people reported long-term follow-up data for 18 people. At a 5 to 7-year follow up, there was no recurrence of lipoedema (Wollina, 2019).

The before-and-after study of 25 people reported no recurrence of lymphoedema after a follow up of 6 months (Rapprich, 2011).

The before-and-after study of 63 people reported no recurrence of excess subcutaneous fat after a follow up of 21.5 months (Witte, 2020).

Conservative therapy use

The before-and-after study of 112 people reported that 67 people had both manual lymphatic drainage and compression before liposuction. After a follow up

of 2 years 11 months after the final liposuction, 80.6% of people had a decrease in the frequency of conservative therapy, were able to stop compression or manual lymphatic drainage, or were able to stop conservative therapy altogether (Schmeller, 2012).

In the long-term follow up of Schmeller (2012), of 60 people followed up to 12 years, 37 had received conservative therapy preoperatively. After a follow up of 12 years, 46% reported that either they required fewer conservative treatments than before, or that they no longer needed either manual lymphatic drainage or compression therapy (Baumgartner, 2021).

The before-and-after study of 25 people reported that 15 people had manual lymphatic drainage and 19 people had compression therapy before the operation. After a follow up of 6 months, 2 people reported use of manual lymphatic drainage and 4 reported use of compression therapy (Rapprich, 2011).

The before-and-after study of 63 people reported that 56 people had manual lymphatic drainage and 60 people wore compression garments before the operation. After a follow up of 21.5 months, there were statistically significant decreases in the number of people who needed manual lymphatic drainage (25 people, $p<0.001$) and compression garments (20 people, $p<0.001$; Witte, 2020).

Safety summary

Death

The coroner's regulation 28 letter NICE received in February 2020 reported 1 death in a person who had liposuction for lipoedema. Before this liposuction procedure, the person had 4 previous liposuctions without complication. In the fifth procedure, the person had a cardiac arrest and despite resuscitation, died the next day. The cause of death was established as fat embolism syndrome with a pre-existing significantly enlarged heart.

Fat embolism

The before-and-after study of 111 people reported that 1 person developed microscopic pulmonary fat embolism. This person had treatment with rivaroxaban. Further liposuctions were well tolerated with perioperative low-molecular heparin prophylaxis (Wollina, 2019).

Thrombosis and phlebitis

The before-and-after study of 111 people reported that 2 people developed mild arm-vein phlebitis. No further information was reported (Wollina, 2019).

The before-and-after study of 25 people reported that 1 person developed deep vein thrombosis in the lower leg. This person had a history of deep vein thrombosis. This was treated promptly and there were no further complications (Rapprich, 2011).

The before-and-after study of 85 people reported 1 case of thrombophlebitis. No further information was reported (Rapprich, 2015).

Methaemoglobinaemia

The before-and-after study of 111 people reported that all had temporary methaemoglobinaemia. This is a potential complication of local anaesthesia using prilocaine. The publication reports that 'the most common [adverse events] were a temporary methaemoglobinaemia (100%), that was treated by intravenous injection of toluidine blue'. It is unclear whether all people received toluidine blue. There is no further information about the severity of methaemoglobinaemia (Wollina, 2019).

Oedema

The before-and-after study of 111 people reported that 1 person developed acute lower arm oedema after toluidine blue extravasation. This was treated with prophylactic antibiosis, prednisolone, and compression (Wollina, 2019).

Infections

Pneumonia

The before-and-after study of 111 people reported that 1 person developed community-acquired atypical pneumonia with aggravation of pre-existent comorbidities that needed admission to intensive care. This was first diagnosed as acute pulmonary oedema (Wollina, 2019).

Abscess

The before-and-after study of 112 people reported 1 case of postoperative lower leg abscess that needed hospital treatment (Schmeller, 2012).

Erysipelas (superficial cellulitis)

The before-and-after study of 112 people reported 4 cases of postoperative erysipelas. This was treated at home with oral antibiotics (Schmeller, 2012).

The before-and-after study of 25 people reported 1 case of erysipelas that needed antibiotics (Dadras, 2017).

Wound infection

The before-and-after study of 106 people reported 4 cases of superficial wound infection. This was treated conservatively (Ghods, 2020).

Haematomas and bruising

The before-and-after study of 112 people reported an unspecified number of people who had postoperative minor haematomas (Schmeller, 2012).

The before-and-after study of 111 people reported that 109 people had postoperative bruising. All cases disappeared without specific intervention (Wollina, 2019).

The before-and-after study of 85 people reported 12 cases of postoperative bruising, including 5 mild haematomas, 4 moderate haematomas, 2 haematomas that needed revision, and 1 seroma that needed treatment (Rapprich, 2015).

The before-and-after study of 106 people reported that 2 people developed seromas. This was treated conservatively (Ghods, 2020).

Other adverse events

Anaemia

The before-and-after study of 111 people reported that 1 person developed postoperative anaemia that needed a blood transfusion (Wollina, 2019).

Bleeding

The before-and-after study of 106 people reported that 1 person had mild postoperative bleeding. This did not need a blood transfusion (Ghods, 2020).

Epileptic attack

The before-and-after study of 111 people reported that 1 person without known comorbidities had an epileptic attack. Further liposuctions did not result in epileptic attacks (Wollina, 2019).

Orthostatic reactions

The before-and-after study of 112 people reported that ‘some patients’ had orthostatic reactions (not further defined). These were resolved without further treatment within the same day. (Schmeller, 2012).

Panniculitis

The before-and-after study of 111 people reported that 1 person developed non-infectious panniculitis of the inner sides of the knees. This was treated with an oral combination of herbal enzymes (Wollina, 2019).

Swelling

The before-and-after study of 112 people reported that an unspecified number of people had postoperative swelling (Schmeller, 2012).

Temporary burning sensation

The before-and-after study of 111 people reported that 91 people had a temporary sensation of burning after surgery. All cases disappeared without specific intervention (Wollina, 2019).

Anecdotal and theoretical adverse events

In addition to safety outcomes reported in the literature, professional experts are asked about anecdotal adverse events (events which they have heard about) and about theoretical adverse events (events which they think might possibly occur, even if they have never happened). For this procedure, professional experts did not list any anecdotal or theoretical adverse events.

Coroner regulation 28 letter findings summary

Number of procedures needed

Seven before-and-after studies reported data on the frequency of liposuctions for lipoedema. Each study reported an average of about 2 to 3 liposuction procedures per person (range 1 to 7). The shortest interval between procedures was 4 weeks or 1 month, reported in 2 studies. The longest interval between procedures was 1 year, reported in 1 study.

The before-and-after study of 112 people reported that people had operations a median of 3 times (range 1 to 7). The minimum time between the operations was 1 month, the maximum was about 1 year (Schmeller, 2012).

The before-and-after study of 111 people reported that people had operations a total of 334 times at 6-to-8-week intervals (Wollina, 2019). This is a mean of about 3 procedures per person (calculated as 334/111=3.01).

The before-and-after study of 25 people reported that people had a mean of 2.5 operations (median 2; range 1 to 5) at 4-week intervals (Rapprich, 2011).

The before-and-after study of 85 people reported that people had a mean of 2.6 operations (median 3; range 1 to 6). The interval between procedures was not reported (Rapprich, 2015).

The before-and-after study of 25 people reported that people had an average of 3 operations (range 1 to 7). The interval between procedures was not reported (Dadras, 2017).

The before-and-after study of 106 people reported that people had a median of 3 operations over an 8-month period (Ghods, 2020). This is about 1 liposuction per 2.67 months, or 11.6 weeks (calculated as 8/3=2.67; 2.67*4.35=11.6).

The before-and-after study of 63 people reported that people had operations a median of 3 times (range 1 to 4). Operations were spaced at intervals of minimum 8 weeks (Witte, 2020).

Volume of fluid infiltrated during the procedure

Six before-and-after studies reported data on the volume of fluid infiltrated into people. Two studies reported mean infiltration volumes of 5,155 ml and 7,707 ml. Two studies reported that a maximum of 6,000 ml was infiltrated per procedure. One study reported that people had infiltration until the skin developed a hard elastic turgor and was blanched. The 1 study that only used water-jet-assisted liposuction reported an initial infiltration volume of 200 ml to 700 ml depending on limb location.

The before-and-after study of 112 people reported that an average of 7,707 ml (range 2,564 ml to 13,450 ml) of tumescent anaesthesia solution was infiltrated per surgery (Schmeller, 2012).

The before-and-after study of 111 people reported that a maximum of 6,000 ml per session of tumescent anaesthesia was infiltrated (Wollina, 2019).

The before-and-after study of 25 people reported that a mean of 5,155 ml (SD 1,304 ml) tumescent anaesthesia was infiltrated per session (Rapprich, 2011).

The before-and-after study of 85 people did not report the volume of tumescent anaesthesia infiltrated. However, the publication notes that infiltration was continued until the skin developed a hard elastic turgor, and until the tissue was blanched by the tissue pressure and the proportion of adrenaline in the tumescence solution (Rapprich, 2015).

The before-and-after study of 106 people reported that people had infiltration with a maximum of 6,000 ml of tumescent solution. This study reports that both power-assisted and water-jet-assisted liposuction techniques were used, but does not describe different infiltration volumes for either (Ghods, 2020).

The before-and-after study of 63 people reported that the infiltration volume at the beginning of the operation was 200 ml to 400 ml for the lower legs, 400 ml to 700 ml for the upper legs and 200 ml to 300 ml for the upper limb. This study used water-jet-assisted liposuction, a technique that simultaneously infiltrates and aspirates tumescent fluid, and so needs less infiltrating fluid at the beginning of the operation (Witte, 2020).

Volume of fluid and fat aspirated during the procedure

One before-and-after study reported that the total volume of fluid removed from people per liposuction procedure was, on average, 2,482 ml, with a pure fat component of 1,909 ml. Five before-and-after studies reported data on the volume of fat aspirated from people. The average amount of fat aspirated per procedure ranged from 1,909 ml to 6,355 ml. Of studies reporting ranges, the lowest volume of fat aspirated per procedure was 450 ml and the highest volume of fat aspirated per procedure was 7,000 ml.

