Leitlinienprogramm Onkologie

Evidenzaufbereitung zum Modul Brustrekonstruktion

Evidenzbericht zur S3-Leitlinie Mammakarzinom, Version 5.01
AWMF Nr. 032-045OL

Evidenzbericht

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1 Abkürzungsverzeichnis

Abkürzung	Erläuterung
95%-CI	95% confidence interval
ABR	Autologous breast reconstruction
ADM	Acellular dermal matrix
AWMF	Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften
BCT	Breast-conserving therapy
BMI	Body Mass Index
BR	Breast reconstruction
CoI	Conflict of Interest
DBR	Delayed breast reconstruction
DGHO	Deutsche Gesellschaft für Hämatologie und Onkologie
DIEP	Deep inferior epigastric artery perforator
DTI	Direct-to-implant
ELD	extended latissimus dorsi
EP	Expander prosthesis
FF	Free flap
FFBR	Free flap breast recosntruction
FTRAM	Free Transverse rectus abdominis musculocutaneous
GRADE	Grading of Recommendations, Assessment, Development and Evaluation
Gy	grey
HR	Hazard Ratio

Abkürzung	Erläuterung
IBR/IBBR	Implant-based breast reconstruction
IGAP	inferior gluteal artery perforator
ILBLR	Ipsilateral breast local recurrence
Incl.	inclusive
IQR	Interquartile range
LDF	Latissimus dorsi flap
LR	Local recurrence
M	mean
Mdn	median
MO	Mastectomy only
MSFT	muscle-sparing free TRAM
N	Number
NAT	Neoadjuvant therapy)
NK	Not known
NR	Not reported
NRCS	Non-randomized controlled study
NRSI	Non-randomized study of intervention
NSM	Nipple-sparing mastectomy
OR	Odds Ratio
OR	Odds Ratio
OS	Gesamtüberleben (Overall Survival)

Abkürzung	Erläuterung
PET/CT	Positronen-Emissions-Tomographie/Computertomographie
PFS	progressionsfreies Überleben (progression-free survival)
PMRT	Post-mastectomy radiotherapy
PTRAM	pedicled transverse rectus abdominis musculocutaneous
QoL	Quality of Life
RCT	Randomized controlled trial
RoB	Risk of Bias
RR	Risk Ratio
RT	Radiotherapy
SD	Standard deviation
SGAP	superior gluteal artery perforator
SIEA	Superficial inferior epigastric artery
SR	Systematic review
TEI	Tissue expander implant
TMG	Transverse musculocutaneous gracilis
TRAM	transverse rectus abdominis myocutaneous
TUG	Transverse upper gracilis

2 Informationen zum Evidenzbericht für das Modul Brustrekonstruktion

2.1 Autor*innen und Beteiligte

Klinik für Frauenheilkunde & Geburtshilfe, Universitätsklinikum Heidelberg: Prof. Dr. med. Jörg Heil, Linda Wilson

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Institut für Öffentliches Gesundheitswesen, Universität zu Köln: Univ-Prof. Dr. med. Nicole Skoetz, Nina Kreuzberger, Ana-Mihaela Zorger, Ina Monsef, Karina Worbes, Christoph Beimborn

3 Methodisches Vorgehen

3.1 Formulierung der Schlüsselfragen und Priorisierung

Nach dem Kick-off-Meeting im Juli 2022 wurden innerhalb der multidisziplinären Arbeitsgruppe in Form eines Brainstormings relevante Fragestellungen zum Thema Brustrekonstruktion nach Mammakarzinom gesammelt. Nachfolgend wurden die Fragestellungen in der Gruppe diskutiert, modifiziert, thematisch sortiert und zusammengefasst. Im Februar 2023 lag eine kondensierte Liste mit insgesamt 27 Fragen im PICO-Format (P = Patient, I = Intervention, C = Comparison, O = Outcome) vor. Anschließend wurde ein modifiziertes Dephi-Verfahren in zwei aufeinanderfolgenden Runden durchgeführt. Die Abstimmung wurde an jeweils 20 zufällig ausgewählte Gynäkolog*innen, Plastische Chirurg*innen und Patientenvertreter*innen versandt. Davon nahmen 31 Personen (9 Gynäkolog*innen, 8 Plastische Chirurg*innen, 14 Patientenvertreter*innen) an der Umfrage teil. Als Ergebnis des Delphi-Verfahrens kristallisierten sich 7 priorisierte PICO-Fragestellungen heraus.

3.2 Klinisch-methodischer Austausch

Nach Finalisierung der Priorisierung im August 2022 wurde ein regelmäßiger virtueller Termin für den engen Austausch zwischen Methodiker*innen und Kliniker*innen festgelegt. In diesen Treffen wurden die Schlüsselfragen genauer definiert, Endpunktgruppen erläutert, systematische Reviews auf Relevanz überprüft und aufkommende Fragen geklärt.

3.3 Systematische Recherche und Sichtung der Literatur

3.3.1 Systematische Reviews

Für die Beantwortung der Schlüsselfragen dieses Leitlinienmoduls wurde auf der Gesamtsuche der Koordination für die Leitlinie Mammakarzinom aufgebaut. Es wurde eine modulspezifische Aktualisierung ergänzt. Diese wurde von einer erfahrenen Informationsspezialistin (IM) entworfen und durchgeführt (siehe Kapitel 4.4).

Die zur Verfügung gestellten Referenzen der Leitlinienkoordination sowie die zusätzliche Recherche wurde von zwei wissenschaftlichen Mitarbeitenden unabhängig voneinander auf Relevanz gesichtet und den definierten PICO-Fragen zugeordnet. Im Anschluss wurden die zugeordneten Reviews dem Kliniker*innenteam vorgestellt und auf ihre Anwendbarkeit überprüft.

3.3.2 Primärstudienrecherchen

Für priorisierte Fragestellungen wurde jeweils das relevanteste systematische Review zugrunde gelegt (Kriterien für die Auswahl waren Aktualität und Qualität des Reviews). Das ausgewählte systematische Review für eine Fragestellung wurde jeweils mit AMSTAR-II (A MeaSurement Tool to Assess systematic Reviews) bewertet und das weitere Vorgehen im Team

besprochen. Bei einem Recherchedatum nach Juli 2022 wurde beschlossen, die Recherchen für priorisierte PICOs zu aktualisieren.

Die erfahrene Informationsspezialistin entwarf, basierend auf den Recherchen im systematischen Review sowie aktuellen Ergänzungen, aktualisierte Recherchestrategien. Diese wurden innerhalb des Teams zirkuliert, um ggf. fehlende klinische Begriffe oder Endpunkte zu ergänzen. Nach finaler Freigabe führte sie die systematischen Recherchen per Schlüsselfrage in verschiedenen relevanten Datenbanken ab dem letzten Suchdatum des zugrundeliegenden systematischen Reviews durch. Die resultierenden Treffer wurden jeweils im zweistufigen Verfahren von wissenschaftlich Tätigen in enger Kooperation mit erfahrenen Kliniker*innen gesichtet und ausgewählt. Die einzelnen Literaturrecherchen mit Suchdatum, Flow Charts, Evidenztabellen und Bewertungen sind per Schlüsselfrage zusammengefasst.

3.4 Datenextraktion und Bewertung des Verzerrungsrisikos (Risk of Bias)

Die identifizierten Studien wurden systematisch von einem Mitarbeitenden in Datenextraktionsformulare via Microsoft Excel extrahiert, und von einem zweiten Mitarbeitenden geprüft. Es wurden jeweils die Endpunkte aus den Meta-Analysen des zugrundeliegenden systematischen Reviews übertragen und durch die zusätzlichen Studien ergänzt. Wenn ein Review nicht alle Endpunkte analysiert hat, wurden diese aus den Primärstudien nachextrahiert. Bei methodischen Unklarheiten wurde ein weiterer Wissenschaftler hinzugezogen, bei klinischen Fragen das Kliniker*innenteam kontaktiert.

RCTs wären mit dem Cochrane Risk of Bias 1 Tool bewertet worden; die Fragen erlaubten keine Beantwortung via RCTs. Entsprechend wurden die nicht-randomisierten Studien mit einer angepassten Version der SIGN Checklist für Kohortenstudien bewertet:

- Populations comparable regarding main confounders, and if not, confounding taken into account?
- Rate of participation/Exclusions reported (selection bias into the study):
- Intervention
    - Was the assessment reliable:
    - Was the intervention assessed more than once:
    - Was the assignment to intervention possibly affected by knowledge of outcome status?
- Drop-out rate & reasons reported?
    - Drop-out rate and reasons similar across groups:
    - If the rate was high: comparison of those lost with available:
- Outcome
    - Outcome measure is well-defined, valid and reliable:
    - Blind outcome assessment to exposure:
    - If not, Knowledge of exposure status likely to influence the outcome?

- Confidence intervals reported:
- Selective reporting (comparison with protocol):
- Other limitations or comments

Die Charakteristika und Endpunktdaten der identifizierten Studien wurden außerdem von den Methodiker*innen in Evidenztabellen nach abgewandelter Vorlage des Onkologischen Leitlinienprogramms extrahiert.

3.5 Meta-analytisches Vorgehen

Meta-analysen wurden mit der Software R oder RevMan erstellt. Es wurde jeweils auf den Analysen der identifizierten systematischen Reviews aufgebaut wo möglich, und Daten zum jeweiligen Endpunkt aus den zusätzlich identifizierten Studien hinzugefügt. Generell wurden Random-Effects Meta-analysen von Odds Ratios durchgeführt. Wenn in einer Studie ein adjustierter Effektschätzer berichtet wurde, so wurde dieser vorzugsweise für die Meta-analyse verwendet. In Fällen, in denen keine adjustierten Schätzer vorlagen, wurden die Odds Ratios aus den unadjustierten absoluten Werten (Events, Stichprobengröße pro Gruppe) berechnet.

3.6 Evidenzklassifikation nach GRADE

Die Bewertung der Evidenz erfolgte nach der GRADE Methodik (Grading of recommendations assessment, development and evaluation). Die GRADE Methodik bewertet das Vertrauen in die Evidenz pro Fragestellung und Endpunkt und berücksichtigt hierbei die folgenden fünf Dimensionen:

- das Verzerrungsrisiko der einzelnen Studien,
- die die Heterogenität der Studien,
- die Direktheit der untersuchten Population, Intervention, Vergleiche und Endpunkte,
- die Präzision der Effektschätzer und
- die Wahrscheinlichkeit eines Publikationsbias.

Bei Obervationsstudien gibt es außerdem die Möglichkeit, den Evidenzkörper aufzuwerden bei einem großen Effekt, einem plausiblen Dosis-Wirkungs-Verhältnis, oder vermutetem residuellem Confounding.

Die Bewertung ist aus den Evidenztabellen (Summary of findings tables) im Evidenzbericht ersichtlich. Die Qualität der Evidenz (Vertrauen in die Evidenz) wird nach GRADE eingeteilt in hoch, moderat, niedrig, und sehr niedrig.

Qualität der Evidenz	Beschreibung	Symbol
Hohe Qualität	Wir sind sehr sicher, dass der wahre Effekt nahe bei dem Effektschätzer liegt.	⊕⊕⊕⊕
Moderate Qualität	Wir haben mäßig viel Vertrauen in den Effektschätzer: der wahre Effekt ist wahrscheinlich	⊕⊕⊕⊖

Qualität der Evidenz	Beschreibung	Symbol
	nahe bei dem Effektschätzer, aber es besteht die Möglichkeit, dass er relevant verschieden ist.	
Geringe Qualität	Unser Vertrauen in den Effektschätzer ist begrenzt: Der wahre Effekt kann durchaus relevant verschieden vom Effektschätzer sein.	⊕⊕⊖⊖
Sehr geringe Qualität	Wir haben nur sehr wenig Vertrauen in den Effektschätzer: Der wahre Effekt ist wahrscheinlich relevant verschieden vom Effektschätzer.	⊕⊖⊖⊖

3.7 Formulierung der Empfehlungen

Die eingeschlossenen Studien (systematisches Review und neu identifizierte Primärstudien), die Evidenztabellen, Meta-Analysen sowie die GRADE-Bewertung der Studien wurde den Kliniker*innen als Grundlage für das Formulieren der Empfehlungen zur Verfügung gestellt.

3.7.1 Schema der Evidenzgraduierung

In der Leitlinie wurde zu allen Empfehlungen zusätzlich die Stärke der Empfehlung (Empfehlungsgrad) ausgewiesen. Hinsichtlich der Stärke der Empfehlung wurden in der Leitlinie drei Empfehlungsgrade unterschieden, die sich auch in der Formulierung der Empfehlungen jeweils widerspiegelten.

Es wurden weiterhin Expertenkonsens-Empfehlungen (in der Leitlinie mit EK gekennzeichnet) generiert, wenn beim Kick-Off-Meeting oder in den darauffolgenden Besprechungen mit den Arbeitsgruppen-Leitungen entschieden wurde, eine spezifische Schlüsselfrage nicht auf Basis einer systematischen Literaturrecherche und -bewertung zu beantworten.

Empfehlungsgrad	Beschreibung	Ausdrucksweise
A	Starke Empfehlung	Soll/ soll nicht
B	Empfehlung	Sollte/ sollte nicht
0	Empfehlung offen	Kann erwogen werden/ kann verzichtet werden

Die Empfehlungsgrade berücksichtigten neben der Qualität der Evidenz auch die klinische Relevanz des Ergebnisparameters, das Ausmaß des Effektes und die Übertragbarkeit der Studienergebnisse auf die Patientenzielgruppe und das deutsche Gesundheitssystem. Bei der Empfehlungsgradierung innerhalb dieser Leitlinie wurde nicht das Evidence-to-Decision Framework von GRADE

angewendet, da dieses aufgrund der nur 2-stufigen Graduierung nicht direkt auf die Leitlinien des Onkologischen Leitlinienprogramms übertragbar ist.

Es konnten zudem Statements zu Fragestellungen gebildet werden, für die entweder keine randomisierten Studien oder nur heterogene Evidenz vorhanden waren. Diese Statements wurden auf Grundlage von Expertenmeinungen oder Studienergebnissen gebildet und entsprechend der Vorgehensweise bei den Empfehlungen im Rahmen eines formalen Konsensusverfahrens als Statement oder als Expertenkonsens verabschiedet.

3.7.2 Festlegung des Empfehlungsgrades

Grundsätzlich erfolgte eine Anlehnung der evidenzbasierten Empfehlungen hinsichtlich ihres Empfehlungsgrades an die Stärke der verfügbaren Evidenz (siehe Abbildung 1), d.h. ein hoher Evidenzgrad (z.B. Metaanalysen/systematische Übersichten von RCTs oder mehrere methodisch hochwertige RCTs), d.h. eine hohe Sicherheit bzgl. der Ergebnisse sollte in der Regel auch zu einer starken Empfehlung (Empfehlungsgrad A, „soll“) führen.

Zusätzlich wurden weitere Kriterien bei der Wahl des Empfehlungsgrades berücksichtigt. Die folgenden berücksichtigten Kriterien konnten zu einem Abweichen der Empfehlungsstärke nach oben oder unten führen:

- Konsistenz der Studienergebnisse

Bsp.: Die Effektschätzer der Studienergebnisse gehen in unterschiedliche Richtungen und zeigen keine einheitliche Tendenz.

- Klinische Relevanz der Endpunkte und Effektstärken

Bsp.: Es liegen zwar Studien mit Ergebnissen in eine Richtung vor, jedoch wird die Bedeutung der gewählten Endpunkte und/oder Effektstärken als nicht relevant eingeschätzt.

- Nutzen-Risiko-Verhältnis

Bsp.: Dem nachgewiesenen Nutzen einer Intervention steht ein relevanter Schadensaspekt gegenüber, der gegen eine uneingeschränkte Empfehlung spricht.

- Ethische Verpflichtungen

Bsp.: Downgrading: Aus ethischen Gründen kann eine Intervention mit nachgewiesenem Nutzen nicht uneingeschränkt angeboten werden. Upgrading: Starke Empfehlung auf Basis von z.B. Fall-Kontroll-Studien, da aus ethischen Gründen ein RCT nicht durchführbar ist.

Patientenpräferenzen

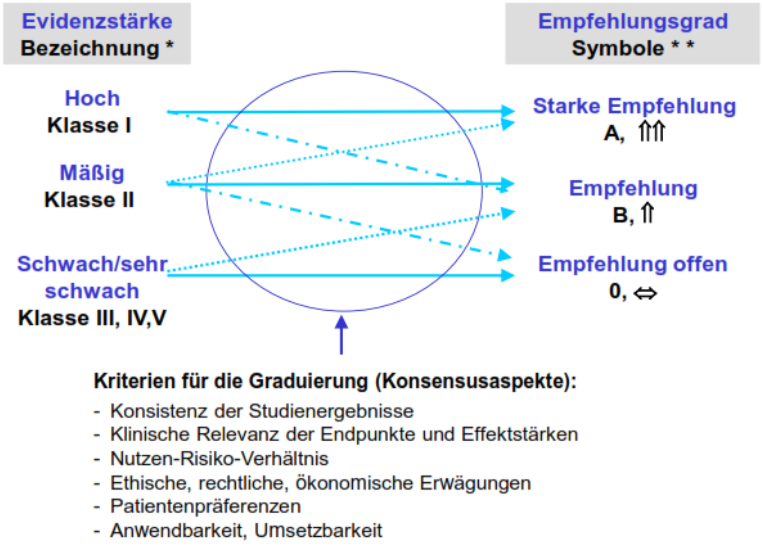
Bsp.: Eine Intervention mit nachgewiesenem Nutzen wird nicht stark empfohlen, da sie von den Patient*innen als belastend oder nicht praktikabel abgelehnt wird.

- Anwendbarkeit, Umsetzbarkeit in der Versorgung

Bsp.: Eine Intervention mit nachgewiesenen positiven Effekten kann nicht empfohlen werden, weil sie im regionalen Versorgungssystem aus strukturellen

Gründen nicht angeboten werden kann.

Abbildung 1: Schema zur Darstellung der kriteriengestützen Entscheidungsprozesse bei der Wahl des Empfehlungsgrades (nach AWMF)



*: blau = Evidenzstärke nach GRADE bzgl. des gesamten ‚body of evidence', schwarz = Evidenzklassifikation bzgl. Einzelstudien, z.B. nach Oxford;
**: Empfehlungsgraduierung im Programm für Nationale Versorgungsleitlinien. Die Empfehlungen werden nach Möglichkeit analog formuliert: Starke Empfehlung: „soll"; (abgeschwächte) Empfehlung: „sollte"; Negativ-Empfehlungen werden entweder rein sprachlich ausgedrückt („nicht" / „kann verzichtet werden") bei gleichen Symbolen oder sprachlich mit zusätzlich nach unten gerichteten Pfeilen; Offene Empfehlungen drücken eine Handlungsoption in Unsicherheit aus („kann erwogen werden" / „kann verzichtet werden").

3.7.3 Formale Konsensusverfahren und Konsensuskonferenzen

Das Kapitel zum Modul Brustrekonstruktion wurde im Oktober/November 2024 für alle Leitlinienbeteteiligten zur Kommentierung und Vorabstimmung zugänglich gemacht. Alle Empfehlungen wurden auch im Rahmen einer formalen Konsensuskonferenz nach NIH-Typ diskutiert und verabschiedet (3. Konsensuskonferenz der Leitlinie Mammakarzinom, November 2024).

Die online Konsensuskonferenz erfolgte unter neutraler Moderation durch Prof. Dr. med. Ina Kopp nach folgendem Schema: Präsentation der abzustimmenden Empfehlungen im Plenum, Gelegenheit zu Rückfragen und Einbringung von begründeten Änderungsanträgen, Abstimmung der Empfehlungen und Änderungsanträge, Diskussion (bei Bedarf), Erarbeitung von Alternativvorschlägen und endgültige Abstimmung. Unterstützt wurde der Prozess von dem OL-Office (Thomas Langer) und des Instituts für öffentliches Gesundheitswesen (Nicole Skoetz, Nina Kreuzberger, Ana-Mihaela Zorger, Karina Worbes). Für jede Empfehlung wurde die prozentuale Zustimmung stimmberechtigter Mandatsträger*innen dokumentiert. Hieraus ergab sich die Konsensstärke gemäß nachfolgender Tabelle.

Konsensstärke	Prozentuale Zustimmung
Starker Konsens	> 95% der Stimmberechtigten
Konsens	>75 – 95% der Stimmberechtigten
Mehrheitliche Zustimmung	50 – 75% der Stimmberechtigten
Keine mehrheitliche Zustimmung	<50% der Stimmberechtigten

4 PICO-übergreifende Resultate

4.1 Definierte Schlüsselfragen im PICO-Format

4.1.1 Vorabbemerkungen

Population

- Grundsätzlich handelt es sich um therapeutische oder prophylaktische Mastektomien. Zwischen therapeutisch und prophylaktisch wurde in den Fragestellungen kein Unterschied gemacht, da dies im Hinblick auf Outcomes und OP-Methodenwahl heutzutage keinen systematischen Einfluss hat.

