Supplementary Material

1. Update to PROSPERO protocol

Initial PROSPERO protocol published 22/05/2020
Protocol update submitted 08/07/2020

Main revisions:

1. Our inclusion criteria were expanded to include implant-based reconstructions as opposed to only autologous reconstructions. This is to encompass all immediate breast reconstructions and increase the scope of our paper.
2. As implant-based reconstructions have been included in our inclusion criteria, we have expanded our primary outcomes to include any of the following pre-defined major complications: total flap loss, partial flap loss, loss of implant/expander, and mastectomy skin flap necrosis. This is because flap loss alone does not occur in implant-based reconstructions and including other major complications will add more valuable information to our systematic review.
3. In addition to reporting our primary outcomes, we included overall complications (as reported by study authors) and delay to adjuvant therapy as secondary outcomes as there was available data and the outcomes are relevant to the paper.
4. As our research yielded predominantly observational cohort studies, we amended our measure of effect to risk ratio as opposed to odds ratio.
5. Upon consulting a statistician, we revised our risk of bias strategy to include both Newcastle-Ottawa Scale and the Cochrane Grade tool to assess the quality of our included studies.
6. We re-defined our subgroups as reconstruction type for subgroup analysis to match our revised review question.
7. Keywords were added to make our review more easily identifiable.
8. In line with the above revisions, we have made the appropriate changes to the following titles on our PROSPERO protocol: review title, anticipated completion date, review stage, review question, condition or domain being studied, paticipants/population, intervention(s), exposure(s), comparator(s)/control, context, main outcome, measure of effect, additional outcomes, measure of effect, data extraction, risk of bias (quality assessment), strategy for data synthesis, analysis of subgroups or subsets, keywords.

2. NOS Score Allué-Cabañuz et al.
NOS score 7

Selection	
1) Is the case definition adequate?	
a) yes, with independent validation ¯	
b) yes, eg record linkage or based on self reports	Y
c) no description	
2) Representativeness of the cases	
a) consecutive or obviously representative series of cases ¯	Y "A retrospective observational analysis was performed to identify patients who had undergone bilateral mastectomy as a treatment for breast cancer with direct prosthetic IBR at our hospital from 2000-2016. From this group, patients with BMIBR after NACT (the NACT group) were selected, which were matched at a maximum ratio of 1:5 versus patients who had not received NACT (control group)."
b) potential for selection biases or not stated	
3) Selection of Controls	
a) community controls ¯	
b) hospital controls	Y "A retrospective observational analysis was performed to identify patients…at our hospital from 2000-2016."
c) no description	
4) Definition of Controls	
a) no history of disease (endpoint) ¯	Y
b) no description of source	
Comparability	
1) Comparability of cases and controls on the basis of the design or analysis	
a) study controls for age ¯	Y "In the NACT group it was 46.6±7.0 years (range 31–61), and in the control group it was 49.3±11.0 years (range 31–87), P = .183."
b) study controls for smoking ¯ (This criteria could be modified to indicate specific control for a second important factor.)	Y Table 1 shows difference between smokers in NACT versus control group is not significant (p=0.806).
Exposure	
1) Ascertainment of exposure	
a) secure record (eg surgical records) ¯	Y "A retrospective observational analysis was performed to identify patients…From this group, patients with BMIBR after NACT (the NACT group) were selected, which were matched at a maximum ratio of 1:5 versus patients who had not received NACT (control group)."
b) structured interview where blind to case/control status ¯	
c) interview not blinded to case/control status	
d) written self report or medical record only	
e) no description	

2) Same method of ascertainment for cases and controls	
a) yes –	Y
b) no	
3) Non-Response rate	
a) same rate for both groups –	Y Retrospective review, so both groups accounted for
b) non respondents described	
c) rate different and no designation	

3. NOS Score Azzawi et al.
NOS score 8

Selection	
1) Representativeness of the exposed cohort	
a) truly representative of the average breast cancer patient (describe) in the community*	Y Mean age 47.8; Mean BMI 27.7
b) somewhat representative of the average _____ in the community*	
c) selected group of users eg nurses, volunteers	
d) no description of the derivation of the cohort	
2) Selection of the non exposed cohort	
a) drawn from the same community as the exposed cohort*	Y "A retrospective case note review of a single surgeon's (C.M.M.) immediate breast reconstructions performed between January of 2000 and December of 2007 was undertaken."
b) drawn from a different source	
c) no description of the derivation of the non exposed cohort	
3) Ascertainment of exposure	
a) secure record (eg surgical records)*	Y "Patients were identified from the Addenbrooke's Hospital records, the operating theater register, the surgeon's log book, and the oncology database."
b) structured interview*	
c) written self report	
d) no description	
4) Demonstration that outcome of interest was not present at start of study	
a) yes*	Y
b) no	
Comparability	
1) Comparability of cohorts on the basis of the design or analysis	
a) study controls for age (select the most important factor)*	Y Table 2 shows difference in mean age is not significant: NACT mean age 27.7, nonrecipients mean age 27.1; p= 0.08
b) study controls for any smoking* (This criteria could be modified to indicate specific control for a second important factor.)	N "…the percentage of smokers in the control group (49 percent) was significantly higher than in the neoadjuvant group (11 percent) (p <0.001)."
Outcome	
1) Assessment of outcome	
a) independent blind assessment*	
b) record linkage*	Y "Patients were identified from the Addenbrooke's Hospital records, the operating theater register, the surgeon's log book, and the oncology database…In addition, the following treatment timings were noted: date of diagnosis, date of definitive surgery, time from end of chemotherapy to surgery, time from surgery to the start of adjuvant radiotherapy, and the reconstructive outcomes."