The before-and-after study of 112 people reported that the average amount of fat removed was 9,846 ml per person (range 1,000 ml to 25,600 ml) or 3,077 ml per procedure (range 450 ml to 7,000 ml), depending on the size and number of operated areas (Schmeller, 2012).

The before-and-after study of 111 people reported that the median amount of removed lipoaspirate was 4,700 ml (SD 7,579 ml) per person, with a range of 950 ml to 14,250 ml (Wollina, 2019). Using a mean of 3 procedures per person, this is about 1,567 ml per procedure (calculated as 4,700/3=1,567).

The before-and-after study of 25 people reported that for each procedure, the aspiration volume was an average of 2,482 ml (SD 968 ml). The pure fat component was on average 1,909 ml (SD 874 ml), or 77% (Rapprich, 2011).

The before-and-after study of 25 people reported that the mean volume of removed fat per procedure was 3,106 ml (range 1,450 ml to 6,600 ml) and the mean volume of total removed fat per person was 9,914 ml (range 4,000 ml to 19,850 ml; Dadras, 2017).

The before-and-after study of 106 people reported that the mean lipoaspirate volume per procedure was 6,355 ml (SD 2,797 ml) with a mean total aspirate volume per person of 17,887 ml (SD 10,341 ml) throughout the entire surgical treatment (Ghods, 2020).

Total volume of fat removed over all treatments

The before-and-after study of 63 people reported that a mean amount of 12,922 ml (SD 2,922 ml) fat was removed per person over the course of all

operations (Witte, 2020). Using a median of 3 procedures per person, this is about 4,307 ml per procedure (calculated as 12,922/3=4,307).

Post-procedure patient recovery

Six before-and-after studies reported details about the postoperative patient recovery plan. Antibiotic prophylaxis was reported by 5 studies, either as a single shot (2 studies) or for 3 days (3 studies). Thrombosis prophylaxis was reported by 3 studies for a duration of 5 to 10 days. Five studies reported use of compression garments. There were differences in the duration of compression, from about 5 weeks to 6 months. Postoperative compression was prescribed by 5 studies. Compression garments were refitted during the follow up to account for decreases in swelling. Manual lymphatic drainage was reported by 4 studies. Manual lymphatic drainage was allowed 2 to 3 days after liposuction, for a duration of at least 6 to 8 weeks.

Also, 1 guideline summarised recommendations from the First International Consensus Conference on Lipoedema. Antibiotic and thrombotic prophylaxis, compression, and manual lymphatic drainage were all noted as part of typical post-procedure recovery.

The before-and-after study of 112 people reported that all had prophylactic oral antibiotics for 3 days after surgery (Schmeller, 2012).

The before-and-after study of 111 people reported that, after surgery, no drains and no prophylactic antibiotics were needed. People were monitored for methaemoglobulinaemia, a complication that can develop with use of prilocaine. People were asked to wear flat-knitted compression garments for at least 6 months, with garments refitted as needed during this time (Wollina, 2019).

The before-and-after study of 25 people reported that, after surgery, people had antibiotic prophylaxis for 3 days and thrombosis prophylaxis for 5 days. Compression garments were worn during the first 7 days after liposuction for 24 hours per day. For liposuction of the lower legs, during the first 2 to 3 days a circumferential compression dressing was applied. Afterward, compression garments were worn during the daytime for only 4 to 6 weeks. Starting on the third day after liposuction, manual lymphatic drainage was done 2 to 3 times per week for at least 6 weeks (Rapprich, 2011).

The before-and-after study of 85 people reported a similar post-procedure recovery plan as Rapprich (2011). Thrombosis prophylaxis was reported for 5 or 10 days (Rapprich, 2015).

The before-and-after study of 25 people reported that people had a single shot of antibiotic prophylaxis. Compression garments were put on immediately after

liposuction. New garments were measured 3 weeks after liposuction. Manual lymphatic drainage was allowed 2 days after surgery (Dadras, 2017).

The before-and-after study of 63 people reported that people were hospitalised overnight and given thrombosis prophylaxis for 7 days and a single shot of antibiotic prophylaxis. Compression bandages were applied immediately after surgery. After 2 days, bandages were removed, and compression garments were worn for 24 hours per day for 6 weeks. People were then weaned from compression for 2 weeks, with the aim of stopping compression 8 weeks after the last operation. Manual lymphatic drainage therapy was started 2 days after surgery with a frequency of 2 sessions per week for at least 8 weeks (Witte, 2020).

The First International Consensus Conference on Lipoedema (as summarised in Existing assessments of this procedure) notes the following statements about the postoperative course (Sandhofer, 2020):

- People who had liposuction treatment using tumescent local anaesthesia may drain lymphatic fluid for several weeks after the procedure.
- Low-dose heparin is given by some European liposuction surgeons as prophylaxis to prevent deep vein thromboses.
- Postoperative antibiotics are given for 1 to 2 weeks.
- Compression stockings are worn for 2 to 4 weeks after surgery to prevent pools of lymphatic fluid forming in suctioned areas. After the first 4 weeks, people may prefer to wear compression stockings daily for comfort and support.
- Manual lymphatic drainage can be given for as long as 4 to 5 weeks after surgery. Acoustic wave therapy may be given for 5 to 10 weeks.
- Low-impact active movements may begin when all liposuction incisions are closed or healed.

The evidence assessed

Rapid review of literature

The medical literature was searched to identify studies and reviews relevant to liposuction for chronic lipoedema. The following databases were searched, covering the period from their start to 28 April 2021: MEDLINE, PREMEDLINE, EMBASE, Cochrane Library and other databases. Trial registries and the internet were also searched. No language restriction was applied to the searches (see the literature search strategy). Relevant published studies identified during consultation or resolution that are published after this date may also be considered for inclusion.

The inclusion criteria were applied to the abstracts identified by the literature search. Where selection criteria could not be determined from the abstracts the full paper was retrieved.

Inclusion criteria for identification of relevant studies

Characteristic	Criteria
Publication type	Clinical studies were included. Emphasis was placed on identifying good quality studies. Abstracts were excluded where no clinical outcomes were reported, or where the paper was a review, editorial, or a laboratory or animal study. Conference abstracts were also excluded because of the difficulty of appraising study methodology, unless they reported specific adverse events that were not available in the published literature.
Patient	People with lipoedema.
Intervention/test	Liposuction.
Outcome	Articles were retrieved if the abstract contained information relevant to the safety and/or efficacy.
Language	Non-English-language articles were excluded unless they were thought to add substantively to the English-language evidence base.

List of studies included in the IP overview

This IP overview is based on 502 people (assuming overlap between Rapprich [2011] and Rapprich [2015], and assuming no overlap between Dadras [2017] and Ghods [2020]) from 8 before-and-after studies.

Other studies that were considered to be relevant to the procedure but were not included in the main summary of the key evidence are listed in the appendix.

Summary of key evidence on liposuction for chronic lipoedema

Study 1 Schmeller W (2012)

Study details

Study type	Single arm, single centre, non-randomised, before-and-after study
Country	Germany
Recruitment period	2003 to 2009
Study population and number	n=112 People with lipoedema who had received liposuction
Age and sex	Mean 38.8 years; 100% female
Patient selection criteria	Inclusion criteria: female people with lipoedema who had completed liposuction for at least 6 months between 2003 and 2009 at the Hanse Clinic.
Technique	**Technique summary:** tumescent anaesthesia liposuction using blunt vibrating microcannulas of 3 and 4 mm in diameter (power-assisted liposuction). **Preoperative treatment:** Nearly all people had received conservative therapy for many years and either had experienced no obvious improvement of complaints or had noticed a progression of subcutaneous fatty volume. **Procedural frequency:** of 112 people, 12 people were operated on once, 29 people twice, 28 people 3 times, 23 people 4 times, 12 people 5 times, 4 people 6 times, and 4 people 7 times. The minimum time between the operations was 1 month, the maximum was approximately 1 year. **Infiltration volume:** the average amount of tumescent anaesthesia solution infiltrated was 7,707 ml (range 2,564 to 13,450 ml), the average time of surgery was 2 hours (40 minutes to 3 hours 35 minutes). **Aspiration volume:** the average amount of fat removed was 9,846 ml per person (range 1,000 to 25,600 ml) or 3,077 ml per session (range 450 to 7,000 ml), depending on the size and number of operated areas. **Postoperative care:** all people received prophylactic oral antibiotics (cefpodoxime proxetil) for 3 days after surgery.
Follow up	Mean 3 years 8 months after the first liposuction; 2 years 11 months after the last liposuction.
Conflict of interest/source of funding	Conflict of interest: the authors declared no conflicts of interest. Source of funding: the authors declared that funding was not received.

*This study and Baumgartner, 2021 were conducted on the same group of people. The authors published 3 analyses:

- Schmeller, 2012 was conducted 4 years after liposuction and includes QoL and safety data on 112 people.
- Baumgartner, 2016 was conducted 8 years after liposuction and includes QoL data on 85 people.
    - As this study does not present safety data and presents shorter follow-up data than Baumgartner, 2021, it is included in the Appendix and is not summarised in the Summary of key evidence.

- Baumgartner, 2021 was conducted 12 years after liposuction and includes QoL data on 60 people.

Analysis

Follow-up issues: A total of 165 people were sent questionnaires, of which 114 were returned and 112 could be analysed. The authors report that many people were also seen clinically or had photographs available for analysis.

Study design issues: This single arm, single centre, non-randomised, before-and-after study assessed the long-term outcomes of liposuction for people with lipoedema. Outcomes assessed included changes in body shape and weight, patient-reported symptoms and complaints, and need for conservative therapy. Changes in body shape were assessed through measurement of the circumference of the hips, legs, and/or arms. Complaints were assessed by a questionnaire comprised of the following 7 items: spontaneous pain, sensitivity to pressure, oedema, bruising, restriction of movement, cosmetic impairment, and reduction in QoL. Responses to these items were captured on a 5-point scale: 0=none, 1=minor, 2=medium, 3=strong, 4=very strong). In addition to the 7 impairment items, an overall impairment value (mean value from all 7 scales) was also evaluated. People completed the questionnaire before surgery and a mean of 2 years 11 months after their final liposuction.