Outcomes

- Outcomegruppe 1:
  - Komplikationen
  - Morbidität
  - Rekonstruktionsverlust
  - Re-Oeration
  - Hospitalisierung
- Outcomegruppe 2:
  - Lebensqualität, Skalen: BREAST-Q, EORTC BR23, etc.
- Outcomegruppe 3:
  - Onkologische Outcomes (Local Recurrence, Overall Survival)
- Zeitbezug für alle Outcomes

4.1.2 Definierte Schlüsselfragen

Implantat vs. Eigengewebe

1. Bei Patientinnen nach Mastektomie (jede Technik): Ist die autologe Brustrekonstruktion der implantatbasierten Brustrekonstruktion im Hinblick auf „Outcomes“ (s.o.) gleichwertig, unter- oder überlegen?

Implantat

2. Bei mastektomierten Patientinnen: Ist die präpectorale der subpectoralen implantatbasierten Brustrekonstruktion im Hinblick auf Outcome gleichwertig, unter- oder überlegen?
3. Bei Patientinnen mit Implantatrekonstruktion: Sind ADM (azelluläre dermale Matrizes) im Vergleich zu synthetischen Netzen (resorbierbar vs. nicht resorbierbar) im Hinblick auf Outcomes gleichwertig, unter- oder überlegen?
4. Bei mastektomierten Patientinnen: ist die implantatbasierte Brustrekonstruktion (epipectoral vs. submusculär) in Kombination mit gewebeverstärkenden Materialien (ADM/Netze) der implantatbasierten Brustrekonstruktion ohne gewebestärkende Materialien (ADM/Netze) im Hinblick auf Outcomes gleichwertig, unter- oder überlegen?
5. Bei mastektierten Patientinnen: besteht bei Verwendung von Implantaten mit glatter Oberfläche im Vergleich zu Verwendung von solchen mit texturierter Oberfläche ein geringeres BIA-ALCL-Risiko?

6. Bei mastektierten Patientinnen: besteht bei Verwendung von Implantaten mit glatter Oberfläche im Vergleich zu Verwendung von solchen mit texturierter Oberfläche ein geringeres BII Risiko?
7. Bei Patientinnen mit Implantatrekonstruktion: haben Patientinnen im Zustand nach Radiatio im Vergleich zu jenen ohne Radiatio ein besseres, schlechteres oder gleiches "Outcome"?

Eigengewebe

8. Bei mastektomierten Patientinnen: Ist die autologe Brustrekonstruktion mit mikrovaskuläre Lappenplastik vom Unterbauch der gestielten myokutanen Lappenplastik vom Unterbauch im Hinblick auf Outcomes, insbesondere Hebestellenmorbidität (bei einer Schwangerschaft) gleichwertig, unter- oder überlegen?
9. Bei mastektomierten Patientinnen: Haben Patientinnen mit autologer Brustrekonstruktion und nachfolgender Radiatio ein gleichwertiger, überlegener oder unterlegener Outcome im Hinblick auf Outcomes im Vergleich zu Patientinnen mit autologer Brustrekonstruktion ohne nachfolgende Radiatio?
10. Bei mastektomierten Patientinnen: Ist die DIEP Lappenplastik der freien muskelsparenden TRAM Lappenplastik im Hinblick auf die Hebestellenmorbidität gleichwertig, unter- oder überlegen?
11. Bei mastektomierten Patientinnen: Ist die Rekonstruktion mit sogenannten „Alternativen Lappenplastiken“ vom Gesäß oder Oberschenkel (z.B. TMG, PAP. GAP) bezüglich des Outcomes, hier insbesondere des ästhetischen Ergebnisses und der Komplikationsrate mit der mikrochirurgische DIEP Lappenplastik gleichwertig, unter- oder überlegen?

Autologer Fetttransfer / Lipofilling

12. Bei mastektomierten Patientinnen: haben Patientinnen nach autologem Fetttransfer (Lipofilling) in Vergleich zu Patientinnen ohne autologem Fetttransfer im HInblck auf Outcomes (hier insbesondere, aber nicht ausschliesslich onkologische Outcomes) gleichwertig, unter- oder überlegen?

Beratung

13. Haben Patientinnen mit einer Indikation zur Mastektomie, die eine gemeinsame Beratung durch onkologische und rekonstruktive ChirurgInnen (Breast surgeons and Reconstructive surgeons) erhalten haben, gleichwertige, bessere oder schlechtere Outcomes?
14. Haben Patientinnen, bei denen in der Beratung zu den operativen Optionen nach Mastektomie persönliche Beratung und schriftliche / app-basierte evidenzbasierte Entscheidungshilfen mit Informationen zu allen drei Optionen (autologe und implantatbasierte Brustrekonstruktion, Aesthetic Flat Closure) kombiniert werden, ein besseres, schlechteres oder

gleiches "Outcome" als Patientinnen, die ohne Entscheidungshilfe beraten werden?

15. Haben Patientinnen, bei denen in der Beratung zu den operativen Optionen nach Mastektomie eine persönliche Beratung und schriftliches, evidenzbasiertes Informationsmaterial in einfacher Sprache zu allen drei Optionen (autologe und implantatbasierte Brustrekonstruktion, Aesthetic Flat Closure) kombiniert werden, ein besserer, schlechterer oder gleicher Outcome als Patientinnen, die ohne patientinnengerechte schriftliche Informationen beraten werden?

Sekundär/primär

16. Bei mastektomierten Patientinnen: Ist die primäre Rekonstruktion der sekundären Rekonstruktion auf die im Hinblick auf Outcome gleichwertig, unter- oder überlegen?
17. Bei mastektomierten Patientinnen: Ist die Expandereinlage mit sekundärer Implantateinlage der sofortigen Implantateinlage bei Patientinnen mit Brustrekonstruktion hinsichtlich der Outcomes gleichwertig, unter- oder überlegen?
18. Bei mastektomierten Patientinnen: Ist die spät-primäre autologe Brustrekonstruktion im Sinne eines zweizeitigen Vorgehens mit Mastektomie und epipectoraler Implantateinlage und nachfolgender autologer Brustrekonstruktion der sofortigen Rekonstruktion mit Eigengewebe hinsichtlich der Outcomes gleichwertig, unter- oder überlegen?

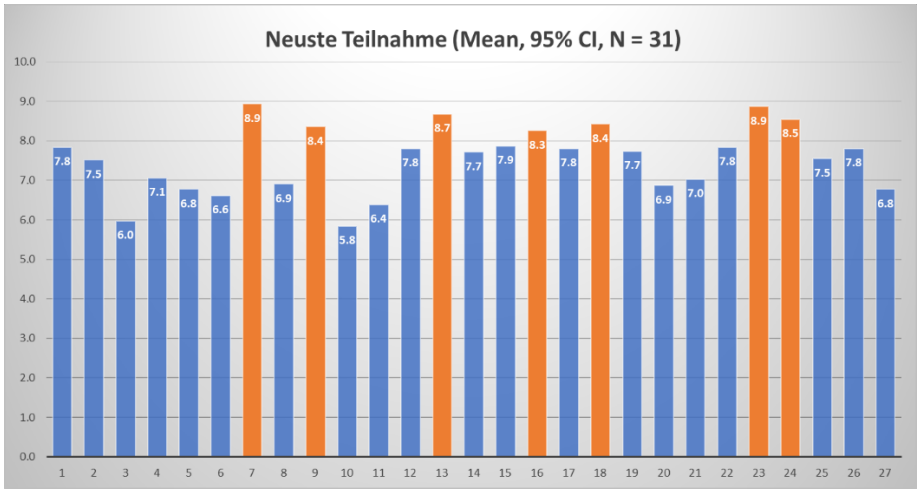
Andere

19. Bei Patientinnen mit Implantatrekonstruktion: Führen prophylaktische Maßnahmen wie Antiseptika/Antibiotika oder eine medikamentöse Therapie (z.B. Leukotrienrezeptorantagonisten) im Vergleich zur Nicht-Anwendung dieser Maßnahmen zu besseren, gleichenwertigen oder schlechteren Outcomes (hier insbesondere Kapselfibroserate)?
20. Bei Patientinnen nach Brustrekonstruktion: Führt die Verwendung von epicutanen Vakuumverbänden im Vergleich zu keinen epicutanen Vakkumverbänden (Hebestelle vs. Empfängerstelle) zu einer Verbesserung, Verschlechterung oder gleichbleibenden Wundheilung?
21. Bei Patientinnen nach Implantatrekonstruktion: Führt eine Liegedauer einer postoperativen Drainage von unter zehn Tagen im Vergleich zu einer Liegedauer von über zehn Tagen bei Patientinnen mit Brustrekonstruktion zu einer erhöhten, verringerten oder gleichbleibenden Bildung von Seromen?
22. Bei Patientinnen mit Indikation zur Mastektomie: Ist die inframammäre Schnittführung bei der NSM im Vergleich zur einer periareolären oder Hockeystick-Inzision bei Patientinnen mit Brustrekonstruktion mit gleichen, besseren oder schlechteren Outcomes (hier insbesondere Asymmetrien und Wundheilungsstörungen) assoziiert?
23. Bei Patientinnen mit Indikation zur Mastektomie: führt die Ablatio ohne Rekonstruktion gegenüber der Mastektomie mit Rekonstruktion

(Implantat vs. Eigengewebe) zu gleichen, besseren oder schlechteren Outcomes (hier insbesondere Brustkrebs(neu)erkrankung und Lebensqualität)?

24. Bei Patientinnen nach Mastektomie (jede Technik): Inwieweit sind die drei Optionen chirurgischer Versorgung nach Mastektomie - autologe Brustrekonstruktion, implantatbasierten Brustrekonstruktion und bewusst gewählte Aesthetic Flat Closure - im Hinblick auf „Outcomes“ gleichwertig, unter- oder überlegen?
25. Bei Patientinnen mit Indikation zur Mastektomie: Ist bei Patientinnen eine bezüglich der Brustgestaltung zwischen Ärzt*innen und Patientinnen abgestimmte Aesthetic Flat Closure (z.B. ob Dekolleté-Ansatz belassen wird, wie Dog Ears, Hautfalten etc. vermieden werden) im Vergleich zur einfachen Entfernung des Brustgewebes und Gestaltung der Brust durch Operateur im Hinblick auf „Outcomes“ gleichwertig, unter- oder überlegen?
26. Haben Patientinnen mit Aesthetic Flat Closure nach Mastektomie einer Brust und bewusst gewählter symmetrischer Angleichung durch Mastektomie und Aesthetic Flat Closure der kontralateralen Brust im Vergleich zu denjenigen Patientinnen ohne Angleichung der zweiten Brust ein besseres, schlechteres oder gleiches "Outcome"?
27. Haben Patientinnen mit Aesthetic Flat Closure einer Brust, die im Alltag eine Epithese tragen, im Vergleich zu denjenigen Patientinnen, die keine Epithese tragen, ein besseres, schlechteres oder gleiches "Outcome" (insbesondere bezüglich orthopädischer Probleme im Schultern- und Rückenbereich)?

4.2 Ergebnisse der Priorisierung (1. Und 2. Runde gemeinsam)



4.3 Priorisierte Schlüsselfragen, final spezifiziert

➢ Frage 1: Bei Patientinnen nach Mastektomie (jede Technik): Inwieweit sind die zwei Rekonsktruktionsoptionen: autologe Brustrekonstruktion vs.

Implantat basierte Brustrekonstruktion- im Hinblick auf Komplikationen (any, major, minor), Lebensqualität- Fokus auf BREAST Q- Satisfaction with outcome, with Breasts, Physical well-being; Reoperationen; Rekonstruktionsverlust (flap/ implant loss) gleichwertig, unter- oder überlegen?

- Frage 7: Haben Patientinnen mit Implantatrekonstruktion und nachfolgender Radiatio ein gleichwertiger, überlegener oder unterlegener Outcome in Bezug auf Nachblutungen, Infektionen, Rekonstruktionsverlust, Reoperation, Hospitalisierung, Lebensqualität, Local Recurrence, oder Overall Suvival im Vergleich zu Patientinnen mit Implantatrekonstruktion ohne nachfolgende Radiatio?

- Frage 9: Bei mastektomierten Patientinnen: Haben Patientinnen mit autologer Brustrekonstruktion und nachfolgender Radiatio ein gleichwertiger, überlegener oder unterlegener Outcome in Bezug auf Nachblutungen, Infektionen, Rekonstruktionsverlust, Reoperation, Hospitalisierung, Lebensqualität, Local Recurrence, oder Overall Suvival im Vergleich zu Patientinnen mit autologer Brustrekonstruktion ohne nachfolgende Radiatio?

- Frage 13: Haben Patientinnen mit einer Indikation zur Mastektomie, die eine gemeinsame oder zusätzliche Beratung durch onkologische und rekonstruktive ChirurgInnen (Breast surgeons and Reconstructive surgeons) erhalten haben, gleichwertige, bessere oder schlechtere Lebensqualität, Ästhetik, Sexualität, Weiblichkeit, & Partizipation als solche, die nur durch eine der beiden Gruppen beraten wurden?

- Frage 16A: Bei mastektomierten Patientinnen: Ist bei der autologen Brustrekonstruktion die primäre Rekonstruktion der sekundären Rekonstruktion (Vergleiche: immediate vs. Delayed vs. immediate-delayed) im Hinblick auf Nachblutungen, Infektionen, Reoperationen, Rekonstruktionsverlust, Hospitalisierung, Recurrence, Overall Survival, und Lebensqualität gleichwertig, unter- oder überlegen?

- Frage 16B: Bei mastektomierten Patientinnen: Ist bei der Implantatrekonstruktion die primäre Rekonstruktion der sekundären Rekonstruktion (Vergleich: direct-to implant (DTI) vs. Tissue expander (TE), auch: one-step versus two-step approach) im Hinblick auf die Outcomes Nachblutungen, Infektionen, Reoperation, Rekonstruktionsverlust, Hospitalisierung, und Lebensqualität gleichwertig, unter- oder überlegen?

- Frage 23: Bei Patientinnen mit Indikation zur Mastektomie (jede Technik): führt die Ablatio ohne Rekonstruktion gegenüber der Mastektomie mit Rekonstruktion (Implantat/ Eigengewebe) zu gleichen, besseren oder

schlechteren Rate an Komplikationen (any, minor, major), Reoperations, Rekonstruktionsverlust (implant/ flap loss) und Lebensqualität (Fokus: BREAST-Q Satisfaction with breasts, Physical well-being)?

- Frage 24: Bei Patientinnen nach Mastektomie (jede Technik): Inwieweit sind die drei Optionen chirurgischer Versorgung nach Mastektomie - autologe Brustrekonstruktion, implantatbasierte Brustrekonstruktion und bewusst gewählte Aesthetic Flat Closure - im Hinblick auf Nachblutungen, Infektionen, Reoperationen, Rekonstruktionsverlust, Hospitalisierung, Recurrence, Overall Survival, und Lebensqualität gleichwertig, unter- oder überlegen?

4.4 Aktualisierte Evidenzrecherche nach systematischen Reviews für das Modul Brustrekonstruktion

Trefferzahlen und Recherchedaten

Date of search for all databases: 01.01.2022 to 15.11.2023	
Database/Register	Update search
MEDLINE ALL (via Ovid) 1946 to present	316
Total	316

4.4.1 Search strategy

MEDLINE (via OVID) 1946 to present

1 exp Breast Neoplasms/ or exp Breast/

2 (breast adj6 (cancer* or neoplasm* or carcinoma* or tumour* or tumor*)).tw.

3 onco*.tw.

4 or/1-3

5 Plastic Surgery Procedures/ or Surgery, Plastic/

6 "prostheses and implants"/ or breast implants/

7 (breast adj6 (reconstruct* or surger*)).tw.

8 (breast adj2 conserving).tw.

9 (breast* adj1 (implant* or prosthes*)).tw.

10 (breast adj5 flap*).tw.

11 exp Mastectomy/ or exp Mammaplasty/

12 (mastectom* or mammaplast* or mammoplast* or postmastectom*).tw.

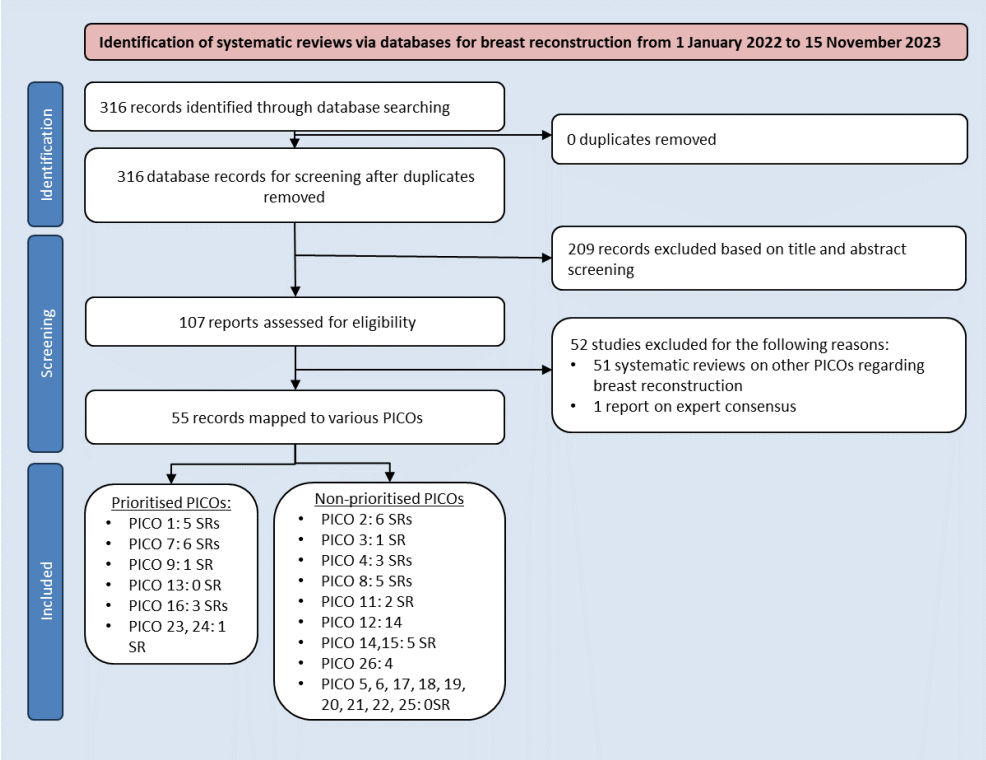
13 or/5-12

14 systematic review.tw. or systematic review.pt. or meta analysis.pt.

15 4 and 13 and 14

16 limit 15 to yr="2022 -Current"

4.4.2 PRISMA Flowdiagramm der aktualisierten Recherche nach systematischen Reviews



Die Auswahl des relevantesten Reviews pro Schlüsselfrage wird jeweils im Bereich der Schlüsselfrage weiter dargestellt.

5 Methodisches Vorgehen

5.1 PICO 1

5.1.1 Fragestellung und geplantes Vorgehen

Bei Patientinnen nach Mastektomie (jede Technik): Inwieweit sind die zwei Rekonsktruktionsoptionen: autologe Brustrekonstruktion vs. Implantat basierte Brustrekonstruktion- im Hinblick auf Komplikationen (any, major, minor), Lebensqualität- Fokus auf BREAST Q-Satisfaction with outcome, with Breasts, Physical well-being; Reoperationen; Rekonstruktionsverlust (flap/ implant loss) gleichwertig, unter- oder überlegen?

PICO 1 ist eine der priorisierten PICOs. In einer aktualisierten Evidenzrecherche nach systematischen Reviews konnten sechs systematische Reviews der PICO zugeordnet werden. Im Folgenden wurden diese systematischen Arbeiten mit dem klinischen Team besprochen und auf Relevanz geprüft.