c) self report	
d) no description	
2) Was follow-up long enough for outcomes to occur	
a) yes (30 days)*	Y "The median follow-up in this study was 21 months (range, 7 to 64 months)."
b) no	
3) Adequacy of follow up of cohorts	
a) complete follow up - all subjects accounted for*	Y All subjects accounted for in results
b) subjects lost to follow up unlikely to introduce bias - small number lost - > ____ % (select an adequate %) follow up, or description provided of those lost)*	
c) follow up rate < ____% (select an adequate %) and no description of those lost	
d) no statement	

4. NOS Score Beugels et al.
NOS score 7

Selection	
1) Representativeness of the exposed cohort	
a) truly representative of the average breast cancer patient (describe) in the community*	Y Mean age 46.3±8.1 Mean BMI 26.8±3.5
b) somewhat representative of the average _____ in the community*	
c) selected group of users eg nurses, volunteers	
d) no description of the derivation of the cohort	
2) Selection of the non exposed cohort	
a) drawn from the same community as the exposed cohort*	Y A retrospective cohort study was conducted based on a prospectively maintained database of all patients who underwent immediate DIEP flap breast reconstruction at Maastricht University Medical Center in the Netherlands…"
b) drawn from a different source	
c) no description of the derivation of the non exposed cohort	
3) Ascertainment of exposure	
a) secure record (eg surgical records)*	Y "A retrospective cohort study was conducted based on a prospectively maintained database of all patients who underwent immediate DIEP flap breast reconstruction …"
b) structured interview*	
c) written self report	
d) no description	
4) Demonstration that outcome of interest was not present at start of study	
a) yes*	Y
b) no	
Comparability	
1) Comparability of cohorts on the basis of the design or analysis	
a) study controls for age (select the most important factor)*	N "Patients who received neoadjuvant chemotherapy were significantly younger (46.3 ± 8.1 years vs. 51.3 ± 9.3 years; $p < 0.001$)."
b) study controls for smoking * (This criteria could be modified to indicate specific control for a second important factor.)	N "Significantly more patients in the control group were active smokers (0% vs. 9.4%;$p = 0.020$) at the time of surgery."
Outcome	
1) Assessment of outcome	
a) independent blind assessment*	
b) record linkage*	Y "A retrospective cohort study was conducted based on a prospectively maintained database of all patients who underwent immediate DIEP flap breast reconstruction at Maastricht…"
c) self report	
d) no description	
2) Was follow-up long enough for outcomes to occur	

a) yes (30 days)*	Y Table 1 - Follow-up median (IQR): NACT patients 14 months (7-20) Control patients 12 months (7-19)
b) no	
3) Adequacy of follow up of cohorts	
a) complete follow up - all subjects accounted for*	Y All patients accounted for
b) subjects lost to follow up unlikely to introduce bias - small number lost - > ____ % (select an adequate %) follow up, or description provided of those lost)*	
c) follow up rate < ____% (select an adequate %) and no description of those lost	
d) no statement	

5. NOS Score D'Alessandro et al.
NOS score 8

Selection	
1) Representativeness of the exposed cohort	
a) truly representative of the average breast cancer patient (describe) in the community*	Y Mean age 41.39; mean BMI 26.71
b) somewhat representative of the average _____ in the community*	
c) selected group of users eg nurses, volunteers	
d) no description of the derivation of the cohort	
2) Selection of the non exposed cohort	
a) drawn from the same community as the exposed cohort*	Y "Data were collected from medical records of 102 patients with cancer who had undergone immediate breast reconstruction with latissimus dorsi flap and silicone implants and were followed up in an outpatient clinic from August 2010 to December 2014."
b) drawn from a different source	
c) no description of the derivation of the non exposed cohort	
3) Ascertainment of exposure	
a) secure record (eg surgical records)*	Y "Data were collected from medical records of 102 patients with cancer who had undergone immediate breast reconstruction…"
b) structured interview*	
c) written self report	
d) no description	
4) Demonstration that outcome of interest was not present at start of study	
a) yes*	Y
b) no	
Comparability	
1) Comparability of cohorts on the basis of the design or analysis	
a) study controls for age (select the most important factor)*	Y Table 1 – mean age 45.09. No significant difference with NACT mean age (p=0.079)
b) study controls for any additional factor * (smoking) (This criteria could be modified to indicate specific control for a second important factor.)	Y Table 2 – smoking habit not significantly different between NACT and control group (p=0.466)
Outcome	
1) Assessment of outcome	
a) independent blind assessment*	
b) record linkage*	Y "Data were collected from medical records of 102 patients with cancer who had undergone immediate breast reconstruction…"
c) self report	
d) no description	
2) Was follow-up long enough for outcomes to occur	
a) yes (30 days)*	
b) no	Y Follow-up time not reported.