Changes in impairments over time were tested for significance using one-way repeated-measures ANOVA with repeated measurements for the 4 measurement points. Effect sizes of 0.20 to 0.50 were considered ‘small’ group differences, those between 0.50 to 0.80 were ‘medium’, and effect sizes 0.80 or more were ‘strong’ differences. $p<0.05$ was considered significant. No adjustment was made for multiple comparisons.

Study population issues: A total of 35 people presented with lipoedema stage 1, 75 people with stage 2 and 2 people with stage 3. The authors report that ‘nearly all’ had received conservative therapy for many years and either had experienced no obvious improvement of complaints or had noticed a progression of subcutaneous fatty volume.

Key efficacy findings

Body shape and weight

Number of people analysed: 112

Follow up at time of assessment: 2 years 11 months after final liposuction

- Mean reductions in the circumference of the limbs of 8 cm (range 1 to 23 cm) in the thighs (inguinal region) and of 4 cm (range 1 to 11 cm) in the middle of the lower legs (calves) were achieved.
- Mean reduction in weight from 79.3 kg (range 50 to 123 kg) to 75.0 kg (range 48.5 to 113.0 kg).
- Reduction in off-the-peg clothing size of 1 size (38% of respondents), 2 sizes (25%), 3 sizes (11%), no change (23%), increase of 1 size (2%).

Complaints/symptoms

Number of people analysed: 112

Follow up at time of assessment: 2 years 11 months after final liposuction

- For all questionnaire items, postoperative scores were statistically significantly lower than preoperative scores (all p<0.001; Table below).
- All effect sizes for the comparison of complaints between pre- and postoperative were substantially above 1 (indicating a 'strong' effect; Table below).
- People with higher severity of lipoedema (stage 2/3) showed a statistically significantly better improvement in 'General impairment' than people with stage 1 lipoedema (p<0.02).

Complaints before and after liposuction in people with lipoedema

Complaint	Questionnaire item score, mean (SD)		p-value (t-test)	Effect size
	Preoperative	Postoperative		
Spontaneous pain	1.88 (1.33)	0.37 (0.60)	<0.001	1.36
Pain because of pressure	2.91 (1.06)	0.91 (0.92)	<0.001	2.01
Oedema	3.06 (1.02)	1.27 (0.88)	<0.001	1.88
Bruising	3.01 (1.03)	1.26 (1.11)	<0.001	1.63
Restriction of movement	2.03 (1.36)	0.28 (0.68)	<0.001	1.58
Cosmetic impairment	3.33 (0.88)	1.08 (0.91)	<0.001	2.52
Reduction in QoL	3.36 (0.86)	0.76 (0.91)	<0.001	2.95
General impairment	2.81 (0.70)	0.86 (0.63)	<0.001	2.93

Abbreviations: QoL, quality of life; SD, standard deviation.

Conservative therapy use

Number of people analysed: 67 people who received combined physical therapy (manual lymphatic drainage and compression) before liposuction.

Follow up at time of assessment: not reported for subgroup.

- 13 people (19.4%) needed manual lymphatic drainage and compression as often as before.
- 20 people (29.9%) continued with manual lymphatic drainage and compression, but less often.
- 13 people (19.4%) used compression garments only.
- 6 people (9.0%) used manual lymphatic drainage only.
- 15 people (22.4%) reported that they no longer required manual lymphatic drainage or compression.

Key safety findings

Number of people analysed: 112 (349 total liposuctions)

Follow up at time of assessment: 2 years 11 months after final liposuction

The following adverse events were reported:

- Postoperative wound infections, n=5
    - In 4 cases, postoperative erysipelas could be treated at home with further oral antibiotics; 1 person with an abscess of the lower leg was treated in hospital.
- Postoperative bleeding, n=1
    - Occurred after removal of 5,400 ml fatty tissue from hips and outer thighs. Treated with oral therapy with iron and folic acid, normal haemoglobin values were reached again within 4 weeks. The following 3 liposuctions (removal of, in total, 16,700 ml of fatty tissue) in this person were performed without any problems.
- Orthostatic reactions, reported as ‘some people’. These were resolved without further treatment within the same day.
- Minor haematomas, number not reported.
- Postoperative swelling, number not reported.
- Indurations of the subcutaneous fatty tissue because of scar formation during wound healing, number not reported.
    - Reported that these indurations ‘disappeared completely within weeks’.

Study 2 Baumgartner A (2021)

Study details

Study type	Single arm, single centre, non-randomised, before-and-after study, long-term follow up of Schmeller, 2012*
Country	Germany
Recruitment period	2003 to 2009
Study population and number	n=60 People with lipoedema who had received liposuction and had responded to questionnaires at 4 years and 8 years
Age and sex	Mean 54.1 years (41.9 years at date of first liposuction); 100% female
Patient selection criteria	Inclusion criteria: female people with lipoedema who had completed liposuction for at least 6 months between 2003 and 2009 at the Hanse Clinic. All people who were evaluated by means of a questionnaire in 2010 and 2014 were written to again in 2019.
Technique	**Technique summary:** Tumescent liposuction. No further details are given for this subset of people, but a more comprehensive description of the treatment of the entire cohort is reported in Schmeller, 2012.
Follow up	12 years
Conflict of interest/source of funding	Conflict of interest: the authors declared no conflicts of interest. Source of funding: the authors declared that funding was not received.

*This study and Schmeller, 2012 were conducted on the same group of people. The authors published 3 analyses:

- Schmeller, 2012 was conducted 4 years after liposuction and includes QoL and safety data on 112 people.
- Baumgartner, 2016 was conducted 8 years after liposuction and includes QoL data on 85 people.
    - As this study does not present safety data and presents shorter follow-up data than Baumgartner, 2021, it is included in the Appendix and is not summarised in the Summary of key evidence.
- Baumgartner, 2021 was conducted 12 years after liposuction and includes QoL data on 60 people.

Analysis

Follow-up issues: Due to changes in address, 14 people could no longer be reached. A further 27 people did not respond. A total of 71 people completed and returned the questionnaires, which corresponds to a return rate of 63.3%. Only people who also completed questionnaires at 4 and 8 years were included in this analysis (n=60).

Study design issues: This single arm, single centre, non-randomised, before-and-after study assessed the long-term outcomes of liposuction for people with lipoedema. Outcomes assessed included patient-reported symptoms/complaints, weight, and need for conservative therapy. Complaints were assessed by a questionnaire comprised of the following 7 items: spontaneous pain, sensitivity to pressure, oedema, bruising, restriction of movement, cosmetic impairment, and reduction in QoL. Responses to these items were captured on a 5-point scale: 0=none, 1=minor, 2=medium, 3=strong, 4=very strong). In addition to the 7 impairment items, an overall impairment value (mean value from all 7 scales) was also evaluated. People completed the questionnaire an average of 4, 8, and 12 years after surgery. Weight was self-reported and unverifiable.

Changes in impairments over time were tested for significance using one-way repeated-measures ANOVA with repeated measurements for the 4 measurement points. Effect sizes of 0.20 to 0.50 were considered 'small' group differences, those between 0.50 to 0.80 were 'medium', and effect sizes 0.80 or more were 'strong' differences. $p<0.05$ was considered significant. No adjustment was made for multiple comparisons.

Study population issues: Of the 60 people in the current study, 18 (30%) had stage 1 lipoedema and 42 (70%) had stage 2 lipoedema prior to liposuction. There were no women with stage 3 lipoedema who had taken part in all 3 questionnaires. The authors state that the underrepresentation of this group was due to comorbidities and adiposity.

Key efficacy findings

Weight

Number of people analysed: 60

Follow up at time of assessment: 12 years

- Average weight increased by 0.5 kg from 79.7 kg (range 50.0 to 116.0 kg) preoperatively, to 80.2 kg (range 40.0 to 130.2 kg) postoperatively.

Complaints/symptoms

Number of people analysed: 60

Follow up at time of assessment: 12 years

- For all questionnaire items, postoperative scores were statistically significantly lower than preoperative (all $p<0.001$; Table below), and these decreases were maintained to 12 years follow up.
- All effect sizes for the comparison of complaints between each measurement time and before surgery were substantially above 0.8 (indicating a 'strong' effect).
- The comparison between the first (4-year) and the second (8-year) evaluation resulted in very low effect sizes for the items spontaneous pain, sensitivity to pressure and oedema. The effect sizes regarding the items bruising, restriction of movement, cosmetic impairment, reduction in QoL and overall impairment were slightly higher, but still evaluated as low, showing a slight increase of these complaints from the 4-year to 8-year evaluation.
- The comparison between the second (8-year) and the most recent measurement (12-year) resulted in very low effect sizes for all items showing no substantial further changes.

Complaints before and after liposuction in people with lipoedema

Questionnaire item	Mean questionnaire score (SD)				ANOVA (F-value)	p-value
	Before liposuction	2010 (4 years)	2014 (8 years)	2019 (12 years)		
Spontaneous pain	1.76 (1.41)	0.33 (0.55)	0.31 (0.51)	0.37 (0.49)	45.33	<0.001
Sensitivity to pressure	2.88 (1.06)	0.88 (0.91)	1.02 (1.03)	0.98 (0.94)	78.80	<0.001
Oedema	3.05 (1.06)	1.42 (0.91)	1.51 (0.93)	1.35 (0.88)	75.98	<0.001
Bruising	3.04 (0.98)	1.16 (0.98)	1.47 (1.23)	1.40 (1.08)	58.28	<0.001
Restriction of movement	2.13 (1.32)	0.20 (0.40)	0.59 (0.71)	0.52 (0.81)	72.70	<0.001
Cosmetic impairment	3.46 (0.91)	1.00 (0.82)	1.46 (1.15)	1.48 (1.08)	101.70	<0.001
Reduction in QoL	3.49 (0.77)	0.69 (0.81)	1.00 (1.04)	0.96 (0.90)	179.50	<0.001
Overall impairment	2.81 (0.69)	0.84 (0.58)	1.05 (0.70)	0.99 (0.66)	182.60	<0.001

Abbreviations: ANOVA, analysis of variance; QoL, quality of life; SD, standard deviation.

