Original article

Short-term cost-effectiveness of one-stage implant-based breast reconstruction with an acellular dermal matrix *versus* two-stage expander-implant reconstruction from a multicentre randomized clinical trial

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Background: Implant-based breast reconstruction (IBBR) is the most commonly performed reconstructive procedure and its economic impact is significant. This study aimed to analyse whether a direct one-stage IBBR with use of an acellular dermal matrix (ADM) is more cost-effective than two-stage (expander-implant) breast reconstruction.

Methods: The BRIOS (Breast Reconstruction In One Stage) study was an open-label multicentre RCT in which women scheduled for skin-sparing mastectomy and immediate IBBR were randomized between one-stage IBBR with ADM or two-stage IBBR. Duration of surgery and hospital stay, and visits for the primary surgery, unplanned and cosmetic procedures were recorded. Costs were estimated at an institutional level. Health status was assessed by means of the EuroQol Five Dimensions 5L questionnaire.

Results: Fifty-nine patients (91 breasts) underwent one-stage IBBR with ADM and 62 patients (92 breasts) two-stage IBBR. The mean(s.d.) duration of surgery in the one-stage group was significantly longer than that for two-stage IBBR for unilateral (2·52(0·55) *versus* 2·02(0·35) h; $P < 0·001$) and bilateral (4·03(1·00) *versus* 3·25(0·58) h; $P = 0·017$) reconstructions. Costs were higher for one-stage compared with two-stage IBBR for both unilateral (€12 448 (95 per cent c.i. 10 722 to 14 387) *versus* €9871 (9373 to 10 445) respectively; $P = 0·025$) and bilateral (€16 939 (14 887 to 19 360) *versus* €13 383 (12 414 to 14 669); $P = 0·002$) reconstructions. This was partly related to the use of relatively expensive ADM. There was no difference in postoperative health status between the groups.

Conclusion: One-stage IBBR with ADM was associated with higher costs, but similar health status, compared with conventional two-stage IBBR. Registration number: NTR5446 (http://www.trialregister.nl).

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Introduction

Worldwide, breast cancer is the most common cancer in women, and its global societal and economic burden is enormous[1,2]. Improving treatment outcomes while controlling costs is a fundamental challenge faced by all healthcare systems[3]. In Western countries, the 5-year survival rate of women diagnosed with breast cancer is approximately 90 per cent[4,5]. Currently, there are more than 3·1 million breast cancer survivors in the USA alone[4]. Over 60 000 new cases of *in situ* breast carcinoma are expected to be diagnosed among women in 2017 in the USA[6],

indicating that the number of breast cancer survivors will increase progressively. More than 90 per cent of women receive surgical treatment, consisting of either lumpectomy or mastectomy[5]. Today, breast reconstruction is offered as a standard treatment option after mastectomy in most developed countries, with the aim of improving long-term outcomes and quality of life. As up to 20 per cent of women undergo breast reconstruction after a mastectomy, it is one of most common reconstructive procedures undertaken by plastic surgeons[7]. An increase in immediate reconstructions has also been noted[8].

There are many surgical options for breast reconstruction, but it is not known which is most cost-effective for an individual patient. Implant-based breast reconstruction (IBBR) methods are used in approximately 80 per cent of reconstructions following mastectomy[9]. IBBR is performed either in one or two stages, with or without the use of an additional tissue matrix. It has been suggested that one-stage reconstruction augmented with an acellular dermal matrix (ADM) is more cost-effective than two-stage IBBR. Having only a single procedure and insertion of a larger breast implant because of enlargement of the subpectoral pocket are advantages of one-stage ADM-assisted IBBR. Improved aesthetic outcome with use of an ADM has been reported as an additional advantage. Several studies[10–14] that compared the cost-effectiveness of different IBBR methods or IBBR with autologous reconstructions have reported conflicting data. In general, the additional use of an ADM was considered cost-effective. In most studies, however, a decision analytical model was used, in which clinical outcomes based on previously published literature were incorporated in the analyses with various probabilities[11,12,14,15]. This method risks selection bias, as clinical outcomes after breast reconstruction vary considerably, with complication rates ranging from 4 to 50 per cent[16–20].