3) Adequacy of follow up of cohorts	
a) complete follow up - all subjects accounted for*	Y All subjects accounted for
b) subjects lost to follow up unlikely to introduce bias - small number lost - > ____ % (select an adequate %) follow up, or description provided of those lost)*	
c) follow up rate < ____% (select an adequate %) and no description of those lost	
d) no statement	

6. NOS Score Donker et al.
NOS score 8

Selection	
1) Representativeness of the exposed cohort	
a) truly representative of the average breast cancer patient in the community*	
b) somewhat representative of the average breast cancer patient in the community*	Y Median age 38, BMI 22.9
c) selected group of users eg nurses, volunteers	
d) no description of the derivation of the cohort	
2) Selection of the non exposed cohort	
a) drawn from the same community as the exposed cohort*	Y Figure 1 shows patients drawn from the same community as the exposed cohort.
b) drawn from a different source	
c) no description of the derivation of the non exposed cohort	
3) Ascertainment of exposure	
a) secure record (eg surgical records)*	Y "Consequently, we were able to include the prospectively gathered data of 37 women (48 mastectomies) who were treated with neoadjuvant chemotherapy and the data of 176 women (215 mastectomies) as controls."
b) structured interview*	
c) written self report	
d) no description	
4) Demonstration that outcome of interest was not present at start of study	
a) yes*	Y
b) no	
Comparability	
1) Comparability of cohorts on the basis of the design or analysis	
a) study controls for age*	N Table 1 – significant difference between median age of NACT patients (38) and control (47); p=0.001.
b) study controls for smoking * (This criteria could be modified to indicate specific control for a second important factor.)	Y Table 1 – difference in smoking between NACT patients and control was not significant: p=0.332.
Outcome	
1) Assessment of outcome	
a) independent blind assessment*	
b) record linkage*	Y "To assess the short-term surgical outcome, postoperative complications that occurred within six weeks after surgery were recorded."
c) self report	
d) no description	
2) Was follow-up long enough for outcomes to occur	
a) yes (30 days)*	Y
b) no	
3) Adequacy of follow up of cohorts	

a) complete follow up - all subjects accounted for*	Y All subjects accounted for
b) subjects lost to follow up unlikely to introduce bias - small number lost - > ____ % (select an adequate %) follow up, or description provided of those lost)*	
c) follow up rate < ____% (select an adequate %) and no description of those lost	
d) no statement	

7. NOS Score Godfrey et al.
NOS score 5

Selection	
1) Representativeness of the exposed cohort	
a) truly representative of the average breast cancer patient (describe) in the community*	
b) somewhat representative of the average _____ in the community*	Y All subjects in the exposed cohort were candidates for immediate breast reconstruction with clinically advanced breast cancer.
c) selected group of users eg nurses, volunteers	
d) no description of the derivation of the cohort	
2) Selection of the non exposed cohort	
a) drawn from the same community as the exposed cohort*	Y Drawn from the same community of patients offered immediate breast reconstruction who received NACT.
b) drawn from a different source	
c) no description of the derivation of the non exposed cohort	
3) Ascertainment of exposure	
a) secure record (eg surgical records)*	
b) structured interview*	
c) written self report	Y No report of hospital/surgical records linkage.
d) no description	
4) Demonstration that outcome of interest was not present at start of study	
a) yes*	Y
b) no	
Comparability	
1) Comparability of cohorts on the basis of the design or analysis	
a) study controls for age (select the most important factor)*	N Age of patients not reported.
b) study controls for any additional factor * (smoking) (This criteria could be modified to indicate specific control for a second important factor.)	N Smoking status of patients not reported.
Outcome	
1) Assessment of outcome	
a) independent blind assessment*	
b) record linkage*	
c) self report	Y No mention of hospital record linkage.
d) no description	
2) Was follow-up long enough for outcomes to occur	
a) yes (30 days)*	Y Table 1 shows all subjects were followed up, from a minimum of 8 months to maximum of 48 months (median 25.2 months)
b) no	
3) Adequacy of follow up of cohorts	
a) complete follow up - all subjects accounted for*	Y All subjects accounted for (Table 1).
b) subjects lost to follow up unlikely to introduce	

bias - small number lost - > ____ % (select an adequate %) follow up, or description provided of those lost)*	
c) follow up rate < ____% (select an adequate %) and no description of those lost	
d) no statement	