Conservative therapy use

Number of people analysed: 37 people who received combined decongestive therapy preoperatively.

Follow up at time of assessment: 12 years

- 20 people (54%) reported that they still received manual lymphatic drainage and wore compression garments.
- 7 people (19%) required fewer conservative treatments than before.
- 10 people (27%) no longer needed either manual lymphatic drainage or compression therapy.

Key safety findings

No safety findings were reported.

Study 3 Wollina U (2019)

Study details

Study type	Single arm, single centre, non-randomised, before-and-after study
Country	Germany
Recruitment period	2007 to 2018
Study population and number	n=111 People with lipoedema unresponsive to complex decongestive therapy
Age and sex	Mean 44 years; 100% female
Patient selection criteria	Inclusion criteria: consecutive people with lipoedema not responding to complex decongestive therapy. Non-responsiveness was defined as treated by complex decongestive therapy for at least 6 months without improvement or even deterioration of pain sensations and/or leg volume.
Technique	**Technique summary:** most people were treated by microcannular liposuction under tumescent anaesthesia with mechanical liposuction, but some people had a 980 nanometre-diode laser-assisted liposuction (not further described). Liposuction was performed with 2 to 3 mm blunt cannulas connected to a vacuum pump (Vacuson 60L, Nouvag, Goldach, Switzerland). **Procedural frequency:** a total of 334 procedures were performed (mean 3 per person), and procedures were spaced 6 to 8 weeks apart. **Infiltration volume:** a maximum of 6,000 ml of tumescent anaesthesia solution was infiltrated. **Aspiration volume:** the median amount of removed lipoaspirate was 4,700 ml (SD 7,579 ml), with a range of 950 to 14,250 ml. **Postoperative care:** no drains and no prophylactic antibiotics were needed. Laboratory monitoring of methaemoglobinaemia was performed. People were instructed to wear flat-knitted compression garments for at least 6 months, with garments refitted as required during this time.
Follow up	Median 2.0 (SD 2.1) years; long-term follow up (5 to 7 years) was available in 18 people
Conflict of interest/source of funding	Conflict of interest: the authors declared no conflicts of interest. Source of funding: not reported.

Analysis

Study design issues: This single arm, single centre, non-randomised, before-and-after study assessed the efficacy and safety of microcannular liposuction in tumescent anaesthesia for people with lipoedema unresponsive to complex decongestive therapy. Outcomes assessed included pre- to postoperative change in limb circumference (in cm), pain perception, mobility, and bruising. Pain was measured by a 10-point visual analogue scale before the first and the last liposuction, with higher numbers indicative of worse pain. Changes in mobility and bruising were assessed on a 3-point scale: 0=no improvement, 1=minor to medium

improvement, 2=marked improvement or no impairment at all. This study reported infiltration of a maximum of 6 litres of tumescent solution containing 0.07% prilocaine. Given the maximum infiltration volume, a person would receive 4.2 g of prilocaine, approximately 10-times greater than the maximum dose of 400 mg listed in the BNF.

Differences before-and-after treatment were analysed by two-tailed Mann–Whitney U test. $p<0.5$ was considered as statistically significant. The authors do not report adjustment for multiple comparisons.

Study population issues: 7 people had lipoedema Stage 1, 50 people with Stage 2, and 48 people with Stage 3. All people had an involvement of the legs, 108 people had a dominance of the upper legs and 2 had a dominance of the lower legs. Twenty-seven people also had an involvement of the arms (24%).

Key efficacy findings

Weight

Number of people analysed: 111

Follow up at time of assessment: 2 years

- **Limb circumference**: The median reduction of limb circumference on thighs was 6 cm (SD 1.6 cm) (no significance test reported).

Complaints/symptoms

Number of people analysed: 111

Follow up at time of assessment: 2 years

- **Pain**: The median pain level before treatment was 7.8 (SD 2.1). There was a statistically significant median reduction of pain sensations of the visual analogue 10-point scale of 2.2 (SD 1.3) at the end of the treatment ($p<0.3$).

- **Mobility**: All people had better perceived mobility following liposuction. Marked improvement or complete loss of impairment was reported by 86% of people, minor to medium improvement was reported by 14% of people.

- **Bruising**: There was a statistically significant improvement in ‘bruising after minor trauma’ – bruising improved somewhat in 21% and completely or almost completely in 29% ($p<0.5$).

Long-term lipoedema relapse

Number of people analysed: 18

Follow up at time of assessment: 5 to 7 years

- None of the 18 people who had follow up between 5 and 7 years after liposuction had a relapse of lipoedema.

Key safety findings

Number of people analysed: 111

Follow up at time of assessment: 2 years

There were 0 deaths, 0 wound infections, and 0 surgical interventions necessary because of adverse events.

The following adverse events were reported:

- Temporary methaemoglobinaemia, n=111
    - The publication reports that 'the most common [adverse events] were a temporary methaemoglobinaemia (100%), that was treated by intravenous injection of toluidine blue'. It is unclear whether all people received toluidine blue. There is no further information about the severity of methaemoglobinaemia.
- Bruising, n=109
    - All disappeared without any specific intervention.
- Temporary burning sensation, n=91
    - All disappeared without any specific intervention.
- Mild arm-vein phlebitis, n=2
- Microscopic pulmonary fat embolism, n=1
    - Treated by rivaroxaban. Further liposuctions were well tolerated with perioperative low-molecular heparin prophylaxis.
- Acute pulmonary oedema (initial diagnosis)/retarded community-acquired atypical pneumonia with aggravation of pre-existent comorbidities (final diagnosis), n=1
    - Required intensive care unit admission.
- Acute lower arm oedema after toluidine blue extravasation, n=1
    - Treated with prophylactic antibiosis, prednisolone, and compression.
- Postsurgical anaemia requiring a blood transfusion, n=1
- Epileptic attack, n=1
    - Person had no known comorbidities. Further liposuctions did not result in epileptic attacks.
- Non-infectious panniculitis of the inner sides of the knees, n=1
    - Treated by an oral combination of herbal enzymes.

Study 4 Rapprich S (2011)

Study details

Study type	Single arm, single centre, non-randomised, before-and-after study
Country	Germany
Recruitment period	2006 to 2008
Study population and number	n=25 People with lipoedema receiving liposuction
Age and sex	Mean 38.0 years; 100% female
Patient selection criteria	Inclusion criteria: people with lipoedema receiving liposuction. The diagnosis of lipoedema was confirmed in all people included in the study on the basis of guideline criteria.
Technique	**Technique summary:** tumescent anaesthesia liposuction with a vibrating device (VibraSat®, Möller Medical, Fulda). **Procedural frequency:** people were treated in 1 to 5 procedures (mean 2.5 [SD 1.1], median 2). Procedures were spaced at 4-week intervals. **Infiltration volume:** in most people, approximately 6,000 ml tumescence solution were infiltrated per session, with a maximum of 7,000 ml, and a minimum of 2,000 ml. The mean was 5,155 ml (SD 1,304 ml). The infiltration was performed with a roll pump with a closed tube system (LipoSat®, Möller Medical, Fulda). **Aspiration volume:** for each procedure, the aspiration volume was an average of 2,482 ml (SD 968 ml) and the pure fat component was on average 1,909 ml (SD 874 ml), or 77%. **Postoperative care:** people were given antibiotic prophylaxis for 3 days and thrombosis prophylaxis for 5 days. Compression garments were worn during the first 7 days after liposuction for 24 hours per day. For liposuction of the lower legs, during the first 2 to 3 days a circumferential compression dressing was applied. Afterward, compression therapy continued during the daytime only for 4 to 6 weeks. Starting on the third day after liposuction, manual lymphatic drainage was performed 2 to 3 times per week for at least 6 weeks.
Follow up	6 months
Conflict of interest/source of funding	Conflict of interest: the authors declared no conflicts of interest. Source of funding: not reported.

Analysis

Follow-up issues: 105 people with lipoedema were treated at this centre during the recruitment period, with 25 who received liposuction included in this analysis. Reasons for exclusion from this analysis included incomplete therapy, 6-month follow up not yet performed, or had not received liposuction.

Study design issues: This single arm, single centre, non-randomised, before-and-after study assessed the safety and efficacy of liposuction for treatment of lipoedema. Outcomes included leg volume, measured by 3D imaging, a self-assessment questionnaire of complaints and symptoms, completed before and 6 months after surgery, and need for conservative therapy. The questionnaire contained 15-items: pain, sensitivity to pressure, bruising, tension, excessive warmth in legs, feeling cold in legs, muscle cramps, heavy legs, tired legs, swelling, skin involvement, itching, difficulty walking, impact on QoL, and satisfaction with appearance. Each item was scored on a 11-point visual analogue scale, with higher scores indicating worse symptoms/complaints/QoL. This study reported infiltration of a maximum of 7 litres of tumescent solution containing 0.05% prilocaine. Given the maximum infiltration volume, a person would receive 3.5 g of prilocaine, approximately 9-times greater than the maximum dose of 400 mg listed in the BNF.

Wilcoxon tests were used to assess statistically significant differences in paired samples with abnormal distribution. In all the tests performed, 2-sided significance testing was performed. A p-value <0.05 for statistical significance was used. The authors do not report adjustment for multiple comparisons.

Study population issues: 20 people had lipoedema affecting the whole leg, 3 had lipoedema of the thigh, and 2 had lower leg involvement only.

Key efficacy findings

Body shape

Number of people analysed: 25

Follow up at time of assessment: 6 months

- After liposuction, there was a reduction in leg volume of 18.0 litres (SD 3.8 litres) to 16.8 litres (SD 3.5 litres). This corresponds to an average reduction of 1.2 litres (SD 1.0 litres), or 6.9%. No test of significance was reported.