The prospective randomized BRIOS (Breast Reconstruction In One Stage) study compared the cost-effectiveness of one-stage ADM-assisted IBBR and two-stage expander-implant breast reconstruction. The BRIOS study was an open-label phase IV multicentre RCT performed in eight hospitals in the Netherlands[21,22].

Methods

The BRIOS study was a prospective multicentre RCT. Eligible women were older than 18 years with breast carcinoma or a gene mutation linked to breast cancer, who intended to undergo skin-sparing mastectomy and immediate IBBR. Women were assigned randomly to undergo one-stage IBBR with ADM or two-stage IBBR.

The objective was to compare outcomes of one-stage IBBR combined with ADM (Strattice™; LifeCell, Branchburg, New Jersey, USA) with outcomes of conventional two-stage tissue expander-implant breast reconstruction. The primary endpoint of the BRIOS study was health-related quality of life assessed using the BREAST-Q at 1 year after placement of the definite implant. The study was open label, and surgeons and patients were informed about the allocated treatment at least 3 days before surgery. The full study design, methodology and surgical techniques have been described previously[21,22]. The secondary outcome of cost-effectiveness is reported here.

The protocol was approved by the institutional review board from each study centre and the study was preregistered in the Netherlands Trial Register (NTR5446). All patients provided written informed consent. The BRIOS study was performed in accordance with the Declaration of Helsinki, the Consort Statement[23] and guidelines for good clinical practice.

Outcome measures

The following data were recorded: duration of surgery, duration of hospital stay, number of outpatient visits for expander fill in patients who had a two-stage procedure, and number of additional outpatient visits if a complication occurred. These data were collected for the primary breast reconstruction procedure, for the operations needed to treat surgical complications, and for secondary reconstructions if an implant was removed. The duration of surgery was defined as the time from first incision to closure of the wound. All planned second-stage procedures were completed.

Cost calculation

Direct costs were calculated, including all expenses listed in *Table 1*. First, costs of the primary procedures only were calculated. Subsequently, costs of breast reconstruction including operations for surgical complications and secondary procedures were included. Costs associated with procedures for cosmetic improvements were also calculated in a separate analysis. The analyses were performed separately for unilateral and bilateral reconstructions. Costs were estimated in euros based on cost statements from the financial department of VU University Medical Centre (Amsterdam, the Netherlands). An overview of costs used in the calculations is shown in *Table 1*. The operation room (OR) costs included materials, OR and anaesthesia care team and cleaning of the OR. The surgeon's fee and

Table 1 Costs used for the analysis

	Cost (€)
Hospital visits	
First outpatient visit	130
Regular outpatient visit (including visits for expander inflation)	70
Surgery (per h)*	1240
Surgeon's fee (per h)	150
Hospital admission	
Day-care patient	400
Inpatient (per day)	550
Materials	
Tissue expander	530
Breast prosthesis	530
ADM (Strattice®)	2370

*Including all materials, operating room and anaesthesia care team, and cleaning of operating room, but excluding surgeon's fee. ADM, acellular dermal matrix.

costs of the implants (tissue expander, breast prosthesis and ADM) were calculated separately. Calculation of the costs was based on a single surgeon performing each operation.

Patient-reported outcomes

Patient-reported outcomes were measured using the EuroQol Five Dimensions 5L questionnaire (EQ-5D-5L™; EuroQol Group, Rotterdam, the Netherlands), a standardized measure of health status, assessing the following five dimensions: mobility, self-care, usual activities, pain/discomfort and anxiety/depression. Each domain has five levels: no problems (score 1), slight problems (2), moderate problems (3), severe problems (4) and extreme problems (5). Answers were converted into index values using the SPSS® (IBM, Armonk, New York, USA) syntax file that can be ordered from the EuroQol office, enabling comparison of these results with the reference values[24]. Self-rated health was measured on a visual analogue scale, the EQ-VAS, using a 20-cm vertical line with scores ranging from 0 (worst health you can imagine) to 100 (best health you can imagine).