8. NOS Score Jiménez-Puente et al.
NOS score 7

Selection	
1) Representativeness of the exposed cohort	
a) truly representative of the average breast cancer patient (describe) in the community*	Y An analysis was made of all the post-mastectomy IBR carried out from April 2002 until June 2009 at the Costa del Sol Hospital… The regimen of neoadjuvant chemotherapy used before 2005 was FEC… After 2005 the AC-T schedule was used…"
b) somewhat representative of the average _____ in the community*	
c) selected group of users eg nurses, volunteers	
d) no description of the derivation of the cohort	
2) Selection of the non exposed cohort	
a) drawn from the same community as the exposed cohort*	Y "An analysis was made of all the post-mastectomy IBR carried out from April 2002 until June 2009 at the Costa del Sol Hospital…In every case, a modified radical mastectomy was carried out, thirteen of them skin-sparing."
b) drawn from a different source	
c) no description of the derivation of the non exposed cohort	
3) Ascertainment of exposure	
a) secure record (eg surgical records)*	Y "Retrospective information was obtained about postoperative complications and the characteristics of patients and treatments applied."
b) structured interview*	
c) written self report	
d) no description	
4) Demonstration that outcome of interest was not present at start of study	
a) yes*	Y
b) no	
Comparability	
1) Comparability of cohorts on the basis of the design or analysis	
a) study controls for age (select the most important factor)*	N Age not specified for NACT versus control group.
b) study controls for any additional factor * (smoking) (This criteria could be modified to indicate specific control for a second important factor.)	N Smoking status not specifies for NACT versus control group.
Outcome	
1) Assessment of outcome	
a) independent blind assessment*	
b) record linkage*	Y "Retrospective information was obtained about the appearance of postoperative complications and possible associated variables, by means of a review of clinical records from October 2009 to March 2010."

c) self report	
d) no description	
2) Was follow-up long enough for outcomes to occur	
a) yes (30 days)*	Y "The minimum follow-up period was 9 months."
b) no	
3) Adequacy of follow up of cohorts	
a) complete follow up - all subjects accounted for*	
b) subjects lost to follow up unlikely to introduce bias - small number lost - > 95 % (select an adequate %) follow up, or description provided of those lost)*	Y One patient lost to follow-up, all others accounted for
c) follow up rate < ____% (select an adequate %) and no description of those lost	
d) no statement	

9. NOS Score Lardi et al.
NOS score 7

Selection	
1) Representativeness of the exposed cohort	
a) truly representative of the average breast cancer patient (describe) in the community*	Y "All patients who underwent Strattice-assisted implant-based breast reconstructions at Guy's and St. Thomas' Hospitals, London, and at Clinic Pyramide, Zurich, from December 2008 to October 2012 were retrospectively reviewed."
b) somewhat representative of the average _____ in the community*	
c) selected group of users eg nurses, volunteers	
d) no description of the derivation of the cohort	
2) Selection of the non exposed cohort	
a) drawn from the same community as the exposed cohort*	Y "All patients who underwent Strattice-assisted implant-based breast reconstructions at Guy's and St. Thomas' Hospitals, London, and at Clinic Pyramide, Zurich, from December 2008 to October 2012 were retrospectively reviewed."
b) drawn from a different source	
c) no description of the derivation of the non exposed cohort	
3) Ascertainment of exposure	
a) secure record (eg surgical records)*	Y "Patient charts were reviewed for…adjunctive therapy (radio- and/or chemotherapy) use…"
b) structured interview*	
c) written self report	
d) no description	
4) Demonstration that outcome of interest was not present at start of study	
a) yes*	Y
b) no	
Comparability	
1) Comparability of cohorts on the basis of the design or analysis	
a) study controls for age (select the most important factor)*	N Age not specified for NACT vs control group.
b) study controls for any additional factor * (smoking) (This criteria could be modified to indicate specific control for a second important factor.)	N Smoking status was not specified for NACT vs control group.
Outcome	
1) Assessment of outcome	
a) independent blind assessment*	
b) record linkage*	Y "Patient charts were reviewed for…incidence of early complications during the follow-up period."
c) self report	
d) no description	
2) Was follow-up long enough for outcomes to occur	
a) yes (30 days)*	Y Mean follow-up 22.2 months. Table 1 shows follow up between different periods.

b) no	
3) Adequacy of follow up of cohorts	
a) complete follow up - all subjects accounted for*	Y All subjects accounted for.
b) subjects lost to follow up unlikely to introduce bias - small number lost - > ____ % (select an adequate %) follow up, or description provided of those lost)*	
c) follow up rate < ____% (select an adequate %) and no description of those lost	
d) no statement	