Complaints/symptoms

Number of people analysed: 25

Follow up at time of assessment: 6 months

- With the exception of the ‘legs feel cold’ item on the questionnaire, the mean visual analogue scale score was statistically significantly lower 6 months postoperatively than the preoperatively (all p<0.001 except excessive warmth in legs [p<0.008] and muscle cramps [p<0.043]) (Table below).

Change in questionnaire item scores pre- and postoperatively

Questionnaire item	Visual analogue scale mean		p-value
	Preoperative	6 months postoperative	
Are the affected areas painful?	7.2	2.1	<0.001
Are the affected areas sensitive to touch or pressure?	6.4	1.9	<0.001
Do you bruise easily?	7.9	4.2	<0.001
Do you feel tension in your legs?	7.7	2.3	<0.001
Do you feel excessive warmth in your legs?	3.0	1.4	<0.008
Do your legs feel cold?	3.8	2.1	<0.120
Do you have muscle cramps?	2.7	1.3	<0.043
Do your legs feel heavy?	8.4	3.6	<0.001
Do your legs feel tired?	8.4	3.5	<0.001
Do you sometimes have swelling?	6.9	3.3	<0.001
Is there skin involvement?	3.5	1.3	<0.001
Is there itching?	4.2	1.9	<0.001
Do you have difficulty walking?	4.6	1.6	<0.001
How much does your condition affect your QoL?	8.7	3.6	<0.001
How satisfied are you with the appearance of your legs?	9.5	5.0	<0.001
Total	92.0	39.0	<0.001

Abbreviations: QoL, quality of life.

Lipoedema relapse

Number of people analysed: 25

Follow up at time of assessment: 6 months

- There was no new incidence of lymphoedema in the follow-up period.

Conservative therapy use

Number of people analysed: 15 people that received manual lymphatic drainage and 19 people that received compression therapy before liposuction.

Follow up at time of assessment: 6 months

- 2 people reported use of manual lymphatic drainage at the follow up, reduced from 15.
- 4 people reported use of compression therapy at the follow up, reduced from 19.

Key safety findings

Number of people analysed: 25

Follow up at time of assessment: 6 months

There was 1 case of deep vein thrombosis of the lower leg in a person with history of deep vein thrombosis.

- This was treated promptly and there were no further complications.

Study 5 Rapprich S (2015)

Study details

Study type	Single arm, single centre, non-randomised, before-and-after study*
Country	Germany
Recruitment period	2003 to 2011
Study population and number	n=85 People with lipoedema receiving liposuction
Age and sex	Mean 38.0 years; 100% female
Patient selection criteria	Inclusion criteria: people with lipoedema receiving liposuction.
Technique	**Technique summary:** tumescent anaesthesia liposuction with a vibrating device. **Procedural frequency:** people were treated in 1 to 6 procedures (median 3; mean 2.61). **Infiltration volume:** the tumescence solution was infiltrated with a continuously operating roll pump system. Infiltration continued until the skin developed a hard elastic turgor and until the tissue was blanched by the tissue pressure and the proportion of adrenaline in the tumescence solution ('blanching effect'). **Postoperative care:** people received postoperative antibiotic prophylaxis for 3 days and thrombosis prophylaxis for 5 or 10 days dependent on the risk profile. The people wore compression stockings 24 hours a day for 1 week and then only during the daytime for a further 4 to 6 weeks. Manual lymphatic drainage sessions were prescribed as further follow-up treatment, 2 to 3 times a week over a period of at least 6 weeks.
Follow up	6 months
Conflict of interest/source of funding	Conflict of interest: not reported. Source of funding: not reported.

*This study was conducted by the same first author as Rapprich, 2011 and uses a similar technique, follow-up timings, and questionnaire. It is therefore likely that the 25 people reported in Rapprich, 2011 are also included in Rapprich, 2015.

Analysis

Study design issues: This single arm, single centre, non-randomised, before-and-after study assessed the safety and efficacy of liposuction for treatment of lipoedema. Outcomes included a questionnaire of complaints and symptoms, completed before and 6 months after surgery. The questionnaire contained 15-items: pain, sensitivity to pressure, bruising, tightness, excessive warmth in legs, feeling cold in legs, muscle cramps, heavy legs, tired legs, swelling, skin involvement, itching, difficulty walking, impact on QoL, and satisfaction with appearance. Each item was scored on a 11-point visual analogue scale, with higher scores indicating worse symptoms/complaints/QoL.

Wilcoxon tests were used to assess statistically significant differences in questionnaire responses. A p-value for statistical significance was not reported. The authors do not report adjustment for multiple comparisons.

Key efficacy findings

Complaints/symptoms

Number of people analysed: 85

Follow up at time of assessment: 6 months

- In every item on the questionnaire, the mean visual analogue scale score was statistically significantly lower 6 months postoperatively than the preoperatively (all p<0.001) (Table below).

Change in questionnaire item scores pre- and postoperatively

Questionnaire item	Visual analogue scale mean		p-value
	Preoperative	6 months postoperative	
Do you have pain in the affected regions?	6.5	2.1	<0.001
Is sensitivity to touch or tenderness present?	6.5	2.4	<0.001
Do you bruise easily?	8.1	4.3	<0.001
Do your legs feel tight?	6.9	2.6	<0.001
Do your legs feel hot?	2.8	1.2	<0.001
Do your legs feel cold?	3.4	1.6	<0.001
Do you have muscle cramps?	2.7	1.3	<0.001
Do your legs feel heavy?	7.8	3.1	<0.001
Do your legs feel tired?	7.4	3.1	<0.001
Do your legs swell?	6.3	3.2	<0.001
Are there skin complications?	3.2	1.1	<0.001
Do your legs itch?	2.8	1.3	<0.001
Is your walking restricted?	4.1	1.2	<0.001
How would you assess the reduction in your QoL?	8.5	3.3	<0.001
Are you satisfied with the appearance of your legs?	9.2	5.0	<0.001
Total	86.2	36.8	<0.001

Abbreviations: QoL, quality of life.

Key safety findings

Number of people analysed: 85

Follow up at time of assessment: 6 months

The following adverse events occurred during the study period:

- Postoperative bruising, n=12
    - Mild haematoma, n=5
    - Moderate haematoma, n=4

  - Haematoma that required revision, n=2
  - Seroma that required treatment, n=1
- Thrombophlebitis, n=1

Study 6 Dadras M (2017)

Study details

Study type	Single arm, single centre, non-randomised, before-and-after study*
Country	Germany
Recruitment period	2010 to 2013
Study population and number	n=25 People with lipoedema receiving liposuction.
Age and sex	Median 45 years; 100% female
Patient selection criteria	Inclusion criteria: people with lipoedema receiving liposuction. Lipoedema diagnosis was clinically confirmed by a lymphologist, ruling out other lymphatic diseases.
Technique	**Technique summary:** tumescent liposuction under general anaesthesia with either vibrating or water-jet-assisted device. **Preoperative treatment:** people had typically already received at least 6 months of combined decongestive therapy without improvement of symptoms. **Procedural frequency:** people received an average of 3 procedures, with a range of 1 to 7 procedures. **Aspiration volume:** the mean volume of removed fat per liposuction was 3,106 ml (range 1,450 to 6,600 ml) and the mean volume of total removed fat per person was 9,914 ml (range 4,000 to 19,850 ml). **Postoperative care:** antibiotics were administered as a single shot for prophylaxis. Compression garments were put on immediately after liposuction. New garments were measured 3 weeks after liposuction. Manual lymphatic drainage was allowed after postoperative day 2.
Follow up	Mean 37 months
Conflict of interest/source of funding	Conflict of interest: the authors declared no conflicts of interest. Source of funding: not reported.

*There may have been some overlap in the people recruited in Dadras, 2017 and Ghods, 2020. This is not explicitly described in the publications; however, both were authored by Ghods M, and had overlapping recruitment periods.

Analysis

Follow-up issues: A total of 33 people received liposuction for lipoedema in the recruitment period. Twenty-five people responded to a standardised questionnaire in 2013 and were available for follow up in 2015.

Study design issues: This single arm, single centre, non-randomised, before-and-after study examined the long-term results of liposuction in people with lipoedema. Outcomes included the severity of complaints and the use of conservative therapy. Outcomes were assessed by a standardised questionnaire with items on spontaneous pain, pain upon pressure, feeling of tension, bruising, cosmetic impairment, and general impairment of QoL. These items were scored on a 0 to 10 scale, with higher scores indicating worse symptoms/complaints/QoL. The questionnaire also included items on frequency of manual lymphatic drainage

per month and the number of hours per day the person wore compression garments. The sum of these 2 values gave a 'combined decongestive therapy score'. People first completed the questionnaire in 2013, assessing both their preoperative QoL and their postoperative QoL. The retrospective nature of the collection of preoperative data is a potential source of bias. In 2015, people were asked to assess their current (postoperative) QoL only.

Statistical analyses were performed using repeated-measures ANOVA with the Bonferroni correction (for multiple comparisons) after meeting the criteria of the Mauchly test of sphericity. All the tests were 2-sided and $p<0.05$ was considered statistically significant.

Study population issues: All people had lipoedema of the lower limb. Additional upper limb involvement was present in 9 people (36%). One person had stage 1 lipoedema, 11 people had stage 2 lipoedema, and 13 people had stage 3 lipoedema.

Key efficacy findings

Weight

Number of people analysed: 25

Follow up at time of assessment: not specified at which postoperative follow-up data were obtained

- BMI was reduced from a mean of 35.3 kg/m^2 (range 24.5 to 50.6 kg/m^2) before liposuction to a mean of 33.9 kg/m^2 (range 22.7 to 47.2 kg/m^2) (significance not reported).

Complaints/symptoms

Number of people analysed: 25

Follow up at time of assessment: Postoperative 1: mean 16 months; Postoperative 2: mean 37 months

- For all questionnaire items on complaints, there were statistically significant decreases in the severity of complaints between preoperative assessment and both postoperative assessments (all $p\leq0.001$; Table below).