Review	Recherche	Thematische Details	Endpunkte	Methodische Notizen
Broyles 2022	23.03.2021	Implant-based vs. autologous reconstruction, review with meta-analyses (40 studies: 2 RCTs, 38 non-RCTs)	psychosocial wellbeing, satisfaction with breasts, sexual wellbeing, satisfaction with surgical outcome, mortality, infections, necrosis, surgical complications, reconstructive failure, seroma, thromboembolic events	RoB assessment *Dieses Review wurde als Basis für die Updatesuche genommen.*
ElAbd 2022	31.12.2020	Autologous reconstruction vs. implant-based reconstruction, (12 controlled studies) P: Obese (BMI > 30)	Patient satisfaction, complications	Rob assessment Population restricted only on obese patients
Guliyeva 2022	10.08.2020	Implant-based reconstruction vs. any other method (11 articles)	pain	No Rob assessment

Review	Recherche	Thematische Details	Endpunkte	Methodische Notizen
Shauly 2023	15.10.2021	Direct-to-implant vs. autologous tissue transfer (21 observational studies)	Patient-reported outcomes only, well-being (sexual, pychosocial, physical), satisfaction overall	No Rob assessment presented
Stefura 2023	09.2021	Implant-based vs. autologous reconstruction (32 studies: 1 RCT, 31 non-RCTs)	BREAST-Q satisfaction with breast, LOS, total costs, complications (capsular contracture, implant leak, implant loss, infections, excessive scarring, hematoma)	No Rob assessment presented
Sinik 2022	03.2020	No comparison of autolog vs. implant, narrative overview of studies including either autologous or implantat reconstruction only (10 studies)	Complications, revisions	Population restricted only on massive weight loss patients

Aufgrund eingeschränkter Patientinnenpopulationen, Interventionen, Outcomes oder methodologischen Schwächen in den Reviews ElAbd 2022, Guliyeva 2022, Shauly 2023, Stefura 2023 und Sinik 2022, wurde nach Absprache mit den Kliniker*innen das Review Broyles 2022 ausgewählt. Das weitere Vorgehen war wie folgt:

- Erstellen einer aktualisierten Recherche ab letztem Datum in Broyles 2022
- Screenen der Treffer der aktualisiserten Suche (zwei Mitarbeitende unabhängig voneinander, Titel- und Abstrakt, Volltext)
- Datenextraktion der bereits eingeschlossenen Studien (aus dem Review übernommen)
    - Prüfung weiterer vorhandener Endpunkte
- RoB-Bewertung der Reviewstudien (aus dem Review übernommen)
- Datenextraktion neu identifizierter Studien
- RoB-Bewertung bereits eingeschlossener Studien
- Meta-Analyse aller Studien

- GRADE (Bewertung der Vertrauenswürdigkeit pro Endpunkt)

5.1.2 Evidenzrecherche

Date of search for all databases: 15.03.2024	
Database/Register	Update search
PubMed 1946 to present	3403
Embase (via Ovid) 1972 to present	1418
CENTRAL CENTRAL (via Cochrane Library) Issue 02, 2024	320
CINAHL	345
Total	5486
Total dedupliziert	4166

Grundlage ist das Review von Broyles 2022: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8916208/

Suchdatum: 23.03.2021
Datenbanken: PubMed, Embase, Cochrane CENTRAL, CINAHL, and ClinicalTrials.gov

MEDLINE (via PubMed)

#1 ("Mastectomy"[Mesh] OR Mastectomy[Title/Abstract] OR Mammectomies[Title/Abstract] OR Mastectomies[Title/Abstract] OR Mammectomy[Title/Abstract]) AND ("Mammaplasty"[MeSH Terms] OR "Breast implants"[MeSH Terms] OR "Breast Implantation"[Mesh] OR mammaplasty OR mammoplasty OR Mammaplasties OR Mammoplasties OR ((breast* OR mammar*) AND (implant OR implants OR Reconstruction* OR prosthe* OR "Prostheses and Implants"[MeSH Terms] OR "Transplantation, Autologous"[Mesh]) OR "Autografts"[Mesh] OR Autotransplantation OR Autotransplantations OR Autografting OR Autograftings OR Autologous OR Autograft OR Autotransplants OR Autotransplant OR "Silicones"[Mesh] OR "Saline Solution"[Mesh] OR "Prosthesis Design"[Mesh] OR Silicone OR silicones OR saline OR "gummy bear" OR nanomaterials OR (("Acellular Dermis"[Mesh] OR "Tissue Expansion Devices"[Mesh] OR acellular OR dermal OR peritoneal) AND (matrices OR matrix)) OR "Surgical Flaps"[Mesh] OR "Adipose Tissue/transplantation"[Mesh] OR "Tissue Transplantation"[Mesh] OR ((flap OR flaps) AND (surgical OR surgery))))

#2 ("Mammaplasty"[MeSH Terms] OR "Breast implants"[MeSH Terms] OR "Breast Implantation"[Mesh] OR mammaplasty OR mammoplasty OR Mammaplasties OR Mammoplasties OR ((breast* OR mammar*) AND (implant OR implants OR Reconstruction* OR prosthe* OR "Prostheses and Implants"[MeSH Terms]))) AND ("Transplantation, Autologous"[Mesh] OR "Autografts"[Mesh] OR Autotransplantation OR Autotransplantations OR Autografting OR Autograftings OR Autologous OR Autograft OR Autotransplants OR Autotransplant OR "Silicones"[Mesh] OR "Saline Solution"[Mesh] OR "Prosthesis Design"[Mesh] OR Silicone OR silicones OR saline OR "gummy bear" OR nanomaterials OR (("Acellular Dermis"[Mesh] OR "Tissue Expansion Devices"[Mesh] OR acellular OR dermal OR peritoneal) AND (matrices OR matrix)) OR "Surgical Flaps"[Mesh] OR "Adipose Tissue/transplantation"[Mesh] OR "Tissue Transplantation"[Mesh] OR ((flap OR flaps) AND (surgical OR surgery))) AND (safe* or adverse* or undesirable or harm or harms or injurious or risk or risks or reaction* or complication* or poison* OR side effect* or safety or unsafe OR ((adverse or undesirable or harm or harms or toxic or injurious or serious or fatal) AND (effect* or reaction* or event* or outcome* or incident*)) OR death or deaths or fatal or fatality or fatalities OR Rupture) NOT ("address"[pt] or "autobiography"[pt] or "bibliography"[pt] or "biography"[pt] or "case reports"[pt] or "comment"[pt] or "congress"[pt] or "dictionary"[pt] or "directory"[pt] or "festschrift"[pt] or "government publication"[pt] or "historical article"[pt] or "interview"[pt] or "lecture"[pt] or "legal case"[pt] or "legislation"[pt] or "news"[pt] or "newspaper article"[pt] or "patient education handout"[pt] or "periodical index"[pt] or "comment on" or ("Animals"[Mesh] NOT "Humans"[Mesh]))

#3 #1 OR #2 Filters: from 2021/3/23 - 2024/3/15

OVID Embase 1974 to present

#	Searches
1	mastectomy/

2 (mammectomies or mastectomies or mammectomy).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword heading word, floating subheading word, candidate term word]

3 or/1-2

4 "breast reconstruction".mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword heading word, floating subheading word, candidate term word]

5 (mammaplasty or mammoplasty or mammaplasties or mammoplasties).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword heading word, floating subheading word, candidate term word]

6 4 and 5

7 autograft.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword heading word, floating subheading word, candidate term word]

8 (dermal and matrix).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword heading word, floating subheading word, candidate term word]

9 (flap or flaps).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword heading word, floating subheading word, candidate term word]

10 5 or 7 or 8 or 9

11 4 or 10

12 3 and 11

13 limit 12 to (article or article in press)

14 limit 13 to em=202112-202411

Cochrane Central Register of Controlled Trials (Central, 2024, Issue 02) (via Cochrane Library)

ID	Search
#1	[mh Mastectomy]
#2	Mastectomy OR Mammectomies OR Mastectomies OR Mammectomy
#3	#1 OR #2
#4	[mh Mammaplasty]
#5	[mh "Breast Implants"]
#6	[mh "Breast Implantation"]
#7	mammaplasty OR mammoplasty OR Mammaplasties OR Mammoplasties
#8	#4 OR #5 OR #6 OR #7
#9	breast* OR mammar*
#10	[mh "Prostheses and Implants"]
#11	[mh "Transplantation, Autologous"]
#12	implant OR implants OR Reconstruction* OR prosthe*
#13	#10 OR #11 OR #12
#14	#9 AND #13
#15	#8 OR #14
#16	[mh Autografts]

#17 [mh Silicones]

#18 [mh "Saline Solution"]

#19 [mh "Prosthesis Design"]

#20 Silicone OR silicones OR saline OR “gummy bear” OR nanomaterials OR Autotransplantation OR Autotransplantations OR Autografting OR Autograftings OR Autologous OR Autograft OR Autotransplants OR Autotransplant

#21 #15 OR #16 OR #17 OR #18 OR #19 OR #20

#22 [mh "Acellular Dermis"]

#23 [mh "Tissue Expansion Devices"]

#24 acellular OR dermal OR peritoneal

#25 #22 OR #23 OR #24

#26 matrices OR matrix

#27 #25 AND #26

#28 #27 OR #21

#29 [mh "Surgical Flaps"]

#30 [mh "Tissue Transplantation"]

#31 ((flap OR flaps) AND (surgical OR surgery))

#32 #28 OR #29 OR #30 OR #31

#33 #32 AND #3 with Cochrane Library publication date Between Mar 2021 and Mar 2024

EBSCO CINAHL

(Mastectomy OR Mammectomies OR Mastectomies OR Mammectomy)

AND

(mammaplasty OR mammoplasty OR Mammaplasties OR Mammoplasties OR ((breast* OR mammar*) AND (implant OR implants OR Reconstruction* OR prosthe*)) OR Silicone OR silicones OR saline OR “gummy bear” OR nanomaterials OR Autotransplantation OR Autotransplantations OR Autografting OR Autograftings OR Autologous OR Autograft OR Autotransplants OR Autotransplant OR ((acellular OR dermal OR peritoneal) AND (matrices OR matrix)) OR ((flap OR flaps) AND (surgical OR surgery)))

Limiters - Publication Date: 20210101-20241231

5.1.3 Studienselektion

5.1.3.1 Ein- und Ausschlusskriterien

Inclusion criteria:

Population

- History of breast cancer, or mixed populations including prophylactic mastectomy
- Mastectomy, both unilateral and bilateral
- Both implant-based reconstruction with tissue expander and later implant, as well as direct to implant techniques- *any implant and any autologous breast reconstruction type*

Intervention

- Autologous breast reconstruction (any type)

Comparator

- Implant-based reconstruction (any type)

Outcomes (prioritized)

- Complications overall (any, major, minor)
- Quality of Life outcomes (BREAST-Q: satisfaction with outcome, with breasts, physical well-being)
- Reoperations
- Reconstruction failure (flap/ implant loss)

Study design

- Prospective cohorts, retrospective cohorts, case-control studies, RCTs

Exclusion criteria:

- Ineligible publication formats (abstracts, letters etc)
- Ineligible study designs (case report, case series, systematic or narrative reviews, protocols)
- Ineligible comparisons (reconstructions vs no reconstruction, different timings, only autologous or only implant-based reconstruction, radiotherapy/ chemotherapy focus)

5.2 PICO 7

5.2.1 Fragestellung und geplantes Vorgehen

Haben Patientinnen mit Implantatrekonstruktion und nachfolgender Radiatio ein gleichwertiger, überlegener oder unterlegener Outcome in Bezug auf Nachblutungen, Infektionen, Rekonstruktionsverlust, Reoperation, Hospitalisierung, Lebensqualität, Local Recurrence, oder Overall Suvival im Vergleich zu Patientinnen mit Implantatrekonstruktion ohne nachfolgende Radiatio?

PICO 7 ist eine der priorisierten PICOs. In einer aktualisierten Evidenzrecherche nach systematischen Reviews (siehe auch Gesamtflowchart dieser Suche) konnten sechs systematische Reviews der PICO zugeordnet werden. Im folgenden wurden diese systematischen Arbeiten mit dem klinischen Team besprochen und auf Relevanz geprüft

Table 1: Evaluation of mapped systematic reviews for PICO 7, with exclusion reasons.

Review	Recherche	Thematische Details	Endpunkte	Methodische Notizen	Ausschlussgrund/ Limitationen
Awadeen 2023	Recherche bis März 2022, 6 Studien eingeschlossen	Pre pectoral IBBR; PMRT after recosntruction vs. nonirradiated breasts	Wound infection, capsular contracture, nipple necrosis, seroma & hematoma, implant loss	RoB assessment	Eingeschränkte Anwendbarkeit, da nur präpektorale Rekonstruktionen eingeschlossen wurden
Du 2022	Recherche 1995 bis 21.12.2021, 22 Studien	immediate breast reconstruction surgery, PMRT or without any radiation, comparison radiation to expander or final implant	Overall complications, capsular contracture	No RoB assessment	*Dieses Review wurde als Basis verwendet, jedoch mit Nachextraktion relevanter Endpunkte und aktualisierter Recherche.*
Guo 2022	Recherche bis Februar 2022	Optimal timing of PMRT	-	-	Anwendbarkeit: nur Zeitpunkt der Bestrahlung, kein Vergleich RT vs. No RT
Saldhana 2022	Suche bis März 2021, 36 studies for different questions	Für AHRQ, verschiedene Fragestellungen; timing of IBR vs. radiation; ADM vs. no ADM,	-	-	Anwendbarkeit: nur Zeitpunkt der Bestrahlung, kein Vergleich RT vs. No RT

Review	Recherche	Thematische Details	Endpunkte	Methodische Notizen	Ausschlussgrund/ Limitationen
		prepectoral vs. partial subpectoral vs. subpectoral, material			
Goel 2022	Recherche bis zum 31.01.2022	Role of radiation for the treatment of hereditary breast cancer	-	-	Anwendbarkeit: nur only familial breast cancer
Gareffa 2023	Recherche von Januar 2010 bis Dezember 2021	Boost radiotherapy	-	-	Anwendbarkeit: nur Boost RT

Aufgrund eingeschränkter Patientinnenpopulationen oder Interventionen in den Reviews Awadeen 2023, Goel 2022, Gareffa 2023, Goel 2023, und Saldhana 2022, wurde das Review Du 2022 ausgewählt, trotz eingeschränkter Berichterstattung von Endpunkten und abwesender Bewertung des Verzerrungsrisikos. Das weitere Vorgehen war wie folgt:

- Erstellen einer aktualisierten Recherche ab letztem Datum in Du 2022
- Screenen der Treffer der aktualisiserten Suche (zwei Mitarbeitende unabhängig voneinander, Titel- und Abstrakt, Volltext)
- Datenextraktion der bereits eingeschlossenen Studien
    - Prüfung weiterer vorhandener Endpunkte
- RoB-Bewertung bereits eingeschlossener Studien
- Datenextraktion neu identifizierter Studien
- RoB-Bewertumg bereits eingeschlossener Studien
- Meta-Analyse aller Studien

5.2.2 Evidenzrecherche

Systematic review Du 2022: "…Studies were searched in citation databases PubMed, Embase, and The Cochrane Library published from January 1, 1995, to December 31, 2021. The term ((radiation therapy) OR (radiotherapy)) AND ((post*) OR (adjuvant) OR (after)) AND ((implant) OR (expander)) AND (breast) is used in the search of PubMed…"

Updatesuchen zu Frage 7:

Table 2: Search results.

Date of search for all databases: 31.12.2021 - 15.12.2023	
Database/Register	Update search
MEDLINE ALL (via Ovid) 1946 to present	183
Embase (via Ovid) 1972 to present	117
Total	300

MEDLINE ALL (via Ovid) 31.12.2021 to December 15, 2023
Search Strategy:

#	Searches
1	exp Breast/ or breast*.tw.
2	exp radiotherapy/ or (radiotherap* or irradiat* or radiat* or radiac*).tw.
3	(implant? or expander*).tw.
4	1 and 2 and 3
5	exp cohort studies/ or exp epidemiologic studies/ or exp clinical trial/ or exp evaluation studies as topic/ or exp statistics as topic/

6	((control and study) or group* or (time and factors) or cohort or program or comparative stud* or evaluation studies or survey* or follow-up* or ci).mp.
7	or/5-6
8	(animals/ not humans/) or comment/ or editorial/ or exp review/ or meta analysis/ or consensus/ or exp guideline/
9	hi.fs. or case report.mp.
10	or/8-9
11	7 not 10
12	4 and 11
13	limit 12 to dt=20211221-20231215

Embase (via Ovid) 31.12.2021 to 15.12.2023
Search Strategy:

#	Searches
1	exp breast/ or breast*.tw.
2	exp radiotherapy/ or (radiotherap* or irradiat* or radiat* or radiac*).tw.
3	(implant? or expander*).tw.
4	1 and 2 and 3
5	Clinical study/
6	(cross sectional adj (study or studies)).tw.
7	exp longitudinal study/
8	exp prospective study/
9	exp follow up/
10	cohort*.tw.
11	exp case control study/
12	(case* and control*).tw.
13	or/5-12

14 4 and 13

15 limit 14 to em=202151-202351

16 limit 15 to embase

5.2.3 Studienselektion

5.2.3.1 Ein- und Ausschlusskriterien

Inclusion criteria:

Population

- History of breast cancer, or mixed populations including prophylactic mastectomy and breast reconstruction
- Mastectomy, both unilateral and bilateral
- Both implant-based reconstruction with tissue expander and later implant, as well as direct to implant techniques

Intervention

- Radiotherapy after breast reconstruction

Comparator

- No radiotherapy after breast reconstruction (this may present comparators who had RT previously, i.e., before mastectomy; mixed populations with and without previous RT, and groups completely without RT)

Outcomes

- Complications
- Oncological outcomes
- Quality of Life outcomes

Study design

- Prospective cohorts, retrospective cohorts, case-control studies, RCTs

Exclusion criteria

- Radiotherapy at unclear or mixed timings (i.e., after mastectomy but before reconstruction, or radiotherapy before mastectomy and breast reconstruction)
- Case report, systematic reviews

5.3 PICO 9

5.3.1 Fragestellung und geplantes Vorgehen

Bei mastektomierten Patientinnen: Haben Patientinnen mit autologer Brustrekonstruktion und nachfolgender Radiatio ein gleichwertiger, überlegener oder unterlegener Outcome in Bezug auf Nachblutungen, Infektionen, Rekonstruktionsverlust, Reoperation, Hospitalisierung, Lebensqualität, Local Recurrence, oder Overall Suvival im Vergleich zu Patientinnen mit autologer Brustrekonstruktion ohne nachfolgende Radiatio?

PICO 9 ist eine der priorisierten PICOs. In der Evidenzrecherche durch das Team Würzburg und einer aktualisierten Evidenzrecherche nach systematischen Reviews durch das Team Köln konnten drei systematische Reviews der PICO zugeordnet werden. Im folgenden wurden diese systematischen Arbeiten mit dem klinischen Team besprochen und auf Relevanz geprüft.

Review	Recherche	Thematische Details	Endpunkte	Methodische Notizen	Ausschlussgrund /Limitations
Liew 2021	Recherche bis November 2020, 21 Studien eingeschlossen	Autologous flaps exposed to PMRT and flaps with no radiation exposure	Clinical comparisons, observer-reported outcomes and patient-reported satisfaction rates	RoB assessment (with ROBINS-I tool)	*Dieses Review wurde als Basis verwendet, jedoch mit Nachextraktion relevanter Endpunkte und aktualisierter Recherche.*
Khajuria 2020	Recherche 01.2000 bis 08.2018, 12 Studien	Neoadjuvant, adjuvant and no RT	Surgical complications	-	Altes Datum der Suche
Saldhana 2022	Suche bis März 2021, 36 studies for different questions	Für AHRQ, verschiedene Fragestellungen; timing of IBR vs. radiation; ADM vs. no ADM, prepectoral vs. partial subpectoral vs. subpectoral, material	-	-	Anwendbarkeit: nur Zeitpunkt der Bestrahlung, kein Vergleich RT vs. No RT

Aufgrund eingeschränkter Interventionen und ältere Suchzeiträume in den Reviews Kjajuria 2020 und Saldhana 2022, wurde das Review Liew 2021 ausgewählt, trotz eingeschränkter Berichterstattung von Endpunkten. Das weitere Vorgehen war wie folgt:

- Erstellen einer aktualisierten Recherche ab letztem Datum in Liew 2021
- Screenen der Treffer der aktualisiserten Suche (zwei Mitarbeitende unabhängig voneinander, Titel- und Abstrakt, Volltext)
- Datenextraktion der bereits eingeschlossenen Studien
    - Prüfung weiterer vorhandener Endpunkte
- Datenextraktion neu identifizierter Studien
- RoB-Bewertung bereits eingeschlossener Studien
- Meta-Analyse aller Studien

5.3.2 Evidenzrecherche

Systematic review Liew 2021: "…A thorough literature search of the online databases MEDLINE (OvidSP), EMBASE (OvidSP) and Cochrane CENTRAL was conducted in November 2020. The search algorithm "(postmastectomy radiation therapy OR PMRT) AND (flap* OR autologous OR autogenous) AND (mamm#plasty OR mastoplasty OR breast reconstruction)" was employed, including MESH terms for "breast neoplasms/rt, su", "radiotherapy, adjuvant", "surgical flaps" and "mammaplasty"…"

Date of search for all databases: 17.01.2024	
Database/Register	Update search
MEDLINE ALL (via Ovid) 1946 to present	257
Embase (via Ovid) 1972 to present	231

Date of search for all databases: 17.01.2024	
CENTRAL (via Cochrane Library)	33
Total	521
Total dedupliziert	416

Basis: Liew 2021: https://pubmed.ncbi.nlm.nih.gov/34565703/ (21 eingeschlossene Studien)

Relevante Referenz: "35397804".ui. (enthalten)

Suche in Liew 2021:

#1 Breast neoplasms/rt,su

#2 (post mastectomy radiation therapy or post radiotherapy or PMRT).mp. or radiotherapy, adjuvant/

#3 (flap* or autologous or autogenous).mp. or Surgical flaps/

#4 Mamm#plasty or mastoplasty or breast reconstruction).mp. or mammaplasty/

#5 or/1-4

Update-Suchstrategien:

MEDLINE ALL (via Ovid) 1946 to January 17, 2024

Searches

1 exp Breast Neoplasms/

2 (breast* adj6 (cancer* or neoplasm* or carcinoma* or tumo?r*)).tw.