10. NOS Score Lee et al.
NOS score 7

Selection	
1) Representativeness of the exposed cohort	
a) truly representative of the average breast cancer patient (describe) in the community*	Y "This study investigated 1116 cases of immediate breast reconstruction that were performed over the period from March 2001 through to September…Cases using other reconstruction methods, including implant or latissimus dorsi flaps, were excluded in order to obtain homogeneous data."
b) somewhat representative of the average _____ in the community*	
c) selected group of users eg nurses, volunteers	
d) no description of the derivation of the cohort	
2) Selection of the non exposed cohort	
a) drawn from the same community as the exposed cohort*	Y "This study investigated 1116 cases of immediate breast reconstruction that were performed over the period from March 2001 through to September…Cases using other reconstruction methods, including implant or latissimus dorsi flaps, were excluded in order to obtain homogeneous data."
b) drawn from a different source	
c) no description of the derivation of the non exposed cohort	
3) Ascertainment of exposure	
a) secure record (eg surgical records)*	Y "Thirteen factors...neoadjuvant chemotherapy…known to be associated with mastectomy flap necrosis were retrospectively analysed."
b) structured interview*	
c) written self report	
d) no description	
4) Demonstration that outcome of interest was not present at start of study	
a) yes*	Y
b) no	
Comparability	
1) Comparability of cohorts on the basis of the design or analysis	
a) study controls for age (select the most important factor)*	N Does not specify age of NACT versus control group.
b) study controls for any additional factor * (smoking) (This criteria could be modified to indicate specific control for a second important factor.)	N Does not specify smoking status of NACT versus control group.
Outcome	
1) Assessment of outcome	
a) independent blind assessment*	
b) record linkage*	Y "All of the data were collected from each patient's breast reconstruction chart,

	which included baseline information and clinical outcomes."
c) self report	
d) no description	
2) Was follow-up long enough for outcomes to occur	
a) yes (30 days)*	Y "Patients…had an average follow-up period of 65.6 months."
b) no	
3) Adequacy of follow up of cohorts	
a) complete follow up - all subjects accounted for*	
b) subjects lost to follow up unlikely to introduce bias - small number lost - > 95 % (select an adequate %) follow up, or description provided of those lost)*	Y "This study investigated 1116 cases of immediate breast reconstruction that were performed…" "Among the 1148 cases analysed in this study…" There is no explanation for this difference in total cases. 1116 cases are accounted for everywhere else in the paper, including in the data tables.
c) follow up rate < ____% (select an adequate %) and no description of those lost	
d) no statement	

11. NOS Score Liu et al.
NOS score 6

Selection	
1) Representativeness of the exposed cohort	
a) truly representative of the average breast cancer patient (describe) in the community*	Y "Between January 2001 and January 2007, we performed IBR using an expander following breast resection in 69 patients (75 breasts) at Tokyo Medical and Dental University (TMDU) Hospital." Mean age 45.3
b) somewhat representative of the average _____ in the community*	
c) selected group of users eg nurses, volunteers	
d) no description of the derivation of the cohort	
2) Selection of the non exposed cohort	
a) drawn from the same community as the exposed cohort*	Y "Between January 2001 and January 2007, we performed IBR using an expander following breast resection in 69 patients (75 breasts) at Tokyo Medical and Dental University (TMDU) Hospital." Mean age 43.3
b) drawn from a different source	
c) no description of the derivation of the non exposed cohort	
3) Ascertainment of exposure	
a) secure record (eg surgical records)*	Y "Between January 2001 and January 2007, we performed IBR…We divided the patients into two groups: one that underwent NAC (NAC group; 9 patients, 12 breasts) and one that did not (non-NAC group; 60 patients, 63 breasts)."
b) structured interview*	
c) written self report	
d) no description	
4) Demonstration that outcome of interest was not present at start of study	
a) yes*	Y
b) no	
Comparability	
1) Comparability of cohorts on the basis of the design or analysis	
a) study controls for age (select the most important factor)*	N P-value not reported.
b) study controls for any additional factor * (smoking) (This criteria could be modified to indicate specific control for a second important factor.)	N Not reported.
Outcome	
1) Assessment of outcome	
a) independent blind assessment*	
b) record linkage*	Y "We investigated all signs of complications…We respectively examined the complication rate in the NAC and non-NAC groups"
c) self report	

d) no description	
2) Was follow-up long enough for outcomes to occur	
a) yes (30 days)*	
b) no	Y Follow-up time not reported
3) Adequacy of follow up of cohorts	
a) complete follow up - all subjects accounted for*	Y All subjects accounted for
b) subjects lost to follow up unlikely to introduce bias - small number lost - > ____ % (select an adequate %) follow up, or description provided of those lost)*	
c) follow up rate < ____% (select an adequate %) and no description of those lost	
d) no statement	

12. NOS Score Moon et al.
NOS score 7

Selection	
1) Representativeness of the exposed cohort	
a) truly representative of the average breast cancer patient (describe) in the community*	Y "This cohort study analyzed data of 214 patients who underwent autologous breast reconstruction with MS-TRAM flap. Mean age of the patients was 43.2 years (range, 28-61 years)."
b) somewhat representative of the average _____ in the community*	
c) selected group of users eg nurses, volunteers	
d) no description of the derivation of the cohort	
2) Selection of the non exposed cohort	
a) drawn from the same community as the exposed cohort*	Y "This cohort study analyzed data of 214 patients who underwent autologous breast reconstruction with MS-TRAM flap. Mean age of the patients was 43.2 years (range, 28-61 years)."
b) drawn from a different source	
c) no description of the derivation of the non exposed cohort	
3) Ascertainment of exposure	
a) secure record (eg surgical records)*	Y "Patient data were linked with hospital records. Linked data were obtained from the Korea University Hospital Data Collection…We collected…patient data…including age, body mass index (BMI), smoking status, neoadjuvant chemotherapy…"
b) structured interview*	
c) written self report	
d) no description	
4) Demonstration that outcome of interest was not present at start of study	
a) yes*	Y
b) no	
Comparability	
1) Comparability of cohorts on the basis of the design or analysis	
a) study controls for age (select the most important factor)*	N Age in NACT compared to Control group not reported.
b) study controls for smoking * (This criteria could be modified to indicate specific control for a second important factor.)	N Smokers in NACT compared to Control group not reported.
Outcome	
1) Assessment of outcome	
a) independent blind assessment*	
b) record linkage*	Y "Outcome data were recorded during a clinical review based on medical charts and electrical hospital patient records. Complications were subdivided into major complications…"
c) self report	
d) no description	
2) Was follow-up long enough for outcomes to	