- In the cosmetic impairment item, the mean score statistically significantly increased between postoperative assessment 1 and 2 ($p<0.01$). The authors theorise that this was due to the excess skin left after extensive liposuction.

Conservative therapy use

Number of people analysed: 25

Follow up at time of assessment: Postoperative 1: mean 16 months; Postoperative 2: mean 37 months

- The combined decongestive therapy score statistically significantly decreased from preoperative to postoperative assessment 2 ($p=0.011$; Table below). Of the 21 people who regularly had manual lymphatic drainage and wore compression garments before liposuction, 14 people had decreased their therapy and 3 people no longer needed conservative therapy at the second postoperative assessment.

Change in questionnaire item scores pre- and postoperatively

Questionnaire item	Preoperative, mean (SD)	Postoperative 1, mean (SD)	Postoperative 2, mean (SD)	p-value, pre. vs. post. 1	p-value, pre. vs. post. 2	p-value, post. 1 vs. post. 2
Complaints						
Spontaneous pain	7.20 (1.46)	3.70 (1.79)	4.28 (2.10)	<0.001	<0.001	0.177
Sensitivity to pressure	7.38 (1.79)	3.98 (1.83)	4.42 (2.08)	<0.001	<0.001	0.115
Feeling of tension	7.52 (1.36)	3.26 (2.28)	4.06 (2.18)	<0.001	<0.001	0.070
Bruising	6.96 (1.58)	4.36 (1.91)	4.64 (1.83)	0.001	0.001	0.511
Cosmetic impairment	8.98 (0.81)	5.10 (1.93)	7.36 (1.66)	<0.001	<0.001	<0.01
General QoL impairment	8.38 (1.06)	4.30 (1.80)	5.16 (1.60)	<0.001	<0.001	0.055
CDT score	20.48 (4.13)	16.38 (6.97)	13.90 (7.32)	0.108	0.011	0.062

Abbreviations: CDT, combined decongestive therapy; QoL, quality of life; SD, standard deviation.

Key safety findings

Number of people analysed: 25

Follow up at time of assessment: 37 months

- One person developed erysipelas which required antibiotics.

Study 7 Ghods M (2020)

Study details

Study type	Single arm, single centre, non-randomised, before-and-after study
Country	Germany
Recruitment period	2009 to 2019
Study population and number	n=106 People with lipoedema receiving liposuction.
Age and sex	Average 41 years; 100% female
Patient selection criteria	Inclusion criteria: people with lipoedema receiving liposuction. Lipoedema diagnosis had been clinically confirmed by a lymphologist, ruling out other lymphatic diseases.
Technique	**Technique summary:** tumescent liposuction under general anaesthesia with either vibrating or water-jet-assisted device. **Preoperative treatment:** all people received preoperative conservative therapy for at least 6 months. **Procedural frequency:** people received a median of 3 operations, spanning a surgical treatment period of 8 months (interquartile range 4 to 14 months). **Infiltration volume:** people were infiltrated with of a maximum of 6,000 ml of tumescent solution. **Aspiration volume:** the mean lipoaspirate volume per operation was 6,355 ml (SD 2,797 ml) with a mean total aspirate volume per person of 17,887 ml (SD 10,341 ml) throughout the entire surgical treatment.
Follow up	Median 20 months (range 6 to 115 months)
Conflict of interest/source of funding	Conflict of interest: the authors declared no conflict of interest. Source of funding: not reported.

Analysis

Follow-up issues: Out of 147 people who received liposuction during the recruitment period, 106 were included after returning a completed postoperative questionnaire.

Study design issues: This single arm, single centre, non-randomised, before-and-after study assessed the efficacy and safety of liposuction in people with liposuction. Outcomes included BMI, comorbid conditions, and complaints/symptoms before and after surgery. Outcomes were assessed by completion of a questionnaire at a median follow up of 20 months (range 6 to 115 months). Both preoperative and postoperative data were collected by this questionnaire. The retrospective nature of the collection of preoperative data is a potential source of bias.

Group differences in the pre/postoperative comparison were assessed using the nonparametric Wilcoxon matched-pairs signed-rank test. A p-value of <0.05 was considered significant in 2-group comparisons. The authors do not report adjustment for multiple comparisons.

Study population issues: There were 11 people with lipoedema stage 1, 61 with stage 2, and 34 with stage 3.

Key efficacy findings

Weight

Number of people analysed: 106

Follow up at time of assessment: 20 months

- At follow up, there was a statistically significant reduction in mean BMI of 2.7 kg/m^2 (IQR 1.1 to 5.2 kg/m^2) ($p<0.0001$).

Complaints/symptoms and comorbid conditions

Number of people analysed: 106

Follow up at time of assessment: 20 months

- **Pain perception**: postoperatively, people reported statistically significant reductions in pain perception ($p<0.0001$) [results not reported].
- **Sex life**: postoperatively, people reported statistically significant improvements in the quality of their sex life ($p<0.0001$) [results not reported].
- **Menstrual cycle**: 19 people had abnormal menstrual bleeding preoperatively. Postoperatively, 10 people (53%) reported normalisation of the menstrual cycle (significance not reported).
- **Hypothyroidism**: 32 people received treatment for hypothyroidism. Postoperatively, there was no statistically significant change in L-thyroxine dose ($p=0.0945$).
- **Migraine**: 24 people were diagnosed with migraine preoperatively. Postoperatively, the number of migraine attacks per month was statistically significantly reduced ($p=0.0002$) [results not reported].
- **Skin disorders**: 20 people had lipoedema-associated dermatoses requiring treatment preoperatively. Postoperatively, 17 people (90%) reported improved symptoms (significance not reported).

Key safety findings

Number of people analysed: 106

Follow up at time of assessment: 20 months

The following adverse events occurred:

- Superficial wound infection, n=4
- Seroma, n=2

- Mild postoperative bleeding which did not necessitate a blood transfusion, n=1

All complications could be treated conservatively.

Study 8 Witte T (2020)

Study details

Study type	Single arm, single centre, non-randomised, before-and-after study
Country	Germany
Recruitment period	2016 to 2017
Study population and number	n=63 People with lipoedema receiving liposuction
Age and sex	Median 35 years; sex not reported
Patient selection criteria	Inclusion criteria: people who were planned to receive liposuction as a treatment for lipoedema during the recruitment period. This study reported the long-term follow up of these people.
Technique	**Technique summary:** water-jet-assisted, tumescent anaesthesia liposuction (body jet/Human Med AG, Schwerin, Germany). **Preoperative treatment:** decongestive measures were applied for at least 6 weeks prior to surgery. People with BMI >40 required preoperative weight reduction. **Procedural frequency:** people received independent operations for lower legs, upper legs/buttocks, and arms (if necessary). Over the course of operative treatment, 6 people (10%) had received 1 operation, 21 people (33%) had received 2, 24 people (38%) had received 3, and 12 people (19%) had received 4 operations. Subsequent operations were performed no earlier than 8 weeks after the previous operation. **Infiltration volume:** at the beginning of the operation, infiltration volume was 200 to 400 ml for the lower legs, 400 to 700 ml for the upper legs and 200 to 300 ml for the upper limb. A mean amount of 12,922 ml (SD 2,922 ml) fat was removed per person over the course of all operations. **Postoperative care:** people were hospitalised overnight. People were given thrombosis prophylaxis for 7 days and a single shot of antibiotic prophylaxis. Compression bandages were applied immediately after surgery. After 2 days, bandages were removed and compression garments were worn for 24 hours per day for 6 weeks, with people then weaned from compression for 2 weeks, with the aim of abandoning compression 8 weeks after the last operation. Manual lymphatic drainage therapy was started at postoperative day 2 with a frequency of 2 sessions per week for at least 8 weeks.
Follow up	Median 21.5 months
Conflict of interest/source of funding	Conflict of interest: 2 authors declared that they are counsellors for Human Med GmbH, the manufacturer of the water-jet-assisted liposuction device used. Source of funding: the authors declared that funding was not received.

Analysis

Follow-up issues: In the time interval, a total of 155 people received liposuction. Among these, 130 people enrolled in the study and preoperative questionnaires were available. A total of 63 people could be followed up and were included in this analysis.

Study design issues: This single arm, single centre, non-randomised, before-and-after study assessed the long-term results of water-jet-assisted liposuction using a standard treatment protocol in the treatment of lipoedema. Outcomes were assessed by a standardised questionnaire given a few days prior to the first surgery and after a median follow up of 21.5 months. The questionnaire included assessment of 11 symptoms/impairments on an 11-point visual analogue scale, with higher scores indicating worse impairment. The 11 symptoms/impairments were: pain, sensitivity to touch, bruising, feeling of tension, feeling of "heavy" leg, swelling, itching, running impairment, occupational impairment, general impairment, and aesthetic impairment. The questionnaire also contained items on the need for conservative therapy.

Statistical analyses were performed with paired, 2-sided t-tests for continuous data and McNemar test for binary variables. $p<0.05$ considered statistically significant. The authors do not report adjustment for multiple comparisons.

Study population issues: 47 people (75%) had lipoedema of both arms and legs; 16 people (25%) had only lipoedema of the legs. Eighteen people (29%) had stage 1 lipoedema and 45 people (71%) had stage 2.

Key efficacy findings

Complaints/symptoms

Number of people analysed: 63

Follow up at time of assessment: 21.5 months

- For all questionnaire items, postoperative scores were statistically significantly lower than preoperative scores (all $p<0.001$; Table below).

Change in questionnaire item scores pre- and postoperatively

Questionnaire item	Preoperative, mean (SD)	Postoperative follow up, mean (SD)	p-value
Pain	6.47 (2.05)	1.39 (1.66)	<0.001
Sensitivity to touch	7.14 (1.90)	1.55 (1.79)	<0.001
Bruising	7.18 (1.93)	2.45 (2.62)	<0.001
Feeling of tension	7.56 (1.72)	1.42 (1.78)	<0.001
Feeling of 'heavy' legs	8.42 (1.80)	1.55 (1.66)	<0.001
Swelling	6.75 (2.41)	1.52 (1.65)	<0.001
Itching	4.00 (3.30)	0.80 (1.30)	<0.001
Running impairment	5.28 (3.04)	0.60 (1.10)	<0.001
Occupational impairment	4.97 (2.63)	0.77 (1.72)	<0.001
General impairment	7.79 (2.11)	0.95 (1.40)	<0.001
Aesthetic impairment	8.71 (2.26)	3.13 (2.48)	<0.001

Abbreviations: SD, standard deviation.