3 or/1-2

4 Radiotherapy, Adjuvant/ or Radiation Oncology/is, mt, st, td [Instrumentation, Methods, Standards, Trends]

5 (radiotherap* or radio-therap* or irradiat* or radiat* or radiac*).tw,kf.

6 PMRT.tw,kf.

7 or/4-6

8 (flap* or autolog* or autogenous*).tw,kf. or exp Surgical flaps/

9 exp Mammaplasty/

10 (((mammectom* or mastectom* or breast) adj2 reconstruction*) or mammaplast* or mastoplast* or mammoplast* or postmastectom*).tw,kf.

11 or/9-10

12 3 and 7 and 8 and 11

13 limit 12 to dt=20201101-20240117

Embase (via Ovid) 1974 to January 17, 2024

Searches

1 exp breast tumor/

2 (breast* adj6 (cancer* or neoplasm* or carcinoma* or tumo?r*)).tw.

3 exp adjuvant radiotherapy/

4 or/1-2

5 exp adjuvant radiotherapy/

6 radiation oncology/

7 exp cancer radiotherapy/

8 exp adjuvant radiotherapy/ or radiation oncology/ or exp cancer radiotherapy/

9 (radiotherap* or radio-therap* or irradiat* or radiat* or radiac*).tw,kw.

10 PMRT.tw,kw.

11 or/8-10

12 (flap* or autolog* or autogenous*).tw,kw.

13 exp breast reconstruction/

14 (((mammectom* or mastectom* or breast) adj2 reconstruction*) or mammaplast* or mastoplast* or mammoplast* or postmastectom*).tw,kw.

15 or/13-14

16 4 and 11 and 12 and 15

17 limit 16 to em=202044-202403

18 limit 17 to embase

Cochrane Central Register of Controlled Trials (via Cochrane Library, Issue 01, 2024)

ID Search

#1 [mh "Breast Neoplasms"]

#2 (breast* NEAR/6 (cancer* or neoplasm* or carcinoma* or tumor* or tumour*)):TI,AB,KW

#3 #1 OR #2

#4 [mh "Radiotherapy, Adjuvant"] OR [mh "Radiation Oncology"]

#5 (radiotherap* or radio-therap* or irradiat* or radiat* or radiac*):TI,AB,KW

#6 PMRT*:TI,AB,KW

#7 #4 OR #5 OR 6

#8 [mh "Surgical flaps"]

#9 (flap* or autolog* or autogenous*):TI,AB,KW

#10 #8 OR #9

#11 [mh Mammaplasty]

#12 (((mammectom* or mastectom* or breast) NEAR/2 reconstruction*) or mammaplast* or mastoplast* or mammoplast* or postmastectom*):TI,AB,KW

#13 #11 OR #12

#14 #3 AND #7 AND #10 AND #13 with Cochrane Library publication date Between Nov 2020 and Jan 2024

5.3.3 Studienselektion

5.3.3.1 Ein- und Ausschlusskriterien

Inclusion criteria:

Population

- History of breast cancer, or mixed populations including prophylactic mastectomy and breast reconstruction

- Mastectomy, both unilateral and bilateral
- Breast reconstruction with all types of flaps was considered (e.g. TRAM Flap- Transverse Rectus Abdominis Myocutaneous Flap, DIEP flap- Deep Inferior epigastric perforator flap or Latissimus Dorsi Flap)

Intervention

- Radiotherapy after breast reconstruction

Comparator

- No radiotherapy after breast reconstruction (this may present comparators who had RT previously, i.e., before mastectomy; mixed populations with and without previous RT, and groups completely without RT)

Outcomes

- Complications
- Oncological outcomes
- Quality of Life outcomes

Study design

- Prospective cohorts, retrospective cohorts, case-control studies, RCTs

Exclusion criteria

- Radiotherapy at unclear or mixed timings (i.e., after mastectomy but before reconstruction, or radiotherapy before mastectomy and breast reconstruction)
- Implant-based reconstruction
- Case reports, systematic or narrative reviews

5.4 PICO 13

5.4.1 Fragestellung und geplantes Vorgehen

Haben Patientinnen mit einer Indikation zur Mastektomie, die eine gemeinsame oder zusätzliche Beratung durch onkologische und rekonstruktive ChirurgInnen (Breast surgeons and Reconstructive surgeons) erhalten haben, gleichwertige, bessere oder schlechtere Lebensqualität, Ästhetik, Sexualität, Weiblichkeit, & Partizipation als solche, die nur durch eine der beiden Gruppen beraten wurden?

PICO 13 ist eine der priorisierten PICOs. In einer aktualisierten Evidenzrecherche nach systematischen Reviews durch das Team Köln konnten keine systematischen Reviews der PICO zugeordnet werden. Dementsprechend war das geplante methodische Vorgehen für diese Schlüsselfrage wie folgt:

- Erstellen einer Primärsuche; relevante Begriffe waren: Breast Surgeon / gynecologist, Reconstructive Surgeon reconstructive / free flap surgeon
- Screenen der Treffer der Literaturrecherche (zwei Mitarbeitende unabhängig voneinander, Titel- und Abstrakt, Volltext)
- Datenextraktion
- Meta-Analyse

5.4.2 Evidenzrecherche

Date of search for all databases: 15.02.2024	
Database/Register	Update search
MEDLINE ALL (via Ovid) 1946 to present	641
Embase (via Ovid) 1972 to present	619
Total	1260

Date of search for all databases: 15.02.2024	
Total dedupliziert	919

Ovid MEDLINE(R) ALL 1946 to February 15, 2024

#	Searches
1	exp Mastectomy/
2	(((mammectom* or mastectom* or breast) adj2 reconstruction*) or mammaplast* or mastoplast* or mammoplast* or postmastectom*).tw.
3	or/1-2
4	"Referral and Consultation"/ or Counseling/
5	decision making/ or decision making, shared/
6	(((make or making) adj2 decision*) or consult* or counsel* or communication* or appointment?).tw. or approach*.ti.
7	or/4-6
8	interprofessional relations/ or interdisciplinary communication/
9	((multidis?iplinar* or interdis?iplinar* or multi-dis?iplinar* or inter-dis?iplinar* or interprofessional* or inter-professional*) adj2 (medical* or team* or approach* or consultation* or physician? or collaborat* or onco* or professionals or conference?)).tw.
10	(surgeon? and oncologist?).tw.
11	((oncolog* or reconstructi* or gynecologist?) adj4 (surger* or surgeon? or surgical*)).tw.

12 ((oncolog* or reconstructi*) adj4 (plastic* or oncoplastic*)).tw.

13 (two-surgeon? or two-team*).tw.

14 or/8-13

15 3 and 7 and 14

16 remove duplicates from 15

Ovid Embase 1974 to present

Searches

1 exp mastectomy/

2 (((mammectom* or mastectom* or breast) adj2 reconstruction*) or mammaplast* or mastoplast* or mammoplast* or postmastectom*).tw.

3 or/1-2

4 consultation/ or counseling/

5 decision making/ or shared decision making/

6 (((make or making) adj2 decision*) or consult* or counsel* or communication* or appointment?).tw. or approach*.ti.

7 or/4-6

8 interdisciplinary communication/

9 ((multidis?iplinar* or interdis?iplinar* or multi-dis?iplinar* or inter-dis?iplinar* or interprofessional* or inter-professional*) adj2 (medical* or team* or approach* or consultation* or physician? or collaborat* or onco* or professionals or conference?)).tw.

10 (surgeon? and oncologist?).tw.

11 ((oncolog* or reconstructi* or gynecologist?) adj4 (surger* or surgeon? or surgical*)).tw.

12 ((oncolog* or reconstructi*) adj4 (plastic* or oncoplastic*)).tw.

13 (two-surgeon? or two-team*).tw.

14 or/8-13

15 3 and 7 and 14

16 limit 15 to embase

remove duplicates from 16

5.4.3 Studienselektion

5.4.3.1 Ein- und Ausschlusskriterien

Inclusion criteria:

Population

- PatientInnen mit Indikation zur Mastektomie

Intervention

- Gemeinsame oder zusätzliche Beratung durch onkologische und rekonstruktive ChirurgInnen (Breast surgeons and Reconstructive surgeons)

Comparator

- Einzelne Beratung durch eine der beiden Gruppen

Outcomes

- Lebensqualität, Ästhetik, Sexualität, Weiblichkeit, & Partizipation

Exclusion criteria

- Case report, systematic reviews, narrative reviews, press articles
- Ineligible interventions: decision aids, surgeon interviews

5.5 PICO 16

5.5.1 Fragestellung und geplantes Vorgehen

Bei mastektomierten Patientinnen: Ist bei der autologen Brustrekonstruktion die primäre Rekonstruktion der sekundären Rekonstruktion (Vergleiche: immediate vs. immediate-delayed vs. delayed) im Hinblick auf Nachblutungen, Infektionen, Reoperationen, Rekonstruktionsverlust, Hospitalisierung, Recurrence, Overall Survival, und Lebensqualität gleichwertig, unter- oder überlegen?

PICO 16A ist eine der priorisierten PICOs. In einer aktualisierten Evidenzrecherche nach systematischen Reviews durch das Team Köln (siehe auch Gesamtflowchart dieser Suche) konnten zwei systematische Reviews der PICO zugeordnet werden. Im folgenden wurden diese systematischen Arbeiten mit dem klinischen Team besprochen und auf Relevanz geprüft.

Review	Recherche	Thematische Details	Endpunkte	Methodische Notizen	Einschluß
Matar 2022	01.05.2021	Immediate vs. delayed	complications, length of postoperative hospital stay, reoperation	30 studies (non-randomized studies, mostly retrospective), No RoB assessment	*Diese Reviews wurden beide als Basis verwendet, jedoch mit Nachextraktion relevanter Endpunkte und aktualisierter Recherche.*

Review	Recherche	Thematische Details	Endpunkte	Methodische Notizen	Einschluß
Bargon 2022	19.11.2020	Immediate vs. delayed BR autologous / implant separately analyzed	local, regional, loco regional, distant, and total breast cancer recurrences	55 studies (non-randomized studies), RoB assessment	

Das weitere Vorgehen war wie folgt:

- Erstellen einer aktualisierten Recherche ab letztem Datum in Bargon 2022
- Screenen der Treffer der aktualisierten Suche (zwei Mitarbeitende unabhängig voneinander, Titel- und Abstrakt, Volltext)
- Datenextraktion der bereits eingeschlossenen Studien
    - Prüfung weiterer vorhandener Endpunkte
- RoB-Bewertung bereits eingeschlossener Studien
- Datenextraktion und RoB-Bewertung neu identifizierter Studien
- Meta-Analyse aller Studien
- Bewertung der Vertrauenswürdigkeit der Evidenz nach GRADE (pro Endpunktebene)

5.5.2 Evidenzrecherche

Systematic review: Bargon 2022: “A comprehensive systematic literature search was performed in MEDLINE (via PubMed), Embase and the Cochrane Library from inception to November 19, 2020”

Updatesuchen zu Frage 16A:

Date of search for all databases: 05.03.2024	
Database/Register	Update search from 19.11.2020 to present
MEDLINE (via PubMed)	1650
Embase (via Ovid)	1588
CENTRAL (via Cochrane Library)	Keine Suche, da wir nicht explizit nach RCTs suchen und ongoing Studies ausschließen.
Total	3238
Total dedupliziert	2614

Ovid MEDLINE(R) ALL 1946 to March 04, 2024

Searches

1 exp "Breast Neoplasms"/ or exp Mastectomy/ or neoplas*.tw. or cancer*.tw. or carcinoma*.tw. or malignan*.tw. or tumor.tw. or tumors.tw. or tumour*.tw. or mammacarcin*.tw. or oncolog*.tw. or mastectom*.tw.

2 exp Mammaplasty/ or mammaplast*.tw. or mammoplast*.tw. or (breast* and reconstruct*).tw. or "deep inferior epigastric arter*".tw. or diep.tw. or "autologous reconstruct*".tw. or "implant reconstruct*".tw. or (autologous and (prosthes* and "of fat graft*")).tw. or "breast implant*".tw. or breastimplant*.tw.

3 exp Mortality/ or "Mortality".fs. or exp Survival/ or exp "Disease-Free Survival"/ or exp "Progression-Free Survival"/ or exp Recurrence/ or exp "Neoplasm Recurrence, Local"/ or (oncologic* and (safety or outcome*)).ti,ab. or mortalit*.ti,ab. or survival.ti,ab. or relaps*.ti,ab. or recrudescence*.ti,ab. or re-crudescence*.ti,ab. or recurrence*.ti,ab.

4 exp Infections/

5 infection*.ti,ab,kf.

6 Seroma/

7 seroma*.ti,ab,kf.

8 exp Skin/ and Necrosis/

9 (skin* adj1 necros*).ti,ab,kf.

10 exp Wound Infection/

11 (wound adj2 (postoperative* or post-operative* or surigal site or surgical* or complication*)).ti,ab,kf.

12 exp hemorrhage/ or hematoma/

13 (bleeding* or postbleeding* or hemorrhage* or haemorrhage* or hematoma* or haematoma*).ti,ab,kf.

14 Reoperation/

15 (((joint or surger*) adj2 (revision* or repeat*)) or reoperation* or re-operation*).ti,ab,kf.

16 (reconstruct* adj1 (failure* or loss)).ti,ab,kf.

17 personal satisfaction/ or Patient Satisfaction/ or "Activities of Daily Living"/ or quality-adjusted life years/ or personal autonomy/ or Happiness/ or Self Concept/ or Family Relations/ or Social Support/ or Financial Support/ or exp Esthetics/

18 (quality of life or life quality or activities of daily living or Quality adjusted life year* or ((patient* or personal) adj1 (autonomy or satisfaction)) or happiness or patient preference* or fear of death or self-concept or family relation* or religion or ((social or financial) adj2 support) or positive experience).tw.

19 (((aesthetic* or esthetic*) adj2 outcome?) or ((aesthetic* or esthetic*) adj1 result?)).ti,ab,kf.

20 (BREAST-Q or BREASTQ or breast satisfaction or well-being or wellbeing).ti,ab,kf.

21 exp Hospitalization/

22 (((readmission* or re-admission*) adj2 (hospital* or patient*)) or rehospitali?ation* or hospitali?ation*).ti,ab,kf.

23 ((major? or minor?) adj2 complication*).ti,ab,kf.

24 (major? adj3 minor?).ti,ab,kf.

25 or/3-24

26 1 and 2 and 25

27 (animals/ not humans/) or comment/ or editorial/ or exp review/ or meta analysis/ or consensus/ or exp guideline/

28 hi.fs. or case report.mp. or case series.mp.

29 case-reports.pt. or case-report.ti. or editorial.pt. or letter.pt.

30 or/27-29

31 26 not 30

32 limit 31 to dt=20201119-20240305

33 remove duplicates from 32

Ovid Embase 1974 to present

#	Searches
1	exp breast tumor/
2	exp mastectomy/
3	(neoplas* or cancer* or carcinoma* or malignan* or tumor or tumors or tumour* or mammacarcin* or oncolog* or mastectom*).ti,ab.
4	or/1-3
5	breast reconstruction/
6	(mammaplast* or mammoplast* or (breast* adj3 reconstruct*) or deep-inferior-epigastric-arter* or diep or autologous-reconstruct* or implant-reconstruct* or (autologous adj3 (prosthes* or fat-graft*)) or breast-implant* or breastimplant*).ti,ab.
7	or/5-6
8	exp mortality/
9	exp survival/
10	exp recurrent disease/
11	((oncologic* adj2 (safety or outcome*)) or mortalit* or survival or recurrence).ti,ab.
12	or/8-11
13	4 and 7 and 12

14 exp breast tumor/ or exp mastectomy/ or (neoplas* or cancer* or carcinoma* or malignan* or tumor or tumors or tumour* or mammacarcin* or oncolog* or mastectom*).ti,ab.

15 breast reconstruction/ or (mammaplast* or mammoplast* or (breast* adj3 reconstruct*) or deep-inferior-epigastric-arter* or diep or autologous-reconstruct* or implant-reconstruct* or (autologous adj3 (prosthes* or fat-graft*)) or breast-implant* or breastimplant*).ti,ab.

16 exp mortality/ or exp survival/ or (mammaplast* or mammoplast* or (breast* adj3 reconstruct*) or deep-inferior-epigastric-arter* or diep or autologous-reconstruct* or implant-reconstruct* or (autologous adj3 (prosthes* or fat-graft*)) or breast-implant* or breastimplant*).ti,ab.

17 disease free survival/

18 exp disease free survival/

19 exp progression free survival/

20 recurrent disease/

21 tumor recurrence/

22 exp mortality/ or exp survival/ or exp disease free survival/ or exp progression free survival/ or recurrent disease/ or tumor recurrence/ or (oncologic* and (safety or outcome*)).ti,ab. or mortalit*.ti,ab. or survival.ti,ab. or relaps*.ti,ab. or recrudescence*.ti,ab. or re-crudescence*.ti,ab. or recurrence*.ti,ab.

23 exp infection/

24 infection*.ti,ab,kw.

25 seroma/

26 seroma*.ti,ab,kw.

27 skin necrosis/

28 ((cutaneous or skin*) adj1 necros*).ti,ab,kf.

29 wound infection/ or infectious complication/

30 (wound adj2 (postoperative* or post-operative* or surigal site or surgical* or complication*)).ti,ab,kf.

31 exp bleeding/ or exp hematoma/

32 (bleeding* or postbleeding* or hemorrhage* or haemorrhage* or hematoma* or haematoma*).ti,ab,kf.

33 reoperation/

34 (((joint or surger*) adj2 (revision* or repeat*)) or reoperation* or re-operation*).ti,ab,kf.

35 (reconstruct* adj1 (failure* or loss)).ti,ab,kf.

36 exp satisfaction/ or patient satisfaction/ or daily life activity/ or quality adjusted life year/ or personal autonomy/ or happiness/ or self concept/ or family relation/ or social support/ or financial management/ or esthetics/

37 (((aesthetic* or esthetic*) adj2 outcome?) or ((aesthetic* or esthetic*) adj1 result?)).ti,ab,kw.

38 (BREAST-Q or BREASTQ or breast satisfaction or well-being or wellbeing).ti,ab,kw.

39 exp hospitalization/

40 (((readmission* or re-admission*) adj2 (hospital* or patient*)) or rehospitali?ation* or hospitali?ation*).ti,ab,kw.

41 ((major? or minor?) adj2 complication*).ti,ab,kw.

42 (major? adj3 minor?).ti,ab,kw.

43 or/16-42

44 14 and 15 and 43

45 (animal experiment/ or Animal experiment/) not (human experiment/ or human/)

46 44 not 45

47 limit 46 to em=202047-202410

48 (books or chapter or conference abstract or conference paper or "conference review" or editorial or letter).pt.

49 (case report or case series).mp.

50 letter/ or note/ or editorial/ or exp "review"/ or exp meta analysis/ or exp consensus/ or exp practice guideline/

51 or/48-50

52 46 not 51

53 limit 52 to em=202047-202410

54 limit 53 to Embas

5.5.3 Studienselektion

5.5.3.1 Ein- und Ausschlusskriterien

Inclusion criteria:

Population

- History of breast cancer and mastectomy, autologous breast reconstruction
- Mastectomy, both unilateral and bilateral

Intervention & Comparator

- Immediate vs. delayed (or for example vs. delayed-immediate)

Outcomes

- Complications (Nachblutungen, Infektionen, Rekonstruktionsverlust, Reoperationen, Hospitalisierung)
- Oncological outcomes (Recurrence, Overall survival)
- Quality of Life outcomes

Study design

- Prospective cohorts, retrospective cohorts, case-control studies, RCTs

Exclusion criteria:

- Unclear timings; implant-based reconstruction, secondary reconstruction after implant failure due to infection
- Case report, systematic or narrative reviews

5.6 PICO 16B

5.6.1 Fragestellung und geplantes Vorgehen

Bei mastektomierten Patientinnen: Ist bei der Implantatrekonstruktion die primäre Rekonstruktion der sekundären Rekonstruktion (Vergleich: direct-to implant (DTI) vs. Tissue expander (TE), auch: one-step versus two-step approach) im Hinblick auf die Outcomes Nachblutungen, Infektionen, Reoperation, Rekonstruktionsverlust, Hospitalisierung, und Lebensqualität gleichwertig, unter- oder überlegen?

PICO 16(B) ist eine der priorisierten PICOs. In einer aktualisierten Evidenzrecherche nach systematischen Reviews (siehe auch Gesamtflowchart dieser Suche) konnten drei systematische Reviews der PICO 16A oder B zugeordnet werden. Im folgenden wurden diese systematischen Arbeiten mit dem klinischen Team besprochen und auf Relevanz geprüft.