occur	
a) yes (30 days)*	Y "Mean follow-up period was 78.3 weeks (range, 10-167 weeks)."
b) no	
3) Adequacy of follow up of cohorts	
a) complete follow up - all subjects accounted for*	Y All subjects accounted for
b) subjects lost to follow up unlikely to introduce bias - small number lost - > ____ % (select an adequate %) follow up, or description provided of those lost)*	
c) follow up rate < ____% (select an adequate %) and no description of those lost	
d) no statement	

13. NOS Score Narui et al.
NOS score 6

Selection	
1) Representativeness of the exposed cohort	
a) truly representative of the average breast cancer patient in the community*	
b) somewhat representative of the average breast cancer patient in the community*	Y Median age 39.5
c) selected group of users eg nurses, volunteers	
d) no description of the derivation of the cohort	
2) Selection of the non exposed cohort	
a) drawn from the same community as the exposed cohort*	Y "Patients admitted to our department (Yokohama City University Medical Center) for mastectomy for breast cancer were informed about the option of immediate reconstruction with autologous grafting."
b) drawn from a different source	
c) no description of the derivation of the non exposed cohort	
3) Ascertainment of exposure	
a) secure record (eg surgical records)*	Y "The patients were divided into two groups: an NACT group and a non-NACT control group… We retrospectively reviewed the data for 201 consecutive patients who underwent immediate reconstruction…"
b) structured interview*	
c) written self report	
d) no description	
4) Demonstration that outcome of interest was not present at start of study	
a) yes*	Y
b) no	
Comparability	
1) Comparability of cohorts on the basis of the design or analysis	
a) study controls for age*	N Table 1 – there is a significant difference in age between NACT patients (median 39.5) and control patients (median 43.0); p =0.008
b) study controls for smoking * (This criteria could be modified to indicate specific control for a second important factor.)	N Not reported
Outcome	
1) Assessment of outcome	
a) independent blind assessment*	
b) record linkage*	Y "Information on postoperative complications was collected from hospital admission records, which included a section on complications described by plastic surgeons."
c) self report	
d) no description	
2) Was follow-up long enough for outcomes to occur	
a) yes (30 days)*	

b) no	Y Follow-up time not reported.
3) Adequacy of follow up of cohorts	
a) complete follow up - all subjects accounted for*	Y All subjects accounted for
b) subjects lost to follow up unlikely to introduce bias - small number lost - > ____ % (select an adequate %) follow up, or description provided of those lost)*	
c) follow up rate < ____% (select an adequate %) and no description of those lost	
d) no statement	

14. NOS Score Peled et al.
NOS score 9

Selection	
1) Representativeness of the exposed cohort	
a) truly representative of the average breast cancer patient (describe) in the community*	Y Mean age 46.4
b) somewhat representative of the average _____ in the community*	
c) selected group of users eg nurses, volunteers	
d) no description of the derivation of the cohort	
2) Selection of the non exposed cohort	
a) drawn from the same community as the exposed cohort*	Y "All women who underwent mastectomy and immediate reconstruction at the Carol Franc Buck Breast Care Center, University of California, San Francisco, between January 1, 2005, and December 31, 2007, were eligible for study inclusion."
b) drawn from a different source	
c) no description of the derivation of the non exposed cohort	
3) Ascertainment of exposure	
a) secure record (eg surgical records)*	Y "With the approval of our institutional review board, patient characteristics and treatment details were retrospectively collected from medical treatment records… Fifty seven patients received neoadjuvant chemotherapy…"
b) structured interview*	
c) written self report	
d) no description	
4) Demonstration that outcome of interest was not present at start of study	
a) yes*	Y
b) no	
Comparability	
1) Comparability of cohorts on the basis of the design or analysis	
a) study controls for age (select the most important factor)*	Y Table 1 shows no significant difference in age between NACT and control groups (p=0.18).
b) study controls for any additional factor * (smoking) (This criteria could be modified to indicate specific control for a second important factor.)	Y Table 1 shows no significant difference in smoking history between NACT and control groups (p=0.63).
Outcome	
1) Assessment of outcome	
a) independent blind assessment*	
b) record linkage*	Y "Surgical outcomes recorded in our prospectively maintained database included wound complications, unplanned return to the operating room, donor-site complications in patients undergoing autologous reconstruction, and cancer outcomes."
c) self report	
d) no description	