Statistical analysis

Descriptive statistics were used for all variables. Differences between groups in duration of surgery and number of hospital visits in the event of complication were assessed by means of Student's *t* tests. Mann–Whitney *U* tests were used to evaluate differences in hospital stay. Bootstrap analysis was used to calculate 95 per cent confidence interval for the costs. The significance of differences in costs, EQ-5D-5L™ index values and EQ-VAS scores was assessed using the Student's *t* test.

Results

Of 142 women enrolled and randomized, 59 who had one-stage IBBR with ADM and 62 who underwent two-stage IBBR were included in the analysis (*Fig. 1*). Comprehensive details of patient demographics were published previously[21]. Mean follow-up after the first operation was 37 months for one-stage IBBR with ADM and 35 months for two-stage IBBR. Significantly more complications occurred in the one-stage group (40 *versus* 14 per cent of reconstructions), which resulted in higher reoperation (32 *versus* 13 per cent) and implant removal (26 *versus* 4 per cent) rates (*Table 2*)[21].

Primary breast reconstruction procedure

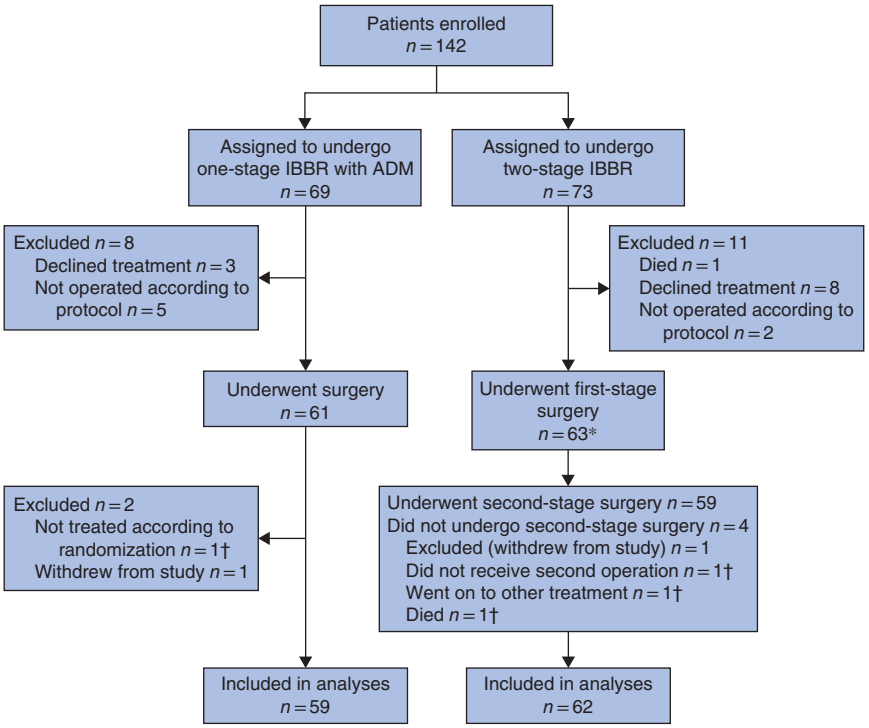
The primary surgery took significantly longer for one-stage IBBR with ADM than two-stage reconstruction, for both unilateral (mean(s.d.) 172(55) *versus* 122(35) min respectively; $P < 0{\cdot}001$) and bilateral (243(60) *versus* 205(58) min; $P = 0{\cdot}017$) reconstructions (*Table 3*). Duration of hospital stay after the primary operation did not differ significantly between the two groups. Combining the two operations in the two-stage group, the total operating time for bilateral two-stage reconstructions was longer than that for bilateral one-stage reconstruction (289(71) *versus* 243(60) min; $P = 0{\cdot}013$). The total median hospital stay was longer for unilateral and bilateral two-stage reconstructions than for one-stage reconstructions (unilateral: median 5 (range 3–10) *versus* 3 (2–8) days respectively, $P = 0{\cdot}002$; bilateral: 5 (2–11) *versus* 4 (2–11) days; $P = 0{\cdot}008$).