Review	Recherche	Thematische Details	Endpunkte	Methodische Notizen	Ausschlussgrund /Limitations
Bargon 2022	19 November 2020 in Medline, Embase, Cochrane Library 55 Studien eingeschlossen	Gemischt Implantat und Eigengewebe	- NA, autolog	-	Recherchedatum weiter zurückliegend als van der Wielen 2023; Autolog (Frage 16A)
Matar 2022	Recherche bis 1. Mai 2021	gemischt Implantat & Eigengewebe, nicht one-stage vs. Two stage bei	Surgical complications (Infections, Fat necrosis,	Kein RoB Assessment	Recherchedatum weiter zurückliegend als van der

Review	Recherche	Thematische Details	Endpunkte	Methodische Notizen	Ausschlussgrund /Limitations
	PubMed, Embase, Cochrane 30 Studien eingeschlossen	Implantat, sondern wirklich immediate vs. Delayed reconstruction	Skin necrosis, Hematoma, seroma,Wound dehiscence) Length of postoperative stay Reoperation		Wielen 2023; Mischung aus Implantat und Eigengewebe
Van der Wielen 2023	Literaturrecherche bis 27 September 2022 in PubMed, Embase, Web of Science, Cochrane Library			Meta-Analyse der Inzidenz, Re-Analyse der Effektschätzer nötig; RoB bewertet mit	

Aufgrund der älteren Recherchedaten in Bargon 2022 und Matar 2022 sowie des Fokus auf der autologen Brustrekonstruktion wurde das Review von van der Wielen 2022 ausgewählt, trotz eingeschränkter Berichterstattung von Endpunkten. Das weitere Vorgehen war wie folgt:

- Da das Recherchedatum im definierten Bereich liegt (definiert als Studien eingeschlossen bis mindestens 07.2022), wurde keine Aktualisierung der Recherche vorgenommen.
- Aufgrund fehlender Endpunkte und Inkongruenzen zwischen Primärstudiendaten und Review, sowie eine Meta-analyse der Prävalenzen anstatt relativer Risiken erfolgte die Datenextraktion der bereits eingeschlossenen Studien.
- Eine RoB-Bewertung bereits eingeschlossener Studien war nicht notwendig, da dies bereits in der Publikation von van der Wielen 2023 vorgenommen wurde.
- Die extrahierten Endpunkte wurden im Anschluss meta-analysiert.

5.6.2 Evidenzrecherche

Es wurde keine eigene Evidenzrecherche durchgeführt, da das Recherchedatum des Reviews im definierten Bereich lag. Die Recherchestrategie wurde im Appendix 1 aufgeführt (kopiert aus van der Wielen 2022):

Search strategy in PubMed.

Search	Query	Results
#5	(#1 OR #2) AND #3 AND #4	1044
#4	"Breast/surgery"[Mesh] OR "Breast/therapy"[Mesh] OR "Mastectomy"[Mesh] OR "Mammaplasty"[Mesh] OR "Breast Neoplasms/surgery"[Mesh] OR "Mastectom*"[tiab] OR "Mammectom*"[tiab] OR "Mammaplast*"[tiab] OR "Mammoplast*"[tiab] OR "breast reconstruct*"[tiab] OR (("mamma*"[tiab] OR "breast"[tiab] OR "breasts"[tiab]) AND ("implant*"[tiab] OR "prosthe*"[tiab] OR "reconstruct*"[tiab]))	95,412
#3	"Breast Implantation"[Mesh] OR "Breast Implants"[Mesh] OR "implant*"[tiab]	461,372
#2	"two stage*"[tiab] OR "second stage*"[tiab] OR "2 stage*"[tiab]	62,322
#1	"one stage*"[tiab] OR "single stage*"[tiab] OR "1 stage*"[tiab] OR "direct to implant"[tiab]	25,540

Search strategy in Embase.com.

Search	Query	Results
#6	#5 NOT ('conference abstract'/it OR 'conference review'/it OR 'conference paper'/it OR 'editorial'/it OR 'erratum'/it OR 'letter'/it OR 'note'/it OR 'short survey'/it)	851
#5	(#1 OR #2) AND #3 AND #4	1191

Search	Query	Results
#4	'breast surgery'/exp OR ('Mastectom*' OR 'Mammectom*' OR 'Mammaplast*' OR 'Mammoplast*' OR 'breast reconstruct*' OR (('mamma*' OR 'breast' OR 'breasts') AND ('implant*' OR 'prosthe*' OR 'reconstruct*'))):ti,ab,kw	127,616
#3	'breast prosthesis'/exp OR ('implant*'):ti,ab,kw	635,414
#2	('two stage*' OR 'second stage*' OR '2 stage*'):ti,ab,kw	80,112
#1	('one stage*' OR 'single stage*' OR '1 stage*' OR 'direct to implant'):ti,ab,kw	34,622

Search strategy in Clarivate Analytics/Web of Science Core Collection.

Search	Query	Results
#6	(#1 OR #2) AND #3 AND #4 and Proceedings Papers or Letters or Editorial Materials or Meeting Abstracts or Corrections or Notes (Exclude – Document Types)	851
#5	(#1 OR #2) AND #3 AND #4	1043
#4	TS=("Mastectom*" OR "Mammectom*" OR "Mammaplast*" OR "Mammoplast*" OR "breast reconstruct*" OR (("mamma*" OR "breast" OR "breasts") AND ("implant*" OR "prosthe*" OR "reconstruct*")))	72,011
#3	TS=("implant*")	560,222
#2	TS=("two stage*" OR "second stage*" OR "2 stage*")	153,422
#1	TS=("one stage*" OR "single stage*" OR "1 stage*" OR "direct to implant")	40,678

Search strategy in Wiley/Cochrane Library.

Search	Query	Results
#5	(#1 OR #2) AND #3 AND #4	48
#4	(“Mastectom*” OR “Mammectom*” OR “Mammaplast*” OR “Mammoplast*” OR “breast reconstruct*” OR ((“mamma*” OR “breast” OR “breasts”) AND (“implant*” OR “prosthe*” OR “reconstruct*”))):ti,ab,kw	477
#3	(“implant*”):ti,ab,kw	14,194
#2	(“two stage*” OR “second stage*” OR “2 stage*”):ti,ab,kw	5347
#1	(“one stage*” OR “single stage*” OR “1 stage*” OR “direct to implant”):ti,ab,kw	1721

5.6.3 Studienselektion

5.6.3.1 Ein- und Ausschlusskriterien

Inclusion criteria:

Population

- History of breast cancer, or mixed populations including prophylactic mastectomy and breast reconstruction
- Mastectomy, both unilateral and bilateral
- Both primary and secondary breast reconstruction

Intervention

- Direct-to-implant breast reconstruction (one-stage breast reconstruction)

Comparator

- Implant-based breast reconstruction with tissue expander (TE; two-stage breast reconstruction)

Outcomes

- Patient satisfaction (i.e., BREAST-Q)
- Aesthetic outcomes
- Complications
- Costs per patient

Study design

- Prospective cohorts, retrospective cohorts, case-control studies, RCTs

Exclusion criteria

- Language other than English
- Case report, systematic reviews
- N < 20

5.7 PICO 23

5.7.1 Fragestellung und geplantes Vorgehen

Bei Patientinnen mit Indikation zur Mastektomie (jede Technik): führt die Ablatio ohne Rekonstruktion gegenüber der Mastektomie mit Rekonstruktion (Implantat/ Eigengewebe) zu gleichen, besseren oder schlechteren Rate an Komplikationen (any, minor, major), Reoperations, Rekonstruktionsverlust (implant/ flap loss) und Lebensqualität (Fokus: BREAST-Q Satisfaction with breasts, Physical well-being)?

PICO 23 ist eine der priorisierten PICOs. In einer aktualisierten Evidenzrecherche nach systematischen Reviews durch das Team Köln konnte eine systematische Übersichtsarbeit der PICO zugeordnet werden. Im Folgenden wurden diese systematischen Arbeiten mit dem klinischen Team besprochen und auf Relevanz geprüft.

Review	Recherche	Thematische Details	Endpunkte	Methodische Notizen	Ausschlussgrund /Limitations
Shen 2021	11.2019	Breast reconstruction vs. mastectomy only	Complications, Oncological outcomes	51 studies, No RoB assessment	Dieses Review wurde als Basis verwendet, jedoch mit Nachextraktion relevanter Endpunkte und aktualisierter Recherche.

Das weitere Vorgehen war wie folgt:

- Erstellen einer aktualisierten Recherche ab letztem Datum in Shen 2021
- Screenen der Treffer der aktualisierten Suche (zwei Mitarbeitende unabhängig voneinander, Titel- und Abstrakt, Volltext)
- Datenextraktion der bereits eingeschlossenen Studien (übernommen aus dem Review)
    - Prüfung weiterer vorhandener Endpunkte
- RoB-Bewertung bereits eingeschlossener Studien
- Datenextraktion neu identifizierter Studien
- RoB-Bewertung bereits eingeschlossener Studien (übernommen aus dem Review)
- Meta-Analyse aller Studien
- Bewertung der Vertrauenswürdigkeit (nach GRADE)

5.7.2 Evidenzrecherche

Basierend auf Shen 2021 Update-Suche https://www.sciencedirect.com/science/article/pii/S1748681520304289?via%3Dihub

Date of search for all databases: 01.04.2024	
Database/Register	Update search from 01.11.2019 to present
MEDLINE (via Ovid)	800
Embase (via Ovid)	857 (not preprint or conference abstracts)
CENTRAL (via Cochrane Library)	90
Total	1747
Total dedupliziert	1067

Ovid MEDLINE(R) ALL 1946 to April 01, 2024

#	Searches
1	exp Breast Neoplasms/
2	(breast adj3 (cancer* or neoplasm* or carcinoma* or tumo?r*)).tw.
3	(mammary adj2 (cancer* or carcinoma*)).tw.
4	or/1-3
5	exp Mastectomy/
6	(mastectom* or mammectomy* or MA or MSM).tw.

7	5 or 6
8	((immediate or delayed or secondary or later) adj3 reconstruction*).tw.
9	4 and 7 and 8
10	limit 9 to dt=20191101-20240402

Ovid Embase 1974 to present

#	Searches
1	exp breast tumor/
2	(breast adj3 (cancer* or neoplasm* or carcinoma* or tumo?r*)).tw.
3	(mammary adj2 (cancer* or carcinoma*)).tw.
4	or/1-3
5	exp mastectomy/
6	(mastectom* or mammectomy* or MA or MSM).tw.
7	or/5-6
8	((immediate or delayed or secondary or later) adj3 reconstruction*).tw.
9	4 and 7 and 8
10	limit 9 to em=201944-202414
11	limit 10 to (conference abstracts or "preprints (unpublished, non-peer reviewed)")

12	10 not 11

CENTRAL (via Cochrane Library) Issue 03, 2024

ID	Search
#1	[mh "Breast Neoplasms"]
#2	(breast NEAR/3 (cancer* or neoplasm* or carcinoma* or tumor* or tumour*)):TI,AB,KW
#3	(mammary NEAR/2 (cancer* or carcinoma*)):TI,AB,KW
#4	#1 OR #2 OR #3
#5	[mh Mastectomy]
#6	(mastectom* or mammectomy* or MA or MSM):TI,AB,KW
#7	#5 OR #6
#8	((immediate or delayed or secondary or later) NEAR/3 reconstruction*):TI,AB,KW
#9	#4 AND #7 AND #8 with Cochrane Library publication date Between Nov 2019 and Apr 2024

5.7.3 Studienselektion

5.7.3.1 Ein- und Ausschlusskriterien

Inclusion criteria

Population

History of breast cancer, or mixed populations including prophylactic mastectomy

Mastectomy, both unilateral and bilateral

Intervention

Any breast reconstruction (autologous/ implant-based)

Comparator

Mastectomy alone, without reconstruction

Clinically prioritized outcomes

Complications overall (any, major, minor)

Quality of Life outcomes (satisfaction with breasts, physical well-being)

Reoperation

Reconstruction loss (flap/ implant loss)

Study design

Prospective cohorts, retrospective cohorts, case-control studies, RCTs

Exclusion criteria

Ineligible comparisons (e.g. comparison different reconstruction types, different timings but no comparison with mastectomy only)

Case report, abstracts, systematic or narrative reviews

5.8 PICO 24

5.8.1 Fragestellung und geplantes Vorgehen

Bei Patientinnen nach Mastektomie (jede Technik): Inwieweit sind die drei Optionen chirurgischer Versorgung nach Mastektomie - autologe Brustrekonstruktion, implantatbasierte Brustrekonstruktion und bewusst gewählte Aesthetic Flat Closure - im Hinblick auf Nachblutungen, Infektionen, Reoperationen, Rekonstruktionsverlust, Hospitalisierung, Recurrence, Overall Survival, und Lebensqualität gleichwertig, unter- oder überlegen?

Fokus PICO 24: *Vergleich mit* „bewusst gewählter *Aesthetic Flat Closure*“

PICO 24 ist eine der priorisierten PICOs. In einer aktualisierten Evidenzrecherche nach systematischen Reviews durch das Team Köln konnten der Schlüsselfrage keine systematischen Reviews zugeordnet werden. Dementsprechend war das geplante methodische Vorgehen für diese Schlüsselfrage wie folgt:

- Erstellen einer Primärsuche; relevante Begriffe waren: „*Aesthetic Flat Closure, go flat, going flat, flat closure*“
- Screenen der Treffer der Literaturrecherche (zwei Mitarbeitende unabhängig voneinander, Titel- und Abstrakt, Volltext)
- Datenextraktion
- Meta-Analyse

5.8.2 Evidenzrecherche

Date of search for all databases: 16.01.2024	
Database/Register	Update search
MEDLINE ALL (via Ovid) 1946 to present	28
Embase (via Ovid) 1972 to present	30

Date of search for all databases: 16.01.2024	
CENTRAL (via Cochrane Library)	3
Total	61
Total dedupliziert	33

Ovid MEDLINE(R) ALL 1946 to present

#	Searches
1	exp Mastectomy/
2	Breast/ and Surgery, Plastic/
3	(mastectom* or breast conserving surger* or mammaplast* or mammoplast* or postmastectom*).tw,kf.
4	exp Mammaplasty/
5	(((mammectom* or mastectom* or breast) adj2 reconstruction*) or mammaplast* or mammoplast* or postmastectom*).tw,kf.
6	or/1-5
7	(flat adj2 closur*).tw.
8	(go* adj2 flat*).tw,kf.
9	6 and 8
10	7 or 9

Ovid Embase 1974 to present

#	Searches
1	exp mastectomy/
2	breast/ and exp plastic surgery/
3	(mastectom* or breast conserving surger* or mammaplast* or mammoplast* or postmastectom*).tw,kw.
4	exp breast reconstruction/
5	(((mammectom* or mastectom* or breast) adj2 reconstruction*) or mammaplast* or mammoplast* or postmastectom*).tw,kw.
6	or/1-5
7	(go* adj2 flat*).tw,kf.
8	(flat adj2 closur*).tw.
9	6 and 7
10	8 or 9

CENTRAL (via Cochrane Library) Issue 01, 2024

ID	Search
#1	[mh Mastectomy]
#2	[mh ^breast] AND [mh ^"Surgery, Plastic"]
#3	(mastectom* or breast conserving surger* or mammaplast* or mammoplast* or postmastectom*):TI,AB,KW

#4	[mh Mammaplasty]
#5	(((mammectom* or mastectom* or breast) adj2 reconstruction*) or mammaplast* or mammoplast* or postmastectom*):TI,AB,KW
#6	#1 OR #2 OR #3 OR #4 OR #5
#7	(go* NEAR/2 flat*):TI,AB,KW
#8	#6 AND #7
#9	(flat* NEAR/2 closur*):TI,AB,KW
#10	#8 OR #9

5.8.3 Studienselektion

5.8.3.1 Ein- und Ausschlusskriterien

Inclusion criteria:

Population

- Mastectomy, both unilateral and bilateral
- Breast reconstruction after mastectomy

Intervention

- ***Aesthetic Flat Closure***

Comparator

- Reconstruction: autologous or implant-based

Outcomes

- Complications
- Oncological outcomes
- Quality of Life outcomes

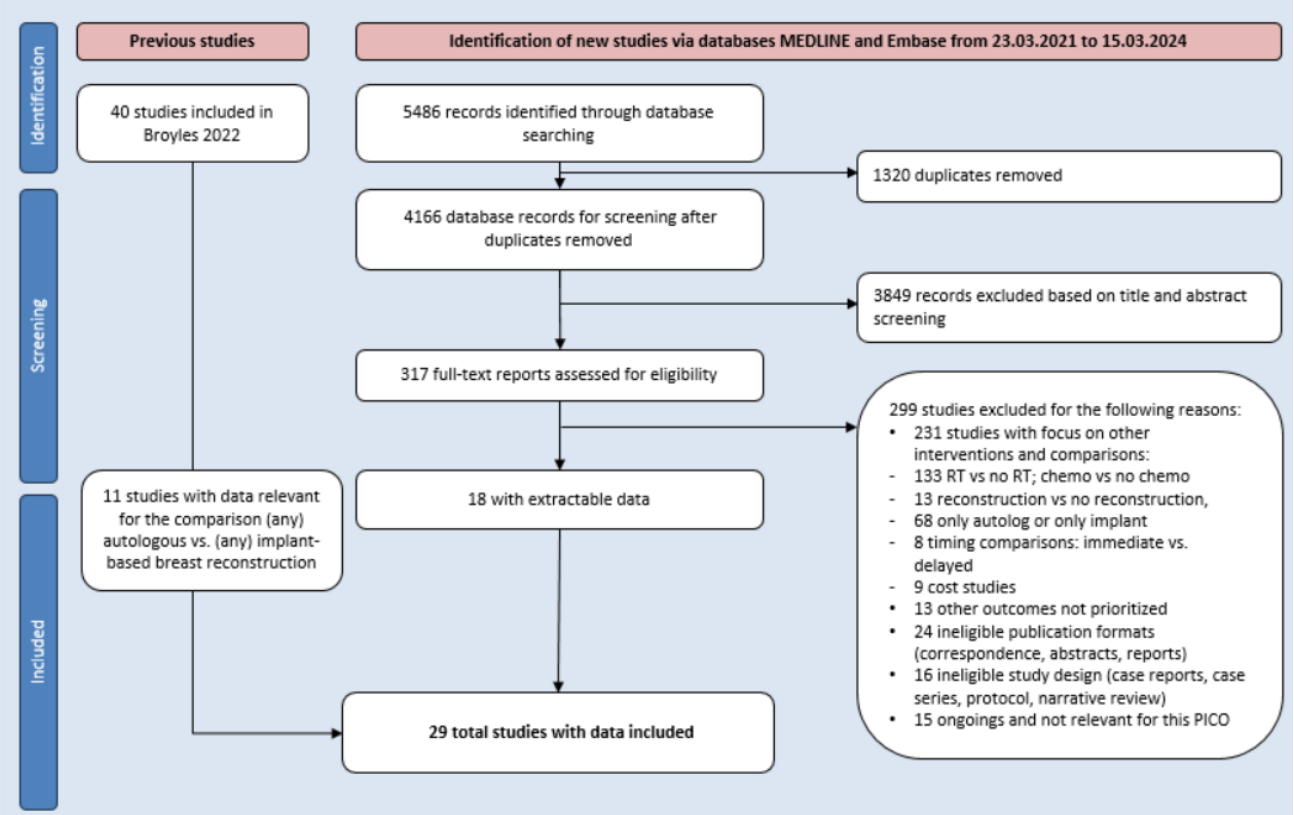
Exclusion criteria

- Case reports, narrative reviews, conference abstracts
- Ineligible interventions: no aesthetic flat closure technique

6 Ergebnisse

6.1 PICO 1

6.1.1 PRISMA Flowdiagramm



6.1.2 Evidenztabellen

6.1.2.1 Systematisches Review

6.1.2.1.1 Evidenztabelle systematisches Review Broyles 2022

Broyles, JM, Balk, EM, Adam, GP, Cao, W, Bhuma, MR, Mehta, S, et.al. Implant-based versus Autologous Reconstruction after Mastectomy for Breast Cancer: A Systematic Review and Meta-analysis. Plast Reconstr Surg Glob Open, 2022. 10 (3)(3): p. e4180., https://pubmed.ncbi.nlm.nih.gov/35291333/.