2) Was follow-up long enough for outcomes to occur	
a) yes (30 days)*	Y "…mean postoperative follow-up of 19.2 months (range, 8-35 months)…"
b) no	
3) Adequacy of follow up of cohorts	
a) complete follow up - all subjects accounted for*	Y All subjects accounted for
b) subjects lost to follow up unlikely to introduce bias - small number lost - > ____ % (select an adequate %) follow up, or description provided of those lost)*	
c) follow up rate < ____% (select an adequate %) and no description of those lost	
d) no statement	

15. NOS Score Radovanovic et al.
NOS score 7

Selection	
1) Representativeness of the exposed cohort	
a) truly representative of the average breast cancer patient (describe) in the community*	Y "From January 2004 till December 2008, 205 consecutive breast cancer patients at the Department of Surgical Oncology, Oncology Institute of Vojvodina, Serbia, undergoing 214 nipple sparing mastectomies followed by immediate breast reconstruction with fixed volume silicone prosthesis were included in this prospective study…39 patients (19%) with locally advanced disease were treated with neoadjuvant chemotherapy."
b) somewhat representative of the average _____ in the community*	
c) selected group of users eg nurses, volunteers	
d) no description of the derivation of the cohort	
2) Selection of the non exposed cohort	
a) drawn from the same community as the exposed cohort*	Y "From January 2004 till December 2008, 205 consecutive breast cancer patients at the Department of Surgical Oncology, Oncology Institute of Vojvodina, Serbia, undergoing 214 nipple sparing mastectomies followed by immediate breast reconstruction with fixed volume silicone prosthesis were included in this prospective study."
b) drawn from a different source	
c) no description of the derivation of the non exposed cohort	
3) Ascertainment of exposure	
a) secure record (eg surgical records)*	Y "…205 consecutive breast cancer…were included in this prospective study…39 patients (19%) with locally advanced disease were treated with neoadjuvant chemotherapy."
b) structured interview*	
c) written self report	
d) no description	
4) Demonstration that outcome of interest was not present at start of study	
a) yes*	Y
b) no	
Comparability	
1) Comparability of cohorts on the basis of the design or analysis	
a) study controls for age (select the most important factor)*	N Age is not specified for NACT versus control group.
b) study controls for any additional factor * (smoking) (This criteria could be modified to indicate specific control for a second important factor.)	N Smoking status is not specified for NACT versus control group.
Outcome	
1) Assessment of outcome	

a) independent blind assessment*	
b) record linkage*	Y "We recorded all early complications and treatment procedures."
c) self report	
d) no description	
2) Was follow-up long enough for outcomes to occur	
a) yes (30 days)*	Y "For this study, postoperative follow-up was six weeks."
b) no	
3) Adequacy of follow up of cohorts	
a) complete follow up - all subjects accounted for*	Y All subjects accounted for
b) subjects lost to follow up unlikely to introduce bias - small number lost - > ____ % (select an adequate %) follow up, or description provided of those lost)*	
c) follow up rate < ____% (select an adequate %) and no description of those lost	
d) no statement	

16. NOS Score Schaverien et al.
NOS score 7

Selection	
1) Representativeness of the exposed cohort	
a) truly representative of the average breast cancer patient (describe) in the community*	Y "A prospective study of all immediate free flap breast reconstructions following skin sparing mastectomy for a single surgeon at a single cancer center was performed to include all patients that had undergone NC from October 2006 to March 2012." Median age 46.5
b) somewhat representative of the average _____ in the community*	
c) selected group of users eg nurses, volunteers	
d) no description of the derivation of the cohort	
2) Selection of the non exposed cohort	
a) drawn from the same community as the exposed cohort*	Y "All patients that received immediate free flap breast reconstruction by the same surgeon without NC during the same study period were used as a comparator group."
b) drawn from a different source	
c) no description of the derivation of the non exposed cohort	
3) Ascertainment of exposure	
a) secure record (eg surgical records)*	Y "A prospective study of all immediate free flap breast reconstructions following skin sparing mastectomy for a single surgeon at a single cancer center was performed to include all patients that had undergone NC…"
b) structured interview*	
c) written self report	
d) no description	
4) Demonstration that outcome of interest was not present at start of study	
a) yes*	Y
b) no	
Comparability	
1) Comparability of cohorts on the basis of the design or analysis	
a) study controls for age (select the most important factor)*	N "The median age in the NC group was 46.5 (range, 35-57) years and in the control group 49 (range, 33-70) years, and the difference between the means was significant (T-test; p . 0.0031)."
b) study controls for smoking * (This criteria could be modified to indicate specific control for a second important factor.)	Y "Although there were more current cigarette smokers in the NC group, this difference was not significant."
Outcome	
1) Assessment of outcome	
a) independent blind assessment*	
b) record linkage*	Y "Tumour pathology, details of neoadjuvant and adjuvant therapy, and complications were

	recorded, including the need for surgical intervention and readmission."
c) self report	
d) no description	
2) Was follow-up long enough for outcomes to occur	
a) yes (30 days)*	
b) no	Y Follow-up time not reported.
3) Adequacy of follow up of cohorts	
a) complete follow up - all subjects accounted for*	Y All subjects accounted for.
b) subjects lost to follow up unlikely to introduce bias - small number lost - > ____ % (select an adequate %) follow up, or description provided of those lost)*	
c) follow up rate < ____% (select an adequate %) and no description of those lost	
d) no statement	