The mean total direct cost for unilateral one-stage IBBR was comparable to that of unilateral two-stage reconstruction (€9052 (95 per cent c.i. 8409 to 9815) *versus* €8940 (8445 to 9537) respectively; $P = 0{\cdot}815$). However, for bilateral reconstruction, the cost of one-stage IBBR was higher than that of two-stage reconstruction (€14 364 (13 672 to 15 088) *versus* €12 566 (11 790 to 13 471); $P = 0{\cdot}004$), owing to higher implant costs in the one-stage group.

Additional procedures owing to surgical complications

Among patients who had a complication, visits to the outpatient clinic were more frequent after one-stage than two-stage reconstruction. This difference was statistically significant for bilateral reconstructions (mean(s.d.)

Fig. 1 Flow diagram for the trial



*The patient underwent two-stage implant-based breast reconstruction (IBBR) because of the surgeon's intraoperative decision, and was included in the two-stage group for analysis. †Included in final analysis. ADM, acellular dermal matrix.

6·00(3·30) *versus* 2·67(2·73); $P = 0·042$) (*Table 4*; *Table S1*, supporting information).

In the one-stage group, nine patients with unilateral reconstructions and 13 with bilateral reconstructions underwent one or more reoperations. In the two-stage group, three and five patients respectively had one or more reoperations (*Table 4*).

Most reconstructions in patients with a failed unilateral procedure were converted to an autologous reconstruction (4 in the 1-stage group, 2 in 2-stage group). In patients with a failed bilateral reconstruction, salvage was achieved with either an implant reconstruction or combination of an implant and autologous tissue (*Table S2*, supporting information). Additional implant materials needed for reconstruction were tissue expanders (18 in 1-stage group, 1 in 2-stage group), breast implants (17 and 1 respectively) and another ADM (1-stage group). In the unilateral two-stage group, two tissue expanders were replaced by autologous flaps (*Table 4*).

Combining costs, including those for complication-related and salvage procedures, the mean costs per patient were higher in the one-stage group compared with the two-stage group for both unilateral (€11 752 (95 per cent c.i. 9987 to 13 611) *versus* €9000 (8551 to 9479) respectively; $P = 0·008$) and bilateral (€16 714 (14 909 to 18 971) *versus* €13 061 (12 039 to 14 233); $P = 0·001$) reconstructions.

Additional procedures not related to surgical complications

During exchange of the tissue expander for the definite implant, a secondary correction was performed in 19 breasts (17 patients) in the unilateral group, and 20 reconstructions (12 patients) in the bilateral group. Secondary revisional surgery was undertaken in 12 breasts (8 patients) in the unilateral one-stage group, nine breasts (9 patients) in the unilateral two-stage group, six breasts (4 patients) in the bilateral one-stage group and 13 breasts (7 patients) in the bilateral two-stage group (*Table 5*).

Including costs for cosmetic procedures, the overall direct costs were higher in the one-stage compared with the two-stage group for both unilateral (€12 448 (95 per cent c.i. 10 722 to 14 387) *versus* €9871 (9373 to 10 445)