Reference/ Study type	Review description	Interventions	Study Population	Ergebnisse der untersuchten Endpunkte	Methodological comments	Included publications
Broyles 2022 Systematisches Review mit Meta-Analyse	**Study design** ◆ RCTs or non-randomized design **Search dates** ◆ From database inception through March 23, 2021 **Databases :** ◆ Medline (via PubMed) ◆ Embase ◆ Cochrane Central Register of Controlled Trials (CENTRAL) ◆ CINAHL ◆ ClinicalTrials.gov **Inclusion criteria:** ◆ NR **Exclusion criteria:** ◆ Does not address any Key Question (n=313)	**Question/ Aim** "Given the preference sensitive nature of breast reconstruction, the evolving nature of the evidence, and the lack of an agreed-upon preferred surgical modality, we conducted a systematic review (SR) with meta-analysis to assess the benefits and surgical complications of IBR versus AR after	40 studies (2 RCTs, 38 NRSIs) published between 1989 and 2021, including 121,525 patients that received reconstruction ◆ IBR: NR ◆ AR: NR **Descriptive statistics** ◆ Age: NR ◆ BMI: NR ◆ Reconstruction type: autologous vs. implant-based (11 studies with extractable data)	**BREAST-Q QoL outcomes** *Satisfaction with breasts* ◆ 7 studies reportedthis outcome ◆ 3 studies (pooled data) ◆ Overall Mean difference: 8.08 (95% CI 6.11 to 10.05) in favor of autologous breast reconstruction *Physical well-being* ◆ 6 studies reported this outcome, no pooled data ◆ Overall Mean difference: NR ◆ "Results were inconsistent across studies." *General Quality of Life* ◆ 3 studies reported this outcome, no pooled data ◆ Overall Mean difference: NR ◆ "For each instrument in each study, differences in general quality of life	**Risk of bias assessment of studies:** 25 of the 38 NRCSs had a high risk of bias (mostly due to critical or serious risk of confounding and lack of blinding) and 13 had a moderate risk (mostly due to lack of blinding). RCTs had moderate risk of bias. **Overall confidence in results of SR (AMSTAR-2):** ◆ PICO elements: partially described ◆ A priori design: no ◆ Justification for design: no ◆ Literature search >= 2 databases, search strategy + other sources: · 3 databases · String for PubMed provided · No further resources searched ◆ Selection in duplicate: yes ◆ Data extraction in duplicate:	**Included and checked for additional outcomes:** ◆ Brito 2020 ◆ Fischer 2014 ◆ Hangge 2013 ◆ Eltahir 2015 ◆ Kouwenberg 2020 ◆ Mioton 2013 ◆ Chetta 2017 ◆ Garvey 2012 ◆ Zhang 2019 ◆ McCarthy 2014 ◆ Tallroth 2021 (RCT)- also identified in our update search **Excluded for this guideline, comparison autologous or implant-based only (immediate**

Broyles, JM, Balk, EM, Adam, GP, Cao, W, Bhuma, MR, Mehta, S, et.al. Implant-based versus Autologous Reconstruction after Mastectomy for Breast Cancer: A Systematic Review and Meta-analysis. Plast Reconstr Surg Glob Open, 2022. 10 (3)(3): p. e4180., https://pubmed.ncbi.nlm.nih.gov/35291333/.

- >=10% of patients underwent breast augmentation (n = 7)
- >=10% of patients underwent revision reconstruction (n=3)
- Does not address breast reconstruction (n = 17)
- Does not address mastectomy for breast cancer (n = 5)
- Does not report any outcome of interest (n=28)
- Protocol/methods only with no results (n = 20)
- NRCS, N<30 participants per arm (n = 103)
- NRCS without adequate adjustment (n = 234)
- Single group studies, N<500 participants (n = 187)
- Single group studies, N> 500 participants, no surgical complications data (n=26)

mastectomy for breast cancer (or prophylaxis)."

Interventions:

A: Autologous

B: Implant

between IBR and AR were not statistically significant."

Psychosocial well-being

- 5 studies reported this outcome
- 3 studies (pooled data)
- Overall Mean difference 3.14 (95% CI 1.26 to 5.02)

Sexual well-being

- 4 studies reported this outcome
- 3 studies (pooled data)
- Overall Mean difference 5.83 (95% CI 3.44 to 8.23) in favor of autologous breast reconstruction

Mortality

- 1 study reported this outcome
- Overall: adjusted OR 0.96, 95% CI 0.89–1.04

Surgical complications

- 3 studies reported this outcome
- No pooled data

Reconstructive failure

- 4 studies reported this outcome

- "All extracted data were confirmed by a second, independent researcher."
- List of excluded studies: no

- sufficient detail on studies: no
- RoB assessed: yes
- Funding of incl. studies: no
- RoB considered in MA: no
- RoB in interpretation: yes
- Heterogeneity explained: no
- Publication bias investigated: no
- Sources of CoI: yes (see Sources of funding)

Sources of funding

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vs. delayed), or no data extractable:

- Abedi 2016
- Brorson 2020a
- Carramaschi 1989
- Dauplat 2021
- De Araujo 2016
- Fischer 2013
- Fischer 2015
- Garbay 1992
- Ha 2020
- Jiang 2013
- Kouwenberg 2019
- Kulkarni 2017
- Laporta 2017
- Lei 2020
- Liu 2014
- Mak 2020
- Merchant 2015
- Momenti 2018
- Naoum 2020a
- Naoum 2020b
- Nasser 2018
- Nelson 2019
- Palve 2020
- Quin 2018
- Roth 2007
- Shiraishi 220020
- Simon 2020
- Woo 2018

Broyles, JM, Balk, EM, Adam, GP, Cao, W, Bhuma, MR, Mehta, S, et.al. Implant-based versus Autologous Reconstruction after Mastectomy for Breast Cancer: A Systematic Review and Meta-analysis. Plast Reconstr Surg Glob Open, 2022. 10 (3)(3): p. e4180., https://pubmed.ncbi.nlm.nih.gov/35291333/.			
	• Case report or series of case reports (n = 7) • Narrative review/commentary (n=55) • Systematic review (n = 20) • Copublication of included study with no new data (n=35) • Unable to retrieve article (n = 20) • Duplicates (n = 70) • Did not address any key question addressed in current review (n = 61) • Single-group studies (n = 86)	• No pooled data	• Wu 2021 • Xu 2018 • Yueh 2009

Characteristics of the systematic review chosen for this PICO 1.

Characteristics of studies included in Broyles 2022 (adapted table from the review)

Study	inclusion criteria	exclusion criteria	study design	enrolment period	age,	BMI kg/m2	Previous chemotherapy	adjuvant chemotherapy	Smoking status	Type of autologous BR	Type of implant BR	Lenth of follow-up
Brito 2020	◆ Women 18 years or older who underwent immediate or delayed primary BR following mastectomy ◆ with implant-based or autologous reconstruction (pedicled TRAM or LD-flap) ◆ at least 12 months after reconstruction	◆ Patients with secondary reconstruction, immediate reconstruction on one breast, and contralateral delayed reconstruction, or hybrid implant and autologous reconstruction (other than LD)	retrospective cohort study	January 2014 and May 2018	48.8	25	NR	NR	34	pedicled TRAM or LD-flap	NR	NR
Eltahir 2015	◆ Women with successful autologous or implant breast reconstruction ◆ good understanding of Dutch language	◆ age younger 18 years ◆ legally incompetent women ◆ presence of metastasis or severe illness ◆ reconstruction failure	prospective multicenter cohort study	2006 and 2010	51 vs. 44	26 vs. 23	NR	23 vs. 12	7 vs. 4	Diep, TMG, TRAM, DIEP + SIEA	implant, LD+ implant, SIEA + Implant	NR

Study	inclusion criteria	exclusion criteria	study design	enrolment period	age,	BMI kg/m2	Previous chemotherapy	adjuvant chemotherapy	Smoking status	Type of autologous BR	Type of implant BR	Lenth of follow-up
	◆ signed informed consent	◆ women who did not give informed consent										
Fischer 2014	◆ Patients who underwent either abdominally based free autologous breast reconstruction (FF) or E/I reconstruction	NR	retrospective review	June 2005 - May 2011,	48.5 vs. 47.9	25.4 vs. 25.4	25.2% vs. 30.3%	40% vs. 47.7%	12.3% vs. 9%	TRAM, DIEP, SIEA	implant	NR
Hangge 2013	◆ women who underwent mastectomy with immediate reconstruction using 1-stage IBBR, 2-stage IBBR, or ATR for invasive breast cancer or ductal carcinoma in situ (DCIS)	NR	retrospective review	2010 - 2017	55.9 vs. 50.9/51.5	29.6 vs. 25/25.4	NR	17 vs. 46/34	1 vs. 3/10	TRAM, DIEP, SIEA	1-stage IBBR, 2-stage IBBR	NR

Study	inclusion criteria	exclusion criteria	study design	enrolment period	age,	BMI kg/m2	Previous chemotherapy	adjuvant chemotherapy	Smoking status	Type of autologous BR	Type of implant BR	Lenth of follow-up
Kouwenberg 2020	◆ Patients who had been surgically treated for nonmetastatic breast cancer in the past 10 years (2008 to 2018).	◆ Patients who had developed distant metastases since curative treatment or who were not proficient in Dutch	retrospective cohort study	2008 - 2018	59.58 vs. 60.05	NR	NR	47.6 vs. 43.9	NR	NR	NR	NR
McCarthy 2014	◆ age ≥ 21 years ◆ history of mastectomy alone, immediate postmastectomy two-stage tissue expander/implant reconstruction, or immediate postmastectomy autogenous tissue flap reconstruction ◆ date of completed mastectomy or reconstruction	◆ a history of irradiation ◆ delayed postmastectomy reconstruction ◆ combined autogenous tissue/implant breast reconstruction ◆ documented local recurrence of breast cancer ◆ and/or history of complex regional pain syndrome	retrospective cohort study	2003–2008	52 vs. 50	30.2 vs. 23.92	29 vs. 85	NR	0 vs. 8	immediate postmastectomy autogenous tissue flap reconstruction	immediate postmastectomy two-stage tissue expander/implant reconstruction	NR

Study	inclusion criteria	exclusion criteria	study design	enrolment period	age,	BMI kg/m2	Previous chemotherapy	adjuvant chemotherapy	Smoking status	Type of autologous BR	Type of implant BR	Lenth of follow-up
	at least 1 year but no more than 5 years prior ◆ able to read and complete a questionnaire booklet written in the English language											
Mioton 2013	◆ patients undergoing either autologous tissue based breast reconstruction or prosthetic breast reconstruction with a tissue expander	◆ Patients with the description code representing “immediate or delayed insertion of a breast prosthesis following mastopexy or mastectomy ◆ Patients with more than one type of reconstruction	retrospective cohort study	2006 - 2010	51.8 vs. 51.02	28.39 vs. 26.93	NR	NR	362 vs. 1386	free flaps, pedicled transverse rectus abdominis myocutaneous (TRAM) flaps and latissimus dorsi (LD) flaps	NR	NR

Study	inclusion criteria	exclusion criteria	study design	enrolment period	age,	BMI kg/m2	Previous chemotherapy	adjuvant chemotherapy	Smoking status	Type of autologous BR	Type of implant BR	Lenth of follow-up
Zhang 2019	• women aged 18–65 years who underwent mastectomy and breast reconstruction with or without PMRT	NR	retrospective cohort study	June 2001 - December 2015	NR	NR	NR	NR	3	NR	NR	58.5 months

Chetta 2017	◆ at least one medical claim for breast reconstruction (immediate or delayed) procedures under the diagnosis of breast cancer/high risk of breast cancer/family history of breast cancer ◆ female sex ◆ age 18 years or older ◆ continuous enrollment for at least 15 months after the index procedure. ◆ Only patients who received radiation therapy for the management of breast cancer or patients who had claims indicating a history of	◆ patients who had a combination of the two techniques in the same reconstruction episode	retrospective study	2009 - 2013	Autologous: 18-34:44/935, 35-44: 219/935, 45-54: 395/935, 55-64: 222/935, ≥65: 55/935 Implant-based: 18-34: 225/3846, 35-44: 1019/3846, 45-54:1524/3846, 55-64: 865/3846, ≥65:213/3846	NR	NR	NR	NR	NR	NR	15 months

	radiation therapy during the study period											

Garvey 2012	• consecutive implant and abdominal-based free flap breast reconstructions • obese patients (body mass index 30 kg/m2)	• patients who were not obese (body mass index 30 kg/m2) • in whom the reconstruction was performed with a technique other than implant only or abdomenbased free flap, who had a “delayed-delayed” or “delayed-immediate” breast reconstruction • who underwent latissimus dorsi– or gluteus-based flap reconstructions	retrospective study	2005 - 2010	Autologous: 48.9 ± 8.9 Implant-based: 52.2 ± 10.3	Autologous: obese: 406/548 morbididly obese: 110/548 superobese: 32/548 Implant-based: obese: 275/442 morbididly obese: 107/442 superobese: 60/442	Autologous: 87/548 (52.4%) Implant-based: 130/442 (29.4%)	Autologouss: 39/548 (7.1%) Implant-based: 58/442 (13.1%)	Autologous: Nonsmoker: 519/548 (52.4%) Active smoker: 29/548 (5.3%) Implant-based: Nonsmoker: 417/442 (94.3%) Active smoker: 25/442 (5.7%)	deep inferior epigastric artery perforator, superficial inferior epigastric artery, and muscle-sparing free transverse rectus abdominis musculocutaneous)	Direct-to-implant, staged TE implant	mean: 17 months (range: 3 - 118) Autologous: 17.8 ± 18.7 Implant-based: 17.4 ± 19.7

6.1.2.1.2 Risk of Bias assessment of Studies included in Broyles 2022 (adapted tables from the review)

Randomized controlled trials (RCTs)

Study, Year	Random Sequence Generation	Allocation Concealment	Blinding of Participants	Blinding of Personnel/ Care Providers	Blinding of Outcome Assessors (Objective Outcomes)	Blinding of Outcome Assessors (Subjective Outcomes)	Incomplete Outcome Data	Selective Outcome Reporting	Other Bias	Eligibility Criteria Prespecified and Clearly Described	Intervention Clearly Described and Consistently Delivered	Outcomes Prespecified, Clearly Defined, Valid, Reliable, and Consistently Assessed	Overall RoB
Tallroth, 2021	Unclear	Unclear	High	High	Low	Unclear	Low	Low	Low	Yes	Yes	Yes	Moderate

Risk of bias assessment of RCT included in Broyles 2022 that were eligible for inclusion for PICO 1.

6.1.2.1.3 Nonrandomized comparative studies, confounding and selection bias

Study, Year	Potential for any Confounding?	Potential for Time-Varying Confounding?	Intervention Switches Related to Prognostic Factors?	Appropriate Analysis Method for Confounding?	Appropriate Confounding Variables Used?	Inappropriate Control of Post-Intervention Variables?	Judgement - Risk of Bias Related to Confounding	Post-Intervention Biased on Post-Intervention Variables?	Post-Intervention Variables Associated with Intervention?	Post-Intervention Variables Associated with Outcome?	Start and Follow-Up (Duration) Coincide	Appropriate Adjustment for Selection Bias	Judgement - Risk of Bias Related to Selection Bias
Brito, 2020	Yes	No	N/A	N	N/A	N	Serious	N	N/A	N/A	Y	N/A	Low
Chetta, 2017	Yes	No	N/A	PN	N/A	N	Serious	N	N/A	N/A	Y	N/A	Low
Eltahir, 2015	Yes	No	N/A	Y	PY	N	Low	N	N/A	N/A	PY	N/A	Low
Fischer, 2014	Yes	No	N/A	N	N/A	N	Serious	N	N/A	N/A	Y	N/A	Low
Garvey, 2012	Yes	No	N/A	Y	Y	N	Low	N	N/A	N/A	Y	N/A	Low
Hangge, 2019	Yes	No	N/A	PN	N/A	N	Serious	N	N/A	N/A	PY	N/A	Low
Kouwenberg, 2020	Yes	No	N/A	Y	Y	N	Low	N	N/A	N/A	PY	N/A	Low

Study, Year	Potential for any Confounding?	Potential for Time-Varying Confounding?	Intervention Switches Related to Prognostic Factors?	Appropriate Analysis Method for Confounding?	Appropriate Confounding Variables Used?	Inappropriate Control of Post-Intervention Variables?	Judgement - Risk of Bias Related to Confounding	Post-Intervention Biased on Post-Intervention Variables?	Post-Intervention Variables Associated with Intervention?	Post-Intervention Variables Associated with Outcome?	Start and Follow-Up (Duration) Coincide	Appropriate Adjustment for Selection Bias	Judgement - Risk of Bias Related to Selection Bias
McCarthy, 2014	Yes	No	N/A	Y	PY	Y	Moderate	PN	N/A	N/A	N	PN	Moderate
Mioton, 2013	Yes	No	N/A	Y	Y	N	Low	PN	N/A	N/A	PY	N/A	Low
Zhang, 2019	Yes	No	N/A	N	N/A	N	Serious	N	N/A	N/A	Y	N/A	Low

Risk of bias assessment of NRSIs included in Broyles 2022 that were eligible for inclusion for PICO 1.

6.1.2.1.4 Nonranomized comparative studies, assesssment of remaining biases, quality, and overall risk of bias

Study, Year	Blinding of Participants	Blinding of Personnel/ Care Providers	Blinding of Outcome Assessors (Objective Outcomes)	Blinding of Outcome Assessors (Subjective Outcomes)	Incomplete Outcome Data	Selective Outcome Reporting	Other Bias	Eligibility Criteria Prespecified and Clearly Described	Intervention Clearly Described and Consistenty Delivered	Outcomes Prespecified, Clearly Defined, Valid, Reliable, and Consistently Assessed	Overall RoB
Brito, 2020	High	High	High	Low	Low	Low	Low	Yes	Yes	Yes	High
Chetta, 2017	High	High	Unclear	N/A	Low	Low	Low	Yes	Yes	Yes	High
Eltahir, 2015	High	Unclear	N/A	Unclear	Low	Low	Low	Yes	Yes	Yes	Moderate
Fischer, 2014	High	High	Low	N/A	Low	Low	Low	Yes	Yes	Yes	High
Garvey, 2012	High	High	High	N/A	Low	Low	Low	Yes	Unclear	Yes	Moderate
Hangge, 2019	High	High	Unclear	N/A	Low	Low	Low	Yes	Yes	Yes	High
Kouwenberg, 2020	High	High	High	High	Unclear	Low	Low	Yes	Unclear	Yes	Moderate
McCarthy, 2014	High	High	N/A	High	Low	Low	Low	Yes	Unclear	Yes	Moderate
Mioton, 2013	High	High	High	High	Low	Low	Low	Unclear	Unclear	Yes	Moderate
Zhang, 2019	High	High	Low	N/A	Low	Low	Low	Yes	Yes	Yes	High

Risk of bias assessment of NRSIs included in Broyles 2022 that were eligible for inclusion for PICO 1.

6.1.2.2 Primärstudien – neu identifiziert

Reference/ Study type	Population	Interventions	Main results	Methodological evaluation
Abdou 2023 Retrospective study	**Inclusion criteria (for analysis):** ◆ Patients who underwent NSM for both prophylactic and therapeutic indications ◆ Only patients undergoing immediate breast reconstruction with either autologous reconstruction or DTI ◆ only patients who underwent FF reconstruction in the autologous group **Exclusion criteria (for analysis):** ◆ Patients who underwent tissue expansion ◆ less than 30-day follow-up **Enrolment period** ◆ January 2014 - January 2020 **Follow-up (median in months)** ◆ Autologous: 9 ◆ Implant-based: 28 **Descriptive statistics** ◆ Age (median in years) · Autologous: 46 · Implant-based: 45.4 ◆ BMI (mean)	**Interventions** A: Autologous · N = 54 B: Implant-based · N = 54 **Analysis** ◆ Fisher exact test + Mann-Whitney tests ◆ No adjustment	**Total flap loss** · Autologous: 2/54 · Implant-based: NA/54 **Reoperation** · Autologous: 27/54 · Implant-based: 15/54	**General information** ◆ **Follow-up:** median 9 vs. 28 months ◆ **Funding**: Dr. Song receives royalties from Elsevier for Plastic Surgery, third and fourth editions, and from Biomet Microfixation for Sternalock. The remaining authors have no financial disclosures, commercial associations, or any other conditions posing a conflict of interest to report. ◆ **CoI**: Dr. Song receives royalties from Elsevier for Plastic Surgery, third and fourth editions, and from Biomet Microfixation for Sternalock. The remaining authors have no financial disclosures, commercial associations, or any other conditions posing a conflict of interest to report. **Risk of bias considerations (adapted from SIGN cohort study checklist)** ◆ Study type: retrospective ◆ Populations comparable (confounding): yes ◆ Rate of participation/ Exclusions reported (selection bias into the study):no ◆ Intervention · Assessment reliable: yes · Assessed more than once: no

Reference/ Study type	Population	Interventions	Main results	Methodological evaluation
	· Autologous: 28.2 · Implant-based: 26 ◆ Stadium: · NR ◆ Neoadjuvant chemotherapy (N yes) · Autologous: 3 · Implant-based: 5 ◆ Adjuvant chemotherapy (N yes) · Autologous: 3 · Implant-based: 13 ◆ Reconstruction type · Autologous: FF · Implant-based: DTI ◆ Smoke (N) · Autologous: 0 · Implant-based: 0			· Possibly affected by knowledge of outcome status? no ◆ Drop-out rate & reasons reported: no ◆ Outcome: yes · Outcome measure is well-defined, valid and reliable; · No blind outcome assessment, however, this is unlikely to affect the results (retrospective) ◆ Main cofounders taken into account: no adjustment ◆ Confidence intervals reported: no ◆ Selective reporting (comparison with protocol): no

Reference/ Study type	Population	Interventions	Main results	Methodological evaluation
Asaad 2023 Retrospective study	**Inclusion criteria (for analysis):** ◆ Patients who underwent subsequent breast reconstruction with free flap-based reconstruction (FFBR) or implant-based reconstruction (IBR) ◆ with or without LD flap **Exclusion criteria (for analysis):** ◆ Patients who had combined IBR and FFBR procedures ◆ Patients who received secondary breast reconstruction without prior radiation **Enrolment period** ◆ January 2000 - March 2016 **Follow-up (median in months)** ◆ Autologous: 90 ◆ Implant-based: 40 **Descriptive statistics** ◆ Age (mean, sd) · Autologous: 52 (8) · Implant-based: 50 (9.5) ◆ BMI (mean, sd) · Autologous: 29 (4) · Implant-based: 27 (6) ◆ Stadium: · NR	**Interventions** A: Autologous · N = 48 B: Implant-based · N = 57 **Analysis** ◆ Fisher exact test + Mann-Whitney tests ◆ No adjustment	**Loss of implant/flap** · Autologous: 0/48 · Implant-based: 15/30 **Any complications:** · Autologous: 21/48 · Implant-based: 15/30 **Major complications** · Autologous: 12/48 · Implant-based: 18/30	**General information** ◆ Follow-up (median in months) Autologous: 90 Implant-based: 40 ◆ Funding: NR ◆ **CoI**: No conflict of interest to report. **Risk of bias considerations (adapted from SIGN cohort study checklist)** ◆ Study type: retrospective study ◆ Populations comparable (confounding): yes ◆ Rate of participation/ Exclusions reported (selection bias into the study):no ◆ Intervention · Assessment reliable: yes · Assessed more than once: no · Possibly affected by knowledge of outcome status? no ◆ Drop-out rate & reasons reported: no ◆ Outcome: yes · Outcome measure is well-defined, valid and reliable; · No blind outcome assessment, however, this is unlikely to affect the results ◆ Main cofounders taken into account: no. ◆ Confidence intervals reported: yes ◆ Selective reporting (comparison with protocol): no

Reference/ Study type	Population	Interventions	Main results	Methodological evaluation
	◆ Neoadjuvant chemotherapy (N) · Autologous: 31 · Implant-based: 19 ◆ Adjuvant chemotherapy (N) · Autologous: 11 · Implant-based: 11 ◆ Reconstruction type · Autologous: Free Flap · Implant-based: IBR ◆ Smoke · NR			
Asaad 2022 retrospective study	**Inclusion criteria (for analysis):** ◆ if patients developed an implant-based breast reconstruction infection requiring explantation with subsequent secondary breast reconstruction **Exclusion criteria (for analysis):** ◆ patients who had implant-based breast reconstruction explantation because complications other than infection before the infection-necessitated implant-based breast reconstruction ◆ patients who underwent primary or secondary breast reconstruction with pedicled latissimus dorsi flaps with or	**Interventions** A: Autologous · N = 44 B: Implant-based · N = 86 **Analysis** ◆ Fisher exact test + Mann-Whitney tests ◆ No adjustment	**Loss of implant/flap** · Autologous: 2/44 · Impant-based: 18/86 **any complicatios:** · Autologous: 11/48 · Implant-based: 31/86 **Major complications** · Autologous: 9/44 · Implant-based: 18/86	**General information** ◆ **Follow-up:** 33 vs. 41 median months ◆ **Funding**: Dr. Song receives royalties from Elsevier for Plastic Surgery, third and fourth editions, and from Biomet Microfixation for Sternalock. The remaining authors have no financial disclosures, commercial associations, or any other conditions posing a conflict of interest to report. ◆ **CoI**: Dr. Song receives royalties from Elsevier for Plastic Surgery, third and fourth editions, and from Biomet Microfixation for Sternalock. The remaining authors have no financial disclosures, commercial associations, or any other conditions posing a conflict of interest to report.