17. NOS Score Terao et al.
NOS score 6

Selection	
1) Representativeness of the exposed cohort	
a) truly representative of the average breast cancer patient (describe) in the community*	Y "The study involved 38 patients who underwent PMRT after immediate reconstruction with a flap and 20 patients who underwent delayed reconstruction with a flap after PMRT between 2006 and 2015...Twenty patients received neoadjuvant chemotherapy."
b) somewhat representative of the average _____ in the community*	
c) selected group of users eg nurses, volunteers	
d) no description of the derivation of the cohort	
2) Selection of the non exposed cohort	
a) drawn from the same community as the exposed cohort*	Y "The study involved 38 patients who underwent PMRT after immediate reconstruction with a flap and 20 patients who underwent delayed reconstruction with a flap after PMRT between 2006 and 2015...Twenty patients received neoadjuvant chemotherapy."
b) drawn from a different source	
c) no description of the derivation of the non exposed cohort	
3) Ascertainment of exposure	
a) secure record (eg surgical records)*	Y In the case of immediate reconstruction, a retrospective study…Twenty patients received neoadjuvant chemotherapy."
b) structured interview*	
c) written self report	
d) no description	
4) Demonstration that outcome of interest was not present at start of study	
a) yes*	Y
b) no	
Comparability	
1) Comparability of cohorts on the basis of the design or analysis	
a) study controls for age (select the most important factor)*	N Study does not differentiate median age for NACT compared to control group.
b) study controls for any additional factor * (smoking) (This criteria could be modified to indicate specific control for a second important factor.)	N Not reported
Outcome	
1) Assessment of outcome	
a) independent blind assessment*	
b) record linkage*	Y Complications reported individually in text based on retrospective review.
c) self report	
d) no description	

2) Was follow-up long enough for outcomes to occur	
a) yes (30 days)*	
b) no	Y Follow-up time not reported.
3) Adequacy of follow up of cohorts	
a) complete follow up - all subjects accounted for*	Y All subjects accounted for.
b) subjects lost to follow up unlikely to introduce bias - small number lost - > ____ % (select an adequate %) follow up, or description provided of those lost)*	
c) follow up rate < ____% (select an adequate %) and no description of those lost	
d) no statement	

18. NOS Score Zweifel-Schlatter et al.
NOS score 6

Selection	
1) Representativeness of the exposed cohort	
a) truly representative of the average breast cancer patient (describe) in the community*	Y "All patients treated with mastectomy and immediate microvascular breast reconstruction after neoadjuvant chemotherapy for locally advanced breast cancer at Guy's and St. Thomas' Hospital, London, from February 1, 2007 to August 2009 were identified using a prospectively maintained database." Median age 47
b) somewhat representative of the average _____ in the community*	
c) selected group of users eg nurses, volunteers	
d) no description of the derivation of the cohort	
2) Selection of the non exposed cohort	
a) drawn from the same community as the exposed cohort*	Y "The control group consisted of patients who underwent immediate breast reconstruction without neoadjuvant chemotherapy between October 2007 and February 2009 at the same institution." Mean age 49
b) drawn from a different source	
c) no description of the derivation of the non exposed cohort	
3) Ascertainment of exposure	
a) secure record (eg surgical records)*	Y "All patients treated with mastectomy and immediate microvascular breast reconstruction after neoadjuvant chemotherapy…were identified using a prospectively maintained database."
b) structured interview*	
c) written self report	
d) no description	
4) Demonstration that outcome of interest was not present at start of study	
a) yes*	Y
b) no	
Comparability	
1) Comparability of cohorts on the basis of the design or analysis	
a) study controls for age (select the most important factor)*	N Significance/p-value not reported.
b) study controls for smoking* (This criteria could be modified to indicate specific control for a second important factor.)	N Significance/p-value not reported.
Outcome	
1) Assessment of outcome	
a) independent blind assessment*	
b) record linkage*	Y "All patients… were identified using a prospectively maintained database…Patients were evaluated for …type of complications.."
c) self report	

d) no description	
2) Was follow-up long enough for outcomes to occur	
a) yes (30 days)*	
b) no	Y Follow-up time not reported.
3) Adequacy of follow up of cohorts	
a) complete follow up - all subjects accounted for*	Y All subjects accounted for.
b) subjects lost to follow up unlikely to introduce bias - small number lost - > ____ % (select an adequate %) follow up, or description provided of those lost)*	
c) follow up rate < ____% (select an adequate %) and no description of those lost	
d) no statement	