Table 2 Surgical complications, reoperations and removal of implant

	Unilateral		Bilateral	
	One-stage IBBR + ADM (*n* = 27 patients)	Two-stage IBBR (*n* = 32 patients)	One-stage IBBR + ADM (*n* = 32 patients; 64 reconstructions)	Two-stage IBBR (*n* = 30 patients; 60 reconstructions)
Surgical complications	12 (44)	4 (13)	24 (38) [16 patients]	9 (15) [7 patients]
Haematoma	2 (7)	1 (3)	1 (2)	1 (2)
Seroma	0 (0)	0 (0)	0 (0)	2 (2)
Burn wound	0 (0)	0 (0)	0 (0)	1 (2)
Blister	0 (0)	0 (0)	0 (0)	1 (2)
Redness without signs of infection	3 (11)	1 (3)	2 (3)	0 (0)
Wound infection	1 (4)	1 (3)	8 (13)	1 (2)
Skin necrosis	3 (11)	0 (0)	8 (13)	1 (2)
Wound dehiscence: exposure				
ADM	3 (11)	–	2 (3)	–
ADM and implant	0 (0)	–	2 (3)	–
Unknown	0 (0)	0 (0)	1 (2)	0 (0)
Suspected perforation of expander	–	1 (3)	–	1 (2)
Pain, capsular contracture	0 (0)	0 (0)	0 (0)	1 (2)
Reoperations				
Haematoma evacuation	2 (11)	1 (3)	1 (2)	3 (5)
Excision of burn wound	0 (0)	0 (0)	0 (0)	1 (2)
Botulinum toxin injection	0 (0)	1 (3)	1 (0)	0 (0)
Necrosectomy	0 (0)	0 (0)	1 (2)	1 (2)
Removal of				
Tissue expander	–	2 (6)	–	1 (2)
Implant	1 (4)	0 (0)	9 (14)	1 (2)
ADM	0 (0)	–	2 (3)	–
ADM + implant	5 (19)	–	7 (11)	–
Change of implant (owing to capsular contracture)	0 (0)	0 (0)	0 (0)	1 (2)

Values in parentheses are percentage of breasts. IBBR, implant-based breast reconstruction; ADM, acellular dermal matrix.

Table 3 Operation details for both primary breast reconstructive procedures (per patient)

	Unilateral			Bilateral		
	One-stage IBBR + ADM (*n* = 27)	Two-stage IBBR (*n* = 32)	*P*‡	One-stage IBBR + ADM (*n* = 32)	Two-stage IBBR (*n* = 30)	*P*‡
Duration of operation (min)*						
First operation	172(55) (*n* = 25)	122(35) (*n* = 30)	< 0·001	243(60)	205(58) (*n* = 29)	0·017
Second operation	–	62(40) (*n* = 30)		–	71(33) (*n* = 22)	
Overall	172(55)	189(55)	0·298	243(60)	289(71)	0·013
Duration of hospital stay (days)†						
First operation	3 (2–8)	3 (2–8)		4 (2–11)	3 (2–6)	
Second operation	–	2 (1–4)		–	2 (1–3) (*n* = 28)	
Overall	3 (2–8)	5·0 (3–10)	0·002§	4 (2–11)	5 (2–11)	0·008§
No. of expander fillings*	–	5·27(2·55)		–	6·17(2·55) (*n* = 29)	

Values are *mean(s.d.) and †median (range). IBBR, implant-based breast reconstruction; ADM, acellular dermal matrix. ‡Student's *t* test, except §Mann–Whitney *U* test.

Table 4 Additional operation details for both breast reconstructive procedures in patients with complications (per patient)

	Unilateral		Bilateral	
	One-stage IBBR + ADM ($n = 10$)	Two-stage IBBR ($n = 4$)	One-stage IBBR + ADM ($n = 15$)	Two-stage IBBR ($n = 6$)
No. of additional outpatient visits	3·10(1·85)	2·75(2·22)	6·00(3·30)	2·67(2·73)
No. of patients requiring additional operation(s)	9	3	13	5
No. of additional reoperations	2·0(0·50)	2·00(2·65)	2·92(1·19)	1·00
Additional operating time (min)	79(102)	134(134)	60(21)	45(17)
Additional duration of hospital stay (days)	3·63(2·96)	4·83(2·32)	2·51(1·52)	3·00(2·83)
Additional materials	Expander 2		Expander 16	Expander 1
	Implant 2		Implant 15	Implant 1
			Other ADM 1	

*Values are mean(s.d.). IBBR, implant-based breast reconstruction; ADM, acellular dermal matrix.