Reference/ Study type	Population	Interventions	Main results	Methodological evaluation
	without tissue expander/permanent implant **Enrolment period** ◆ January 2006 - December 2019 **Follow-up (median in months)** ◆ Autologous: 33 ◆ Implant-based: 41 **Descriptive statistics** ◆ Age (median, range) · Autologous: 53 · Implant-based: 48 ◆ BMI (mean) · Autologous: 29 · Implant-based: 28 ◆ Stadium: · NR ◆ Neoadjuvant chemotherapy (% yes) · Autologous: 35 · Implant-based: 36 ◆ Adjuvant chemotherapy (% yes) · Autologous: 1 · Implant-based: 5 ◆ Reconstruction type · Autologous: FF (Free Flap)			**Risk of bias considerations (adapted from SIGN cohort study checklist)** ◆ Study type: retrospective study ◆ Populations comparable (confounding): yes ◆ Rate of participation/ Exclusions reported (selection bias into the study):no ◆ Intervention · Assessment reliable: yes · Assessed more than once: no · Possibly affected by knowledge of outcome status? no ◆ Drop-out rate & reasons reported: no ◆ Outcome: yes · Outcome measure is well-defined, valid and reliable; · No blind outcome assessment, however, this is unlikely to affect the results ◆ Main cofounders taken into account: no. ◆ Confidence intervals reported: no Selective reporting (comparison with protocol): no

Reference/ Study type	Population	Interventions	Main results	Methodological evaluation
	· Implant-based: IBR (implant-based Breast Reconstruction) ◆ Smoke · Autologous: 1 · Implant-based: 1			
Cai 2022 prospective cohort study	**Inclusion criteria (for analysis):** ◆ adult female patients older than 18 years ◆ previously undergone either autologous breast reconstruction or implant-based breast reconstruction by the senior author ◆ at least 1 year of postoperative follow-up **Exclusion criteria (for analysis):** ◆ NR **Enrolment period** ◆ NR **Follow-up** ◆ NR **Descriptive statistics**	**Interventions** A: Autologous · N = 38 B: Implant-based · N = 25 **Analysis** ◆ NR ◆ No adjustment	**Loss of implant/flap** · Autologous: 1/69 · Implant-based: 0/40 **Breast –Q (Mean, SD)** ◆ Satisfaction with breasts · Autologous: 84.7 (18.6) · Implant-based: 77.0 (19.1)	**General information** ◆ Follow-up: NR ◆ **Funding**: None. ◆ **CoI**: None **Risk of bias considerations (adapted from SIGN cohort study checklist)** Study type: prospective cohort study ◆ Populations comparable (confounding): no ◆ Rate of participation/ Exclusions reported (selection bias into the study):no ◆ Intervention · Assessment reliable: yes · Assessed more than once: no

Reference/ Study type	Population	Interventions	Main results	Methodological evaluation
	◆ Age (median, range) · Autologous: 51 · Implant-based: NR ◆ BMI (mean, SD) · Autologous: 27.5 · Implant-based: NR ◆ Stadium: · NR ◆ Neoadjuvant chemotherapy (% yes) · NR ◆ Adjuvant chemotherapy (% yes) · NR ◆ Reconstruction type · NR ◆ Smoke · NR			· Possibly affected by knowledge of outcome status? no ◆ Drop-out rate & reasons reported: no ◆ Outcome: yes · Outcome measure is well-defined, valid and reliable; · No blind outcome assessment, however, this is unlikely to affect the results ◆ Main cofounders taken into account: no. ◆ Confidence intervals reported: no Selective reporting (comparison with protocol): no
Deek 2021 retrospective cohort	**Inclusion criteria (for analysis):** ◆ NR **Exclusion criteria (for analysis):** ◆ NR **Enrolment period** ◆ 1 January 2009 - 31 December 2018 **Follow-up** ◆ NR **Descriptive statistics**	**Interventions** A: Autologous · N = 128 B: Implant-based · N = 186 **Analysis** ◆ Kolmogorov-Smirnov (K-S)	**Loss of implant/flap** · Autologous: 6/128 · Implant-based: 2/185 **Reoperation:** · Autologous: 18/128 · Implant-based: 24/185 **Any complications:** · Autologous: 66/128 · Implant-based: 62/185	**General information** ◆ Follow-up: NR ◆ **Funding**: No forms of funding were acquired for this research. ◆ **CoI**: None **Risk of bias considerations (adapted from SIGN cohort study checklist)** ◆ Study type: retrospective cohort ◆ Populations comparable (confounding): no ◆ Rate of participation/ Exclusions reported (selection bias into the study):no

Reference/ Study type	Population	Interventions	Main results	Methodological evaluation
	◆ Age (median, range) · Autologous: 50.6 · Implant-based: NR ◆ BMI (mean, SD) · Autologous: 28.1 · Implant-based: NR ◆ Stadium (overall population): · I, II = 287 · III, IV = 26 (8.3) ◆ Neoadjuvant chemotherapy (% yes) · NR ◆ Adjuvant chemotherapy (% yes) · NR ◆ Reconstruction type · Autologous: Free TRAM (Transverse Rectus Abdominis Myocutaneous Flap), Latissimus Dorsi Alone, DIEP (Deep Inferior Epigastric Perforator Flap) · Implant-based: Tissue Expander, Implant only, Lat Dorsi, Expander ◆ Smoke · Autologous: 0 · Implant-based: NR	non-parametric test ◆ Adjustment: no		◆ Intervention · Assessment reliable: yes · Assessed more than once: no · Possibly affected by knowledge of outcome status? no ◆ Drop-out rate & reasons reported: no ◆ Outcome: yes · Outcome measure is well-defined, valid and reliable; · No blind outcome assessment, however, this is unlikely to affect the results ◆ Main cofounders taken into account: no. ◆ Confidence intervals reported: no ◆ Selective reporting (comparison with protocol): no

Reference/ Study type	Population	Interventions	Main results	Methodological evaluation
Emanuele 2023 retrospective case-control multicenter study	**Inclusion criteria (for analysis):** ◆ female patients ◆ age over 18 years at the time of diagnosis ◆ patients who had undergone mastectomy and immediate reconstruction with implant in one or two stages or with autologous flaps with or without adjuvant radiotherapy **Exclusion criteria (for analysis):** ◆ patients with prior breast or chest wall irradiation ◆ delayed reconstruction ◆ patients lost to follow-up **Enrolment period** ◆ January 2014 - January 2020 **Follow-up (months)** ◆ Autologous: 9 ◆ Implant-based (DTI + TE/I): 28 **Descriptive statistics** ◆ Age (median, range) · Autologous: 50 · Implant-based (DTI only): 47 · Implant-based (TE/I only): 50 ◆ BMI (mean, sd) · Autologous: 25.4 · Implant-based (DTI only): 22 · Implant-based (TE/I only): 23.4	**Interventions** A: Autologous · N = 187 B: Implant-based · N = 2932 · B1: DTI · B2: TE/I **Analysis** ◆ Multivariable hierarchical logistic regression ◆ Adjusted for: postmastectomy radiotherapy, age, the BMI, smoking habits, diabetes, other autoimmune diseases, type of chemotherapy, and axillary dissection (*still not for the relevant outcomes*)	**Any complications** · Autologous: 73/187 · Implant-based (DTI + TE/I): 1145/2932 **Minor complications:** · Autologous: 33/187 · Implant-based (DTI + TE/I): 288/2932 **Major complications** · Autologous: 9/187 · Implant-based (DTI + TE/I): 589/2932 **Reoperation:** · Autologous: 6/187 · Implant-based (DTI + TE/I): 68/2932	**General information** ◆ Follow-up (months) Autologous: 9 Implant-based (DTI + TE/I): 28 ◆ Funding: NR ◆ **CoI**: The authors declare that they have no conflicts of interest **Risk of bias considerations (adapted from SIGN cohort study checklist)** ◆ Study type: retrospective case-control multicenter study ◆ Populations comparable (confounding): yes ◆ Rate of participation/ Exclusions reported (selection bias into the study):no ◆ Intervention · Assessment reliable: yes · Assessed more than once: no · Possibly affected by knowledge of outcome status? no ◆ Drop-out rate & reasons reported: no ◆ Outcome: yes · Outcome measure is well-defined, valid and reliable; · No blind outcome assessment, however, this is unlikely to affect the results ◆ Main cofounders taken into account: no. ◆ Confidence intervals reported: yes

Reference/ Study type	Population	Interventions	Main results	Methodological evaluation
	◆ Stadium: · NR ◆ Neoadjuvant chemotherapy (% yes) · Autologous: 43 · Implant-based (DTI only): 294 · Implant-based (TE/I only): 279 ◆ Adjuvant chemotherapy (% yes) · Autologous: 99 · Implant-based (DTI only): 447 · Implant-based (TE/I only): 727 ◆ Reconstruction type · Autologous: Flap · Implant-based: DTI (Direct to Implant); Tissue expander/immediate ◆ Smoke · Autologous: 18 · Implant-based (DTI only): 184 · Implant-based (TE/I only): 245			Selective reporting (comparison with protocol): no
Gao 2022 retrospective cohort study	**Inclusion criteria (for analysis):** ◆ all women aged 18 years old and older ◆ first-time breast reconstruction with LDF or one-stage implant for cancer treatment at the National Cancer Center of China **Exclusion criteria (for analysis):** ◆ contraindications with porcine **Enrolment period** ◆ August 2010 - April 2019	**Interventions** A: Autologous · N = 56 B: Implant-based · N = 79 **Analysis** ◆ chi-square test	**Loss of implant/flap** · Autologous: 0/56 · Implant-based: 5/79 **Minor complications:** · Autologous: 6/56 · Implant-based: 5/79 **Major complications** · Autologous: 5/56 · Implant-based: 5/79	**General information** ◆ **Follow-up:** 66.97 vs. 17.55 ◆ **Funding**: This work was supported by the Natural Science Foundation of China (No. 81872160, No. 82072940), the China National Key R&D (or Research and Development) Program (No. 2020AAA0105000 and No. 2020AAA0105004), the Beijing Municipal Natural Science Foundation (Key Project) (No. 7191009), the Beijing Municipal Natural

Reference/ Study type	Population	Interventions	Main results	Methodological evaluation
	Follow-up ◆ Autologous: 66.97 ◆ Implant-based: 17.55 **Descriptive statistics** ◆ Age (median, range) · Autologous: 39.52 · Implant-based: 41.14 ◆ BMI (mean, sd) · Autologous: 30.08 · Implant-based: 21.73 ◆ Stadium: · NR ◆ Neoadjuvant chemotherapy (% yes) · Autologous: 12 · Implant-based: 9 ◆ Adjuvant chemotherapy (% yes) · Autologous: 46 · Implant-based: 46 ◆ Reconstruction type · Autologous: LDF (Latissimus Dorsi Flap) · Implant-based: SIS matrix-assisted DTI (Direct to Implant) ◆ Smoke · Autologous: 0 · Implant-based: 0	◆ No adjustment	**Breast -Q (Mean, SD)** ◆ Satisfaction with breasts · Autologous: 61.6 (15.99) · Implant-based: 60.27 (17.71) ◆ Physical well-being · Autologous: 36.0 (20.30) · Implant-based: 39.60 (17.39)	Science Foundation (No. 7204293), the Special Research Fund for Central Universities, Peking Union Medical College (No. 3332019053), the Beijing Hope Run Special Fund of Cancer Foundation of China (No. LC2019B03, No. LC2019L07, No. LC2020L01), the Golden Bridge Project Seed Fund of Beijing Association for Science and Technology (No. ZZ20004), the 2021 Chaoyang District Social Development Science and Technology Plan Project (Medical and Health Field) (No. CYSF2115), the Chinese Young Breast Experts Research project (No. CYBER-2021-005), the XianSheng Clinical Research Special Fund of China International Medical Foundation (No. Z-2014-06-2103), and the Beijing Xisike Clinical Oncology Research Foundation (No. Y-Young2021-0017). ◆ **CoI**: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest. **Risk of bias considerations (adapted from SIGN cohort study checklist)** ◆ Study type: retrospective cohort study ◆ Populations comparable (confounding): yes ◆ Rate of participation/ Exclusions reported (selection bias into the study):no ◆ Intervention · Assessment reliable: yes

Reference/ Study type	Population	Interventions	Main results	Methodological evaluation
				· Assessed more than once: no · Possibly affected by knowledge of outcome status? no ◆ Drop-out rate & reasons reported: no ◆ Outcome: yes · Outcome measure is well-defined, valid and reliable; · No blind outcome assessment, however, this is unlikely to affect the results ◆ Main cofounders taken into account: no. ◆ Confidence intervals reported: no Selective reporting (comparison with protocol): no
Han 2021 retrospectíve study	**Inclusion criteria (for analysis):** ◆ All breast cancer patients who underwent bilateral mastectomy with immediate reconstruction **Exclusion criteria (for analysis):** ◆ Patients with a previous history of surgery for breast cancer, such as breast-conserving surgery ◆ Patients who had undergone hybrid reconstruction using autologous tissue in addition to implants **Enrolment period** ◆ January 2014 - January 2020 **Follow-up (months)**	**Interventions** A: Autologous · N = 48 B: Implant-based · N = 52 **Analysis** ◆ Fisher exact test + Mann-Whitney tests ◆ No adjustment	**Minor complications:** · Autologous: 4/48 · Implant-based: 21/52 **Major complications** · Autologous: 8/48 · Implant-based: 7/52	**General information** ◆ **Follow-up:** 12.93 vs. 12.39 (months) ◆ Funding: NR ◆ **CoI**: No potential conflict of interest relevant to this article was reported. **Risk of bias considerations (adapted from SIGN cohort study checklist)** ◆ Study type: retrospective study ◆ Populations comparable (confounding): yes ◆ Rate of participation/ Exclusions reported (selection bias into the study):no ◆ Intervention · Assessment reliable: yes · Assessed more than once: no

Reference/ Study type	Population	Interventions	Main results	Methodological evaluation
	◆ Autologous: 12.93 ◆ Implant-based: 12.39 **Descriptive statistics** ◆ Age (median, range) · Autologous: 44.88 · Implant-based: 48.38 ◆ BMI (mean, sd) · Autologous: 26.65 · Implant-based: 22.82 ◆ Stadium: · NR ◆ Neoadjuvant chemotherapy (% yes) · Autologous: 8 · Implant-based: 7 ◆ Adjuvant chemotherapy (% yes) · Autologous: 6 · Implant-based: 2 ◆ Reconstruction type · Autologous: DIEP (deep inferior epigastric perforator) · Implant-based: DTI (Direct to Implant) ◆ Smoke · Autologous: 0 · Implant-based: 1			· Possibly affected by knowledge of outcome status? no ◆ Drop-out rate & reasons reported: no ◆ Outcome: yes · Outcome measure is well-defined, valid and reliable; · No blind outcome assessment, however, this is unlikely to affect the results ◆ Main cofounders taken into account: no. ◆ Confidence intervals reported: no Selective reporting (comparison with protocol): no

Reference/ Study type	Population	Interventions	Main results	Methodological evaluation
Hart 2021 prospective cohort study	**Inclusion criteria (for analysis):** ◆ Patients 18 years or older ◆ first-time breast reconstruction after mastectomy for breast cancer treatment or prophylaxis ◆ Reconstruction options: direct-to-implant, tissue expander plus implant, latissimus dorsi flap with and without implant, pedicle transverse rectus abdominis musculocutaneous (TRAM) flap, free TRAM flap, deep inferior epigastric perforator flap, superficial inferior epigastric perforator flap, superior gluteal artery perforator flap, and inferior gluteal artery perforator flap procedures **Exclusion criteria (for analysis):** ◆ Patients who had undergone prophylactic mastectomy, delayed reconstruction, or mixed-timing reconstruction (immediate and delayed) ◆ if they received bilateral reconstruction with implant-based reconstruction on one side and autologous reconstruction on the other ◆ Women with latissimus dorsi, superior gluteal artery perforator, or inferior gluteal artery perforator flaps ◆ Patients who underwent both neoadjuvant and adjuvant chemotherapy **Enrolment period** ◆ January 1, 2012 - December 31, 2017	**Interventions** A: Autologous · N = 508 B: Implant-based · N = 1373 **Analysis** ◆ Multivariable analyses ◆ No adjustment	**Any complications:** · Autologous: 264/508 · Implant-based: 373/1373 **Major complications** · Autologous: 165/508 · Implant-based: 273/1373	**General information** ◆ **Follow-up:** NR ◆ **Funding**: This study was supported by grant RO1CA152192 from the National Cancer Institute (NCI). ◆ **CoI**: NR **Risk of bias considerations (adapted from SIGN cohort study checklist)** ◆ Study type: prospective cohort study ◆ Populations comparable (confounding): no ◆ Rate of participation/ Exclusions reported (selection bias into the study):no ◆ Intervention · Assessment reliable: yes · Assessed more than once: no · Possibly affected by knowledge of outcome status? no ◆ Drop-out rate & reasons reported: no ◆ Outcome: yes · Outcome measure is well-defined, valid and reliable; · No blind outcome assessment, however, this is unlikely to affect the results ◆ Main cofounders taken into account: no. ◆ Confidence intervals reported: no ◆ Selective reporting (comparison with protocol): no

Reference/ Study type	Population	Interventions	Main results	Methodological evaluation
	Follow-up ◆ NR **Descriptive statistics** ◆ Age (median, range) · NR ◆ BMI (mean, sd) · NR ◆ Stadium: · NR ◆ Neoadjuvant chemotherapy (% yes) · Autologous: 47 · Implant-based: 153 ◆ Adjuvant chemotherapy (% yes) · Autologous: 178 · Implant-based: 490 ◆ Reconstruction type · Autologous: NR · Implant-based: NR ◆ Smoke · NR			
Lee 2023 retrospective cohort study	**Inclusion criteria (for analysis):** ◆ Patients with breast cancer who underwent immediate breast reconstruction after total mastectomy	**Interventions** A: Autologous · N = 302 B: Implant-based · N = 1078	**Loss of implant/flap** · Autologous: 64/302 · Implant-based: 2/1078 **Reoperation:** · Autologous: 7/302 · Implant-based: 16/1078	**General information** ◆ **Follow-up:** median 58 months ◆ **Funding:** NR ◆ **CoI**: The authors declare no competing interests.