Lipoedema relapse

Number of people analysed: 63

Follow up at time of assessment: 21.5 months

- No recurrence of excess subcutaneous fat was observed in the people in the follow-up period.

Conservative therapy use

Number of people analysed: 56 people receiving manual lymphatic drainage preoperatively; 60 people wearing compression garments preoperatively

Follow up at time of assessment: 21.5 months

- 56 people (88.9%) received manual lymphatic drainage preoperatively. Postoperatively, statistically significantly fewer people required manual lymphatic drainage (25 people; 39.7%; p<0.001).
- 60 people (95.2%) received compression garments preoperatively. Postoperatively, statistically significantly fewer people required compression garments (20 people; 31.7%; p<0.001).

Key safety findings

Number of people analysed: 63

No significant complications occurred in any of the people.

Validity and generalisability of the studies

- The studies were homogenous regarding person age and sex. However, there were differences in the lipoedema stage of included people.
- Studies were similar in the number and frequency of liposuction procedures. There were differences in the volume of fluid infiltrated and aspirated.
- Two studies included people who had received either vibrating cannula-assisted or water-jet-assisted liposuction, and 1 study used a water-jet-assisted liposuction technique only. It is unclear which, if either, liposuction technique produces more favourable outcomes. One study reported that some people had 'a 980 nm-diode laser-assisted liposuction', but this was not described in detail (Wollina, 2019).
- CE marked devices were used in Rapprich, 2011, Wollina, 2019, and Witte, 2020.
- Outcomes were collected primarily through person self-report using questionnaires that were not validated.
- All the studies were conducted in Germany. There may exist differences in clinical practice between the UK and Germany that prevent generalisation of the study findings to a UK context.
- Two studies reported retrospective collection of preoperative data via questionnaires completed postoperatively. This method of data collection is a potential source of bias.
- Most studies did not report adjustment for multiple comparisons. Testing many hypotheses without adjustment for multiple comparisons increases the likelihood of finding a statistically significant difference between data that are only different due to chance.
- All studies had a before-and-after design. There were no randomised experimental studies identified.
- The longest follow-up assessment was 12 years.

Existing assessments of this procedure

In 2019, the Canadian Agency for Drugs and Technologies in Health (CADTH) published a rapid response report on liposuction for the treatment of lipoedema

(CADTH, 2019). Evidence was identified by a limited literature search of electronic sources. The CADTH report concluded that 'treatment with liposuction resulted in a significant improvement of pain, sensitivity to pressure, oedema, bruising, feeling of tension, and QoL', 'the benefits of liposuction remained even at long-term (up to 88 months) follow up assessments', and 'liposuction was generally well tolerated'. However, the report cautions that 'the quality of evidence was limited, with sources of uncertainty such as systematic biases due to lack of randomisation, and the use of instruments that have not been validated for the collection of data and assessment in lipoedema-related complaints' (CADTH, 2019). Of note, this report is based on 5 clinical studies, 4 of which are summarised in the Key Evidence section (Dadras, 2017; Wollina, 2019; Schmeller, 2012; Rapprich, 2011) and 1 that is summarised in the Appendix (Baumgartner, 2016) of the IP1843 Overview.

In 2017, Wounds UK published Best Practice Guidelines: The management of lipoedema (Wounds UK, 2017). The methods used to develop the guidelines are not well described in the publication. The guidelines note the following key points on the use of liposuction for lipoedema:

1. There is no evidence that liposuction cures lipoedema, but it may reduce limb bulk and so improve functioning and mobility.
2. People should be advised to try at least 6 to 12 months' non-surgical treatment before undergoing liposuction.
3. Preoperative counselling is important to ensure people understand the non-curative nature of liposuction, the long often painful postoperative course, and the need for ongoing wear of compression therapy (Wounds UK, 2017).

In 2017, the First Dutch guidelines on lipoedema were published (Halk, 2017). These guidelines were produced by a task force organised by the Dutch Society of Dermatology and Venereology. Evidence was collected by a systematic review of English and German language literature. Members of the task force discussed the evidence and recommended tumescent liposuction 'as part of the therapeutic armamentarium in the management of lipoedema'. However, the task force noted that 'tumescent liposuction is only the treatment of choice for people with a suitable health profile and/or inadequate response to conservative and supportive measures' and 'before using tumescent liposuction, associated deteriorating components, such as oedema, obesity, unhealthy lifestyle, lack of physical activity, lack of knowledge about the disease, and psychosocial distress, should be addressed.' The recommendations do not report a level of evidence or strength of recommendation (Halk, 2017).

In 2017, the German Society of Phlebology published the S1 guidelines: Lipoedema (Reich-Schupke, 2017). The methods used to develop the guidelines are not described in the publication. The guidelines state that liposuction 'is

indicated in people with persistent symptoms despite consistent conservative treatment, or if there is further disease progression (volume of subcutaneous fat) and/or exacerbation of symptoms (pain, oedemas)'. Further, the guidelines state that liposuction is 'associated with a pronounced improvement as regards spontaneous pain, tenderness to pressure, oedema, easy bruising; the difference between preoperative and postoperative symptoms is significant', and that 'In the majority of cases, clinical improvement persists for many years'. The guidelines also note that 'morbid obesity associated with lipoedema should be therapeutically addressed prior to liposuction' (Reich-Schupke, 2017). Of note, these guidelines heavily cite German language publications; this literature was not considered in the IP1843 Overview.

In 2020, the First International Consensus Conference published a consensus statement on the prevention of lipoedema using tumescent local anaesthesia (Sandhoefer, 2020). The guidelines were developed by convening a group of international experts. It is not reported how evidence was collected or whether a literature review was performed. The consensus statement concludes that 'multiple studies from Germany have reported long-term benefits for as long as 8 years after liposuction for lipoedema using tumescent local anaesthesia' (Sandhoefer, 2020).

From 2018 to 2020, a group of authors published a series of articles on lipoedema myths and facts (Bertsch, 2020). The 5th and final article, subtitled 'European Best Practice of Lipoedema – Summary of the European Lipoedema Forum consensus', summarises the recommendations of this group. The methods used to collect evidence are not described in the publication. The group question the quality of evidence available on the benefits of liposuction. The group note that benefits of liposuction depend strongly on a clearly defined patient selection. To maximise patient benefit, the group recommend the following criteria for patient selection:

1. Symptoms persist despite at least 12 months of conservative treatment.
2. The person has considerable functional disabilities (for example, restricted mobility).
3. The patient's weight has been stable for at least 12 months.
4. A preoperative psychological assessment is available (Bertsch, 2020).

Related NICE guidance

Below is a list of NICE guidance related to this procedure.

Interventional procedures

IP overview: Liposuction for chronic lipoedema

- Liposuction for chronic lymphoedema. This guidance is currently under review and is expected to be updated in 2022. For more information, see https://www.nice.org.uk/guidance/IPG588

Additional information considered by IPAC

Professional experts' opinions

Expert advice was sought from consultants who have been nominated or ratified by their professional Society or Royal College. The advice received is their individual opinion and is not intended to represent the view of the society. The advice provided by professional experts, in the form of the completed questionnaires, is normally published in full on the NICE website during public consultation, except in circumstances but not limited to, where comments are considered voluminous, or publication would be unlawful or inappropriate. Two Professional expert questionnaires for liposuction for lipoedema were submitted and can be found on the NICE website.

Patient organisation opinions

Patient organisation submissions for liposuction for lipoedema were received and can be found on the NICE website.

Patient commentators' opinions

NICE received 29 completed questionnaires from people with lipoedema.

The patient commentators' views on the procedure were consistent with the published evidence and the opinions of the professional experts. See the patient commentary summary for more information.

Company engagement

A structured information request was sent to 1 company who manufacture a potentially relevant device for use in this procedure. NICE received 1 completed submission. This was considered by the IP team and any relevant points have been taken into consideration when preparing this overview.

Issues for consideration by IPAC

- There was a significant amount of German language literature identified that is not included in this Overview.

References

Key evidence

1. Schmeller W, Hueppe M, and Meier-Vollrath I. (2012) Tumescent liposuction in lipoedema yields good long-term results. The British Journal of Dermatology 166(1):161-8.
2. Baumgartner A, Hueppe M, Meier-Vollrath I et al. (2021) Improvements in patients with lipedema 4, 8 and 12 years after liposuction. Phlebology 36(2):152-9.
3. Wollina U and Heinig B. (2019) Treatment of lipedema by low-volume micro-cannular liposuction in tumescent anesthesia: Results in 111 patients. Dermatologic Therapy 32(2):e12820.
4. Rapprich S, Dingler A, and Podda M. (2011) Liposuction is an effective treatment for lipedema-results of a study with 25 patients. Journal der Deutschen Dermatologischen Gesellschaft = Journal of the German Society of Dermatology 9(1):33-40.
5. Rapprich S, Baum S, Kaak I et al. (2015) Treatment of lipoedema using liposuction: Results of our own surveys. Phlebologie 44(3):121-32.
6. Dadras M, Mallinger PJ, Corterier CC et al. (2017) Liposuction in the treatment of lipedema: A longitudinal study. Archives of Plastic Surgery 44(4):324-31.
7. Ghods M, Georgiou I, Schmidt J et al. (2020) Disease progression and comorbidities in lipedema patients: A 10-year retrospective analysis. Dermatologic Therapy 33(6):e14534.
8. Witte T, Dadras M, Heck FC et al. (2020) Water-jet-assisted liposuction for the treatment of lipedema: Standardized treatment protocol and results of 63 patients. Journal of Plastic, Reconstructive & Aesthetic Surgery 73(9):1637-44.