Table 5 Additional procedures not directly related to surgical complications

	Unilateral		Bilateral	
	One-stage IBBR + ADM ($n = 27$ patients)*	Two-stage IBBR ($n = 32$ patients)*	One-stage IBBR + ADM ($n = 32$ patients; 64 reconstructions)†	Two-stage IBBR ($n = 30$ patients; 60 reconstructions)†
Corrections during second operation	0 (0)	17 (53) [19 reconstructions]	0 (0)	20 (33) [12 patients]
Scarification of capsule	0 (0)	1 (3)	0 (0)	0 (0)
Lipofilling	0 (0)	2 (6)	0 (0)	5 (8) [3 patients]
Capsulotomy or capsulectomy	0 (0)	3 (9)	0 (0)	13 (22) [7 patients]
Contralateral/unilateral symmetrization‡	0 (0)	6 (19)	0 (0)	1 (2) [1 patient]
Combination§	0 (0)	5 (16) [7 breasts]	0 (0)	11 (2) [1 patient]
Secondary revision surgery	8 (30) [12 reconstructions]	9 (28)	6 (9) [4 patients]	13 (22) [7 patients]
Redundant tissue¶	0 (0)	1 (3)	1 (2)	4 (7) [2 patients]
Layer thickness#	2 (7)	1 (3)	3 (5) [2 patients]	0 (0)
Position of implant**	2 (7)	4 (13)	0 (0)	5 (8) [3 patients]
Contralateral preventive mastectomy	0 (0)	1 (3)	0 (0)	0 (0)
Combination††	4 (15) [8 reconstructions]	2 (6)	2 (3) [1 patient]	4 (7) [2 patients]

Values in parentheses are percentage of *patients and †breasts. ‡Contralateral symmetrization reduction mammoplasty or augmentation. §Combination of other procedures (scarification of capsule, capsulotomy or capsulectomy or lipofilling). ¶Dog-ear correction and scar revision. #Lipofilling. **Lowering of inframammary fold, new implant, contralateral symmetrization reduction mammoplasty or augmentation. ††Combination of other procedures (redundant tissue, layer thickness or position of implant).

Table 6 Health status measured using EQ-5D-5L™ before and after operation

	Unilateral			Bilateral		
	One-stage IBBR + ADM ($n = 27$)	Two-stage IBBR ($n = 32$)	*P**	One-stage IBBR + ADM ($n = 32$)	Two-stage IBBR ($n = 30$)	*P**
Preoperative						
EQ-5D-5L™ score	0·78(0·17) ($n = 17$)	0·86(0·12) ($n = 17$)		0·93(0·08) ($n = 15$)	0·86(0·14) ($n = 14$)	
EQ-VAS (0–100)	69·0(17·4) ($n = 17$)	78·8(17·9) ($n = 17$)		89·0(9·6) ($n = 15$)	74·9(11·2) ($n = 14$)	
Postoperative						
EQ-5D-5L™ score	0·89(0·08) ($n = 22$)	0·93(0·10) ($n = 24$)	0·220	0·92(0·11) ($n = 26$)	0·93(0·08) ($n = 20$)	0·648
EQ-VAS (0–100)	79·7(12·9) ($n = 20$)	79·9(14·8) ($n = 18$)	0·967	85·4(11·5) ($n = 25$)	82·3(9·4) ($n = 17$)	0·354

Values are mean(s.d.). IBBR, implant-based breast reconstruction; ADM, acellular dermal matrix. *Student's *t* test.

respectively; $P = 0{\cdot}025$) and bilateral (€16 939 (14 887 to 19 360) *versus* €13 383 (12 414 to 14 669); $P = 0{\cdot}002$) procedures.

Health outcomes

The EQ-5D-5L™ questionnaire was completed before operation by 63 patients (52·1 per cent) and after surgery by 92 patients (76·0 per cent). Mean(s.d.) scores were 0·86(0·14) and 0·92(0·10) respectively. In general, scores were higher after operation in all groups (*Table 6*). There were no significant differences between postoperative EQ-5D-5L™ or EQ-VAS scores between one-stage IBBR with ADM and two-stage IBBR for both unilateral and bilateral reconstructions.

Discussion

This RCT could not confirm the hypothesis that ADM-assisted one-stage IBBR is more cost-effective than two-stage IBBR. The direct costs of one-stage IBBR with ADM were higher than those of two-stage reconstruction, and health outcomes did not differ between the groups.