Existing assessments of this procedure

9. CADTH (2019) Liposuction for the treatment of lipedema: a review of clinical effectiveness and guidelines. (CADTH rapid response report: summary with critical appraisal).
10. Wounds UK (2017) Best Practice Guidelines: The Management of Lipoedema.
11. Halk AB and Damstra RJ. (2017) First Dutch guidelines on lipedema using the international classification of functioning, disability and health. Phlebology 32(3):152-9.

12. Reich-Schupke S, Schmeller W, Brauer WJ et al. (2017) S1 guidelines: Lipedema. Journal der Deutschen Dermatologischen Gesellschaft = Journal of the German Society of Dermatology 15(7):758-67.

13. Sandhofer M, Hanke WC, Habbema L et al. (2020) Prevention of Progression of Lipedema With Liposuction Using Tumescent Local Anesthesia: Results of an International Consensus Conference. Dermatologic Surgery: official publication for American Society for Dermatologic Surgery 46(2):220-8.

14. Bertsch T, Erbacher G, Corda D Lipoedema - myths and facts, Part 5. European Best Practice of Lipoedema – Summary of the European Lipoedema Forum consensus. Phlebologie 49(1):31-49.

Literature search strategy

Databases	Date searched	Version/files
Cochrane Database of Systematic Reviews – CDSR (Cochrane Library)	28/04/2021	Issue 4 of 12, April 2021
Cochrane Central Database of Controlled Trials – CENTRAL (Cochrane Library)	28/04/2021	Issue 4 of 12, April 2021
International HTA database	28/04/2021	-
MEDLINE (Ovid)	28/04/2021	1946 to April 27, 2021
MEDLINE In-Process (Ovid) & MEDLINE ePubs ahead of print (Ovid)	28/04/2021	1946 to April 27, 2021 April 27, 2021
EMBASE (Ovid)	28/04/2021	1974 to 2021 April 26

Trial sources searched

- Clinicaltrials.gov
- ISRCTN
- WHO International Clinical Trials Registry

Websites searched

- National Institute for Health and Care Excellence (NICE)
- NHS England
- Food and Drug Administration (FDA) - MAUDE database
- Australian Safety and Efficacy Register of New Interventional Procedures – Surgical (ASERNIP – S)
- Australia and New Zealand Horizon Scanning Network (ANZHSN)
- General internet search

MEDLINE search strategy

The following search strategy was used to identify papers in MEDLINE. A similar strategy was used to identify papers in other databases.

Number	Search term
1	Lipedema/
2	(Lipoedema* or Lipidema* or lipodema* or lipedema* or lipolymphedema* or adiposalgia* or adipoalgesia* or lipalgia* or "lipohyperplasia dolorosa" or "lipohypertrophy dolorosa").tw.
3	painful fat syndrome*.tw.
4	(subcutaneous* adj2 (adipos* or fat*) adj2 (build-up* or disorder* or disease* or increase* or deposit*)).tw.

5	((fat* or adipos*) adj4 (tissue* or cell*) adj4 (swell* or swollen or enlarge* or build-up* or disorder* or disease*)).tw.
6	or/1-5
7	Lipectomy/
8	(lipectom* or lipoplast* or lipolysis or liposuction* or lipo-suction*).tw.
9	adipectom*.tw.
10	dermolipectom*.tw.
11	(fat* adj4 (suction* or excision*)).tw.
12	Adipose Tissue/su [Surgery]
13	(adipose tissue adj4 surg*).tw.
14	plastic surgery/
15	((plastic or cosmetic or esthetic) adj4 surger*).tw.
16	or/7-15
17	6 and 16
18	Vitruvian infiltration pump*.tw.
19	Vacusat power*.tw.
20	or/17-19
21	animals/ not humans/
22	20 not 21

Appendix

The following table outlines the studies that are considered potentially relevant to the IP overview but were not included in the summary of the key evidence. It is by no means an exhaustive list of potentially relevant studies.

Additional papers identified

Article	Number of patients/ follow up	Direction of conclusions	Reasons for non-inclusion in summary of key evidence section
Bauer AT, von Lukowicz D, Lossagk K et al. (2019) New Insights on Lipedema: The Enigmatic Disease of the Peripheral Fat. Plastic and Reconstructive Surgery 144(6):1475-84	n=209 FU=mean 1 year	Quality of life increases after liposuction with a reduction of pain and swelling and decreased tendency to easy bruising.	Unclear use of statistics to determine treatment effect.
Baumgartner A, Hueppe M, Schmeller W et al. (2016) Long-term benefit of liposuction in patients with lipoedema: a follow-up study after an average of 4 and 8 years. The British Journal of Dermatology 174(5):1061-7	n=85 FU=8 years	People were previously examined 4 years after liposuction. This examination, 8 years after liposuction, found that the improvement in spontaneous pain, sensitivity to pressure, oedema, bruising, and restriction of movement persisted. Improvements in patient self-assessment of cosmetic appearance, quality of life, and overall impairment were also maintained.	People are assessed at 12 years in Baumgartner, 2021.
Chen SG, Hsu SD, Chen TM et al. (2004) Painful fat syndrome in a male patient. British Journal of Plastic Surgery 57(3):282-6	n=1 FU=3.5 years	Report on an extremely rare presentation of lipoedema in a male patient. Tumescent liposuction with postoperative pressure garments provided a satisfactory treatment.	Case report.

Article	Number of patients/ follow up	Direction of conclusions	Reasons for non-inclusion in summary of key evidence section
Peled AW, Slavin SA, and Brorson H. (2012) Long-term Outcome After Surgical Treatment of Lipedema. Annals of Plastic Surgery 68(3):303-7	n=1 FU=4 years	Person was treated with suction-assisted lipectomy and use of compression garments, with successful treatment of the lipodystrophy and maintenance of improved aesthetic results at 4-year postoperative follow up.	Case report.
Sandhofer M, Hofer V, Sandhofer M et al. (2021) High Volume Liposuction in Tumescence Anesthesia in Lipedema Patients: A Retrospective Analysis. Journal of Drugs in Dermatology 20(3):326-34	n=27	Liposuction under high volume tumescent anaesthesia for the treatment of lipoedema people is a safe procedure. The procedures lasted an average of 118 minutes and an average of 6,111 ml of aspirate was removed. No relevant complications associated with drug side effects, hypovolemia or hypervolemia or blood loss were detected.	Studies with more people and longer follow up were included.

Article	Number of patients/ follow up	Direction of conclusions	Reasons for non-inclusion in summary of key evidence section
Schmeller W and Meier-Vollrath I. (2006) Tumescent liposuction: a new and successful therapy for lipedema. Journal of Cutaneous Medicine and Surgery 10(1):7-10	n=28 FU=mean 12.2 months	All people showed great improvement, with normalisation of body proportions. Spontaneous pain, sensitivity to pressure, and bruising either disappeared completely or improved markedly. Other than minor swelling for a few days, no complications could be observed following surgery. All people reported an increase in their quality of life. Physical therapy had to be continued to a much lower degree.	Conducted in the same clinic as Schmeller, 2012. Likely to be significant overlap in patient population.
Schmidt J, Kruppa P, Georgiou I et al. (2021) Management of large volume liposuction in lipedema patients with von Willebrand disease: A systematic review and treatment algorithm. Clinical hemorheology and microcirculation	Systematic review	The evidence for large volume liposuctions in people with lipoedema with von Willebrand disease is limited. Experience is largely based on operations with similar bleeding risks. A safe performance requires an adjustment of the surgical technique and a customised perioperative drug substitution plan. According to the current literature, perioperative thromboembolic events appear to be rare with adequate drug treatment.	Considers people with lipoedema and von Willebrand disease only.

Article	Number of patients/ follow up	Direction of conclusions	Reasons for non-inclusion in summary of key evidence section
van de Pas CB, Boonen RSM, Stevens S et al. (2020) Does tumescent liposuction damage the lymphatic vessels in lipoedema patients? Phlebology 35(4):231–6	n=117 FU=6 months	Lipoedema legs have a delayed lymphatic transport. Tumescent liposuction does not diminish the lymphatic function in lipoedema people, thus tumescent liposuction can be regarded as a safe treatment.	Lymphatic system function not a key outcome.
Wollina U, Goldman A, and Heinig B. (2010) Microcannular tumescent liposuction in advanced lipedema and Dercum's disease. Giornale italiano di dermatologia e venereologia: organo ufficiale, Societa italiana di dermatologia e sifilografia 145(2):151-9	n=2 FU=mean 27 months	The total amount of lipoaspirates varied between 1,800 ml and 3,600 ml. Large adipose tissue removal implies a better the outcome for pain. Patient's satisfaction with treatment was "high" or "very high" in both people.	Studies with more people included.
Wollina U and Heinig B. (2012) Tumescent microcannular (laser-assisted) liposuction in painful lipedema. The European Journal of Aesthetic Medicine and Dermatology 2(2):56-69	n=18 FU=mean 18 months	In contrast to conservative complex decongestive therapy, microcannular tumescent liposuction reduced adipose tissue, pain and improved mobility. The total amount of lipoaspirate was 3,200 ml to 12,000 ml. No signs of lymphedema development after liposuction were observed.	Studies with more people included. Likely to be significant overlap in patient population with Wollina, 2019.

Article	Number of patients/ follow up	Direction of conclusions	Reasons for non-inclusion in summary of key evidence section
Wollina U, Heinig, B, and Nowak A. (2014) Treatment of elderly patients with advanced lipedema: A combination of laser-assisted liposuction, medial thigh lift, and lower partial abdominoplasty. Clinical, Cosmetic and Investigational Dermatology 7:35-42	n=3 FU=range 2 to 4 years	Reports on 3 women aged 55–77 years with advanced lipoedema of the legs and multiple comorbidities. Using microcannular laser-assisted liposuction, a short operation time and early mobilisation were possible. Minor adverse effects were temporary methaemoglobinaemia after tumescent anaesthesia and postsurgical pain. No severe adverse effects were seen. Patient satisfaction was high.	Studies with more people included.

Abbreviations: FU, follow up.