The way in which healthcare is financed differs considerably between countries and healthcare costs can be calculated from various viewpoints. In the Netherlands, all citizens have mandatory health insurance, which is partly sponsored by the government. Reimbursement by health insurers is based on Diagnosis Related Groups (DRGs) using average costing; therefore, reimbursement amounts do not reflect actual costs of specific procedures, similar to payment systems in many other countries. This implies that the sum reimbursed is payable regardless of the actual costs to the hospital providing the relevant care. When comparing the costs of breast reconstruction with and without the additional use of ADM, it seems inappropriate to use reimbursement amounts as these do not reflect the actual costs associated with its use. Even if the costs of ADMs were reimbursed separately, this may not reflect the actual costs. For example, Krishan and colleagues[11] reported that a large discrepancy exists between the actual cost of an ADM (US $4890; €4278, exchange rate 2 January 2019) and its reimbursement ($214·10; €187·31). Therefore, costs were calculated from a hospital perspective in the present study. This way of calculating costs is not without problems, however, as costs may differ considerably across institutions; costs of overheads, implants, personnel required, financing strategies and private interests can all vary. For this reason, the data for underlying variables were also reported (such as duration of operation time and hospital stay) to enable comparison with other studies and to allow cost calculations using different tariffs.

The results indicate that, from an institutional perspective, costs of one-stage IBBR with ADM reconstruction are higher than those of two-stage reconstruction, whereas reimbursement for the one-stage reconstruction is lower. This was true when the primary procedure alone was taken into account. The difference in costs between the two methods increased when the costs of additional procedures to treat surgical complications were also included. The major factors contributing to this difference were the price of the implant material and costs related to a higher complication rate.

Previous authors have used a mixture of perspectives to estimate costs, such as a third-party payer perspective with supplementary costs of ADM included in the calculations. Only a few studies[13–15,25] have reported on costs of ADMs in one-stage implant-based breast reconstruction. None of these analyses was based on prospectively collected data, but costs were derived theoretically by adopting a third-party payer perspective, and analyses usually included data from literature reviews to estimate complication rates. Using this method, de Blacam and co-workers[14] compared one-stage IBBR *versus* ADM with two-stage IBBR with and without ADM. ADM-assisted one-stage IBBR was the least expensive approach; this was still the case if the incremental costs of complications were included. The probability of complications was based on previously published literature. However, when an ADM was used, the authors adjusted for the extended duration of operation only and did not include the material costs of ADM. The authors noted that Medicare reimbursement of breast reconstruction with ADM is erroneously low, that the relative increase in cost incurred by the use of ADM is substantial when extrapolated nationwide, and that the excess costs associated with ADMs are amplified by the higher incidence of complications associated with their use. Johnson *et al.*[13] also compared ADM-assisted one-stage IBBR with conventional two-stage IBBR. They used retrospective data from 24 patients in the one-stage and 22 in the two-stage group to assess surgery-related variables and complications. Costings were based on the tariffs governing reimbursement in the National Health Service in England, and the actual costs of ADM were added to the cost calculations. In contrast to actual costs, tariffs in England are the same for unilateral and bilateral procedures, giving a rather skewed picture, where one-stage IBBR seemed less costly than two-stage IBBR in unilateral procedures, but more costly in bilateral procedures. In another retrospective cohort study[25], no significant cost differences between two-stage IBBR and one-stage ADM-assisted IBBR were reported,

but details regarding the perspective and methods to calculate costs were lacking. In a Canadian study[15], costs of direct-to-implant reconstruction with AlloDerm® (LifeCell, Branchburg, New Jersey, USA) were compared with two-stage non-AlloDerm® reconstruction. The payment system in Canada is not based on DRGs, and costs from the third-party payer perspective corresponded closely to direct costs from the hospital perspective. Expected costs were calculated by means of a decision analytical model using data from previous studies. Based on similar complication rates in both groups and an assumed 10 per cent lower capsular contraction rate in the one-stage group, expected costs of one-stage reconstruction were lower. Total costs were sensitive to the price of the ADM and duration of operation; it was shown that variation in these factors may tip the balance of cost advantage between the two procedures.

ADMs are relatively expensive, with reported prices of biological ADMs varying from £1292 (€1433, exchange rate 2 January 2019) to £4890 (€5425)[11,13–15]. In the present study in a Dutch hospital setting, the costs of an ADM in a one-stage procedure outweighed the costs of additional duration of surgery in a two-stage procedure. With costs of the implant material and overall duration of surgery time being the primary differentiating cost drivers, the costs of one ADM (€2370) corresponded to those of over 1·5 h of surgery (including surgeon's fee). Less expensive alternatives to ADMs have, however, been introduced. One example is the TiLOOP® Bra (pfm medical, Cologne, Germany), a titanized mesh. However, the effectiveness and safety of each of these products have to be evaluated. A small RCT[26] comparing TiLOOP® with another porcine ADM, Protexa® (Tecnos, Turin, Italy), showed a higher severe complication rate with implant loss in the Protexa® group. Larger studies are needed to confirm these results and demonstrate cost-effectiveness.

A more costly procedure may be justifiable if it creates more value for the patient. To assess whether a procedure is cost-effective, it is necessary to determine its actual costs and value with regard to health outcomes. It has been suggested that the use of ADM in breast reconstruction gives aesthetically better results and that it reduces capsular contracture rates. For instance, Krishan and colleagues[12] concluded that the use of ADMs in two-stage IBBR was cost-effective despite higher costs and a higher complication rate in ADM-assisted IBBR. This was based on the assumption that quality of life is better in women treated with ADMs, resulting in higher quality-adjusted life-years (QALYs). However, this assumption was not based on patient-reported outcomes, but on the expert opinion of plastic surgeons. Actual data on health-related quality of life after one-stage IBBR with and without use of ADM were lacking[17]. In the present study, patient-reported health status assessed using the EQ-5D-5L™ was no different between groups. Furthermore, there was no difference between groups in specific patient-reported outcomes regarding quality of life and satisfaction[27]. Based on these outcomes at 1 year after definite placement of the breast implant, there was no indication of differences in QALYs between the two groups. Therefore, this study cannot confirm that one-stage ADM-assisted IBBR is more cost-effective than two-stage IBBR. Health status improved after the reconstruction, with postoperative EQ-5D™ index values being higher than preoperative values. Remarkably, postoperative scores in the present study were also higher than reference values for the Dutch general population (mean(s.d.) for women 0·86(0·17))[24], indicating the importance of postmastectomy breast reconstruction in restoring emotional health and self-esteem.

This is the first randomized study to compare both costs and health status between ADM-assisted one-stage IBBR and two-stage IBBR. To deal with the unknown distribution of cost for this type of surgery, estimation of costs was done using bootstrapping and no further assumptions were made in the comparison. The study, however, has several limitations. Costs were calculated from an institutional perspective. Direct costs may vary considerably between institutions, and should be reassessed for different settings. Furthermore, socioeconomic costs were not taken into account. The impact on patients was addressed only partly by the EQ-5D-5L™ questionnaire. Social implications and consequences of multiple operations, resulting in patient burden, absence from work and travel expenses, were not measured. It may be argued that the impact of a two-stage reconstruction is greater owing to multiple outpatient visits for filling of the expander and a second operation. This applies only to an uneventful postoperative course. In the present study, it was noted that multiple additional procedures were carried out, especially in the one-stage group owing to a much higher complication rate. The specific burden of these treatments was not considered in the cost analyses. Future studies are needed to address this issue. Another limitation is that the trial had a relatively small sample size and not all women completed the EQ-5D-5L™, which reduced the statistical power of the analyses. Finally, follow-up was too short to assess possible differences in capsular contracture rates.

With similar health outcomes and increased costs, ADM-assisted one-stage IBBR was not cost-effective relative to two-stage IBBR. The additional costs of ADM in ADM-assisted one-stage IBBR and increased costs related

to higher complication rates exceeded the costs saved by reduced operating times.

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Supporting information

Additional supporting information can be found online in the Supporting Information section at the end of the article.