Reference/ Study type	Population	Interventions	Main results	Methodological evaluation
	◆ Patients who had undergone DIEP flap surgery (DIEP flap group) or two-stage TE/I for breast reconstruction (TE/I group) **Exclusion criteria (for analysis):** ◆ those who used other reconstruction modalities, such as latissimus dorsi myocutaneous or direct-to-implant flaps ◆ those who did not complete both stages during the follow-up period owing to causes unrelated to complications ◆ those who underwent the second stage of exchange-to-implant in another clinic ◆ those who had planned conversion to autologous tissue reconstruction following tissue expander insertion ◆ those who had been lost to follow-up within 2 years postoperatively **Enrolment period** ◆ 2012 - 2017 **Descriptive statistics** ◆ Age (median, range) · Autologous: 46.3 · Implant-based: 43.6 ◆ BMI (mean, sd) · Autologous: 23.6 · Implant-based: 22.2 ◆ Stadium: · NR	**Analysis** ◆ Fisher exact test + Mann-Whitney tests ◆ No adjustment	**Major complications** · Autologous: 14/302 · Implant-based: 112/1078	**Risk of bias considerations (adapted from SIGN cohort study checklist)** ◆ Study type: retrospective cohort study ◆ Populations comparable (confounding): yes ◆ Rate of participation/ Exclusions reported (selection bias into the study):no ◆ Intervention · Assessment reliable: yes · Assessed more than once: no · Possibly affected by knowledge of outcome status? no ◆ Drop-out rate & reasons reported: no ◆ Outcome: yes · Outcome measure is well-defined, valid and reliable; · No blind outcome assessment, however, this is unlikely to affect the results ◆ Main cofounders taken into account: no. ◆ Confidence intervals reported: no Selective reporting (comparison with protocol): no

Reference/ Study type	Population	Interventions	Main results	Methodological evaluation
	◆ Neoadjuvant chemotherapy (% yes) · Autologous: 34 · Implant-based: 83 ◆ Adjuvant chemotherapy (% yes) · Autologous: 105 · Implant-based: 449 ◆ Reconstruction type · Autologous: (DIEP) deep inferior epigastric perforator · Implant-based: TE/I (Two-stage tissue expander/implant) ◆ Smoke · Autologous: 7 · Implant-based: 19			
Misere 2021 multicenter, cross-sectional survey	**Inclusion criteria (for analysis):** ◆ Women who underwent immediate or delayed IBR or ABR **Exclusion criteria (for analysis):** ◆ bilateral reconstruction with unilateral IBR and contralateral ABR or a mixed timing ◆ tertiary breast reconstruction (after failed reconstruction or unsatisfactory results) ◆ breast reconstruction by autologous fat transfer (AFT) ◆ currently no breast reconstruction after previously failed reconstruction ◆ currently distant metastases **Enrolment period**	**Interventions** A: Autologous · N = 224 B: Implant-based · N = 112 **Analysis** ◆ Multivariable linear regression analysis ◆ Adjusted for: age, BMI, cup size preoperatively,	**Breast –Q (Means, SD)** ◆ Satisfaction with breasts · Autologous: 68.3 (19.4) · Implant-based: 55.5 (18.4) · Adjusted mean difference: 14.10 (95% CI: 8.3- 21.0) ◆ BREAST-Q Satisfaction with overall outcome · Autologous: 70.9 (21.6) · Implant-based: 60 (20.8) · Adjusted mean difference: 14.90 (95% CI: 8.0- 21.9) ◆ BREAST-Q Physical well-being · Autologous: 68.7 (17.2) · Implant-based: 64.2 (17.6)	**General information** ◆ **Follow-up:** Mean 46.7 months (SD 14.8) ◆ **Funding**: This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors. ◆ **CoI**: None **Risk of bias considerations (adapted from SIGN cohort study checklist)** ◆ Study type: multicenter, cross-sectional survey ◆ Populations comparable (confounding): yes ◆ Rate of participation/ Exclusions reported (selection bias into the study):no ◆ Intervention

Reference/ Study type	Population	Interventions	Main results	Methodological evaluation
	◆ November - December 2020. **Follow-up** ◆ Mean 46.7 months (SD 14.8) **Descriptive statistics** ◆ Age (median, range) · Autologous: 55 · Implant-based: 56.4 ◆ BMI (mean, sd) · Autologous: 26.3 · Implant-based: 24.2 ◆ Stadium (overall population) · 1: 82 vs. 43 · 2: 63 vs. 28 · 3: 8 vs. 5 ◆ Neoadjuvant chemotherapy (% yes) · NR ◆ Adjuvant chemotherapy (% yes) · Autologous: 126 · Implant-based: 54 ◆ Reconstruction type · Autologous: NR · Implant-based: NR ◆ Smoke · Autologous: 10 · Implant-based: 21	smoking, educational level, tumor classification (T stage, N stage), radiotherapy, hormone therapy, reconstruction type, reconstruction timing, follow-up duration after reconstruction.	· Adjusted mean difference: 6.20 (95% CI: 0.8- 11.7)	· Assessment reliable: yes · Assessed more than once: no · Possibly affected by knowledge of outcome status? no ◆ Drop-out rate & reasons reported: no ◆ Outcome: yes · Outcome measure is well-defined, valid and reliable; · No blind outcome assessment, however, this is unlikely to affect the results ◆ Main cofounders taken into account: adjusted for some main characteristics ◆ Confidence intervals reported: yes Selective reporting (comparison with protocol): no
Nelson 2022	**Inclusion criteria (for analysis):**	**Interventions**	**Breast –Q (Mean, SDs)**	**General information**

Reference/ Study type	Population	Interventions	Main results	Methodological evaluation
retrospective cohort study	◆ Women who underwent immediate ABR or IBR for therapeutic or prophylactic indications ◆ ABR procedures employed a deep inferior epigastric artery perforator flap, a superficial inferior epigastric artery flap, a muscle-sparing transverse rectus abdominis myocutaneous flap, or a free transverse rectus abdominis myocutaneous flap ◆ IBR procedures were two stages, with submuscular placement of the tissue expander **Exclusion criteria (for analysis):** ◆ Patients were excluded from the study if they underwent a nonabdominal free flap procedure, delayed reconstruction, or radiotherapy as part of oncologic treatment, in an effort to remove potential confounders. **Enrolment period** ◆ January 2007 - June 2017 **Follow-up** ◆ NR **Descriptive statistics** ◆ Age (median, range) · Autologous: 49.6 · Implant-based: 50.1 ◆ BMI (mean, sd)	A: Autologous · Year 1 N = 97 · Year 2 N = 70 B: Implant · Year 1 N = 134 · Year 2 N = 116 **Analysis** ◆ linear regression ◆ No matching ◆ No adjustment	◆ Satisfaction with breasts (year 1) · Autologous: 69.4 (20.3) · Implant-based: 67 (16.8) ◆ Satisfaction with breasts (year 2) · Autologous: 69.7 (20.5) · Implant-based: 68.1 (16.3) ◆ Satisfaction with breasts (longest follow-up) · Autologous: 69.3 (19.9) · Implant-based: 66.5 (16.6) ◆ Physical well-being (year 1) · Autologous: 74.8 (15.9) · Implant-based: 75.3 (15.5) ◆ Physical well-being (year 2) · Autologous: 77.0 (14.2) · Implant-based: 77.6 (16.0) ◆ Physical well-being (longest follow-up) · Autologous: 75.2 (15.3) · Implant-based: 76.2 (16.3)	◆ **Follow-up:** NR ◆ **Funding**: Dr. Pusic is a code developer of the BREAST-Q questionnaire, which is owned by Memorial Sloan Kettering Cancer Center. She receives a portion of the licensing fees (royalty payments) when the questionnaire is used in industry-sponsored clinical trials. Dr. Dayan is a paid consultant for Stryker Corp. All other authors had no competing interests. Dr. Mehrara is an Advisor to PureTech Corp; investigator-initiated grant Regeneron corp. This research was funded in part through the NIH/NCI Cancer Center Support Grant P30 CA008748. ◆ **CoI**: NR. **Risk of bias considerations (adapted from SIGN cohort study checklist)** ◆ Study type: retrospective cohort study ◆ Populations comparable (confounding): yes ◆ Rate of participation/ Exclusions reported (selection bias into the study):no ◆ Intervention · Assessment reliable: yes · Assessed more than once: no · Possibly affected by knowledge of outcome status? no ◆ Drop-out rate & reasons reported: no ◆ Outcome: yes · Outcome measure is well-defined, valid and reliable;

Reference/ Study type	Population	Interventions	Main results	Methodological evaluation
	· NR ◆ Stadium: · NR ◆ Neoadjuvant chemotherapy (% yes) · Autologous: 0 · Implant-based: 11 ◆ Adjuvant chemotherapy (% yes) · Autologous: 1 · Implant-based: 93.5 ◆ Reconstruction type · Autologous: NR · Implant-based: NR ◆ Smoke · Autologous: 4 · Implant-based: 1.7			· No blind outcome assessment, however, this is unlikely to affect the results ◆ Main cofounders taken into account: no. ◆ Confidence intervals reported: no Selective reporting (comparison with protocol): no
Palve 2022 retrospective cohort study	**Inclusion criteria (for analysis):** ◆ All women with DIEP, TMG, LD and implant reconstructions **Exclusion criteria (for analysis):** ◆ Patients without complete data of the reconstruction process or other reconstruction methods **Enrolment period** ◆ 1 January 2008 - 31 December 2019 **Follow-up** ◆ Autologous: 68 months	**Interventions** A: Autologous · N = 591 B: Implant-based · N = 202 **Analysis** ◆ Fisher exact test + Mann-Whitney tests ◆ No adjustment	**Reoperation:** · Autologous: 119/591 · Implant-based: 58/202 **Minor complications:** · Autologous: 148/591 · Implant-based: 83/202 **Major complications** · Autologous: 109/591 · Implant-based: 33/202	**General information** ◆ **Follow-up:** median 73 months ◆ **Funding**: This study was funded by Tampere University Hospital Support Foundation. ◆ **CoI**: None. **Risk of bias considerations (adapted from SIGN cohort study checklist)** ◆ Study type: retrospective cohort study ◆ Populations comparable (confounding): yes ◆ Rate of participation/ Exclusions reported (selection bias into the study):no ◆ Intervention · Assessment reliable: yes

Reference/ Study type	Population	Interventions	Main results	Methodological evaluation
	◆ Implant-based: 79 months **Descriptive statistics** ◆ Age (median, range) · Autologous: 53 · Implant-based: 56 ◆ BMI (mean, sd) · Autologous: 26.3 · Implant-based: 24.7 ◆ Stadium: · NR ◆ Neoadjuvant chemotherapy (% yes) · NR ◆ Adjuvant chemotherapy (% yes) · NR ◆ Reconstruction type · Autologous: DIEP (deep inferior epigastric perforator) flap, LD (latissimus dorsi) without implant, TMG (transverse musculocutaneous gracilis) flap · Implant-based: immediate permanent implant-two-stage-LD with implant ◆ Smoke · Autologous: 50 · Implant-based: 25			· Assessed more than once: no · Possibly affected by knowledge of outcome status? no ◆ Drop-out rate & reasons reported: no ◆ Outcome: yes · Outcome measure is well-defined, valid and reliable; · No blind outcome assessment, however, this is unlikely to affect the results ◆ Main cofounders taken into account: no. ◆ Confidence intervals reported: no Selective reporting (comparison with protocol): no

Reference/ Study type	Population	Interventions	Main results	Methodological evaluation
Pedreira 2023 retrospective cohort study	**Inclusion criteria (for analysis):** ◆ NR **Exclusion criteria (for analysis):** ◆ NR **Enrolment period** ◆ September of 2016 - September of 2019 **Follow-up** ◆ Autologous: 25.9 months ◆ Implant-based: 25.2 months **Descriptive statistics** ◆ Age (median, range) · Autologous: 49 · Implant-based: 49 ◆ BMI (mean, sd) · Autologous: 27.5 · Implant-based: 24 ◆ Stadium: · NR ◆ Neoadjuvant chemotherapy (% yes) · NR ◆ Adjuvant chemotherapy (% yes) · NR ◆ Reconstruction type	**Interventions** A: Autologous · N = 107 B: Implant-based · N = 107 **Analysis** ◆ Fisher exact test + Mann-Whitney tests ◆ No adjustment	**Flap loss:** · Autologous: 2/64 · Implant-based: NA **Any complications:** · Autologous: 29/107 · Implant-based: 36/107 **Major complications:** · Autologous: 8/107 · Implant-based: 29/107 **Minor complications:** · Autologous: 21/107 · Implant-based: 7/107	**General information** ◆ **Follow-up:** 25.9 vs. 25.2 months ◆ **Funding:** NR ◆ **CoI**: NR. **Risk of bias considerations (adapted from SIGN cohort study checklist)** ◆ Study type: retrospective cohort study ◆ Populations comparable (confounding): yes ◆ Rate of participation/ Exclusions reported (selection bias into the study):no ◆ Intervention · Assessment reliable: yes · Assessed more than once: no · Possibly affected by knowledge of outcome status? no ◆ Drop-out rate & reasons reported: no ◆ Outcome: yes · Outcome measure is well-defined, valid and reliable; · No blind outcome assessment, however, this is unlikely to affect the results ◆ Main cofounders taken into account: no. ◆ Confidence intervals reported: no Selective reporting (comparison with protocol): no

Reference/ Study type	Population	Interventions	Main results	Methodological evaluation
	· Autologous: unilateral or bilateral abdominal free tissue transfer (either muscle-sparing transverse rectus abdominis muscle or deep inferior epigastric perforator flaps) · Implant-based: immediate prepectoral reconstruction with tissue expander(s) and acellular dermal matrix ◆ Smoke · NR			
Persichetti 2022 retrospective cohort study	**Inclusion criteria (for analysis):** ◆ patients who underwent to breast reconstruction for cancer ◆ follow-up of at least 2 years ◆ fluent in the Italian language ◆ signed the study consent ◆ Patients having undergone prophylactic mastectomy due to genetic indication from deleterious BRCA1/2 or CDH1 mutations **Exclusion criteria (for analysis):** ◆ if they underwent delayed procedures ◆ follow-up of less than 2 years ◆ postoperative complications that compromised reconstruction ◆ legally incompetent ◆ women who did not sign the consent form to participate to this study **Enrolment period** ◆ January 2014 - January 2020	**Interventions** A: Autologous · N = 133 B: Implant-based · N = 192 **Analysis** ◆ Linear regression ◆ No adjustment	**Breast –Q (Mean, SD)** ◆ Satisfaction with breasts · Autologous: 62.7 (16.2) · Implant-based: 52.9 (12.1) ◆ Satisfaction with overall outcome · Autologous: 77.7 (18.8) · Implant-based: 66.5 (17.2) ◆ Physical well-being · Autologous: 73.3 (16.6) · Implant-based: 65.2 (9.5)	**General information** ◆ **Follow-up:** NR ◆ **Funding**: No intramural or extramural funding supported any aspect of this work. ◆ **CoI**: The authors do not have any commercial associations that might pose or create a conflict of interest with information presented in this communication. **Risk of bias considerations (adapted from SIGN cohort study checklist)** ◆ Study type: retrospective cohort study ◆ Populations comparable (confounding): yes ◆ Rate of participation/ Exclusions reported (selection bias into the study):no ◆ Intervention · Assessment reliable: yes · Assessed more than once: no · Possibly affected by knowledge of outcome status? no

Reference/ Study type	Population	Interventions	Main results	Methodological evaluation
	Follow-up ◆ NR **Descriptive statistics** ◆ Age (median, range) · Autologous: 51.3 · Implant-based: 51.9 ◆ BMI (mean, sd) · Autologous: 25.2 · Implant-based: 26.2 ◆ Stadium: · NR ◆ Neoadjuvant chemotherapy (% yes) · Autologous: 32 · Implant-based: 57 ◆ Adjuvant chemotherapy (% yes) · Autologous: 8 · Implant-based: 25 ◆ Reconstruction type · Autologous: (DIEP) deep inferior epigastric perforator · Implant-based: IBR (implant-based Breast Reconstruction) ◆ Smoke · Autologous: 37 · Implant-based: 54			◆ Drop-out rate & reasons reported: no ◆ Outcome: yes · Outcome measure is well-defined, valid and reliable; · No blind outcome assessment, however, this is unlikely to affect the results ◆ Main cofounders taken into account: no. ◆ Confidence intervals reported: no Selective reporting (comparison with protocol): no

Reference/ Study type	Population	Interventions	Main results	Methodological evaluation
Sadok 2023 prospective multicenter cohort study	**Inclusion criteria (for analysis):** ◆ prospective multicenter cohort study in women undergoing autologous or alloplastic BR ◆ aged 18 years and older **Exclusion criteria (for analysis):** ◆ NR **Enrolment period** ◆ 2012 - 2019 **Follow-up** ◆ NR **Descriptive statistics** ◆ Age (median, range) · Autologous: 49 · Implant-based: 47 ◆ BMI (mean, sd) · Autologous: 27 · Implant-based: 25 ◆ Stadium: · NR ◆ Neoadjuvant chemotherapy (% yes) · Autologous: 6 · Implant-based: 8 ◆ Adjuvant chemotherapy (% yes) · Autologous: 2 · Implant-based: 14	**Interventions** A: Autologous · N = 63 B: Implant-based · N = 75 **Analysis** ◆ Generalized linear regression ◆ No matching ◆ No adjusted data reported	**Flap loss** · Autologous: 1/63 · Implant-based: 0/75 **Any complications** · Autologous: 39/63 · Implant-based: 38/75 **Breast –Q (Means, SDs)** ◆ Satisfaction with breasts (6 months post-operative) · Autologous: 68 (17) · Implant-based: 57 (19) ◆ Satisfaction with overall outcome (6 months post-operative) · Autologous: 74 (23) · Implant-based: 71 (19) ◆ Physical well-being (6 months post-operative) · Autologous: 74 (18) · Implant-based: 73 (13)	**General information** ◆ **Follow-up:** NR ◆ **Funding**: Prof. Werker is SERB member for Fidia Ltd., Milan, Italy ◆ **CoI**: All the other authors have no financial interest to declare in relation to the content of this article. **Risk of bias considerations (adapted from SIGN cohort study checklist)** ◆ Study type: prospective multicenter cohort study ◆ Populations comparable (confounding): yes ◆ Rate of participation/ Exclusions reported (selection bias into the study): yes ◆ Intervention · Assessment reliable: yes · Assessed more than once: no · Possibly affected by knowledge of outcome status? no ◆ Drop-out rate & reasons reported: no ◆ Outcome: yes · Outcome measure is well-defined, valid and reliable; · No blind outcome assessment, however, this is unlikely to affect the results ◆ Main cofounders taken into account: no. ◆ Confidence intervals reported: no Selective reporting (comparison with protocol): no

Reference/ Study type	Population	Interventions	Main results	Methodological evaluation
	◆ Reconstruction type · Autologous: The autologous technique was a deep inferior epigastric perforator (DIEP) flap BR · Implant-based: direct implant (one stage), tissue expander followed by implant (two stages), or tissue expander/implant combined with a latissimus dorsi flap) ◆ Smoke · Autologous: 1 · Implant-based: 16			
Von Glinski 2022 retrospective cohort study	**Inclusion criteria (for analysis):** ◆ history of ABR or IBR after skin/nipple-sparing mastectomy ◆ follow-up after reconstruction of at least one year ◆ free of cancer or metastases ◆ conversant in German **Exclusion criteria (for analysis):** ◆ Patients with an ABR after IBR and vice versa ◆ any patient undergoing reconstruction with a pedicled flap or a mixed approach (bilateral reconstruction with unilateral flap and unilateral implant or additional use of a pedicled flap) **Enrolment period** ◆ January 2014 - May 2020	**Interventions** A: Autologous · N = 36 B: Implant-based · N = 72 **Analysis** ◆ Fisher exact test + Mann-Whitney tests ◆ No adjustment	**Reoperation:** · Autologous: 7/36 · Implant-based: 13/72 **Minor complications:** · Autologous: 8/36 · Implant-based: 8/72 **Major complications** · Autologous: 3/36 · Implant-based: 22/72 **Breast –Q (Means, SD)** ◆ Satisfaction with breasts · Autologous: 67.7 (15.6) · Implant-based: 59.9 (17.9) ◆ Satisfaction with overall outcome · Autologous: 78.4 (19.0) · Implant-based: 73.2 (20.2)	**General information** ◆ **Follow-up:** 34.9 vs. 27.1 months ◆ **Funding**: We acknowledge support from the Open Access Publication Funds of the Ruhr-Universität Bochum. ◆ **CoI**: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest. **Risk of bias considerations (adapted from SIGN cohort study checklist)** ◆ Study type: retrospective cohort study ◆ Populations comparable (confounding): yes ◆ Rate of participation/ Exclusions reported (selection bias into the study):no ◆ Intervention · Assessment reliable: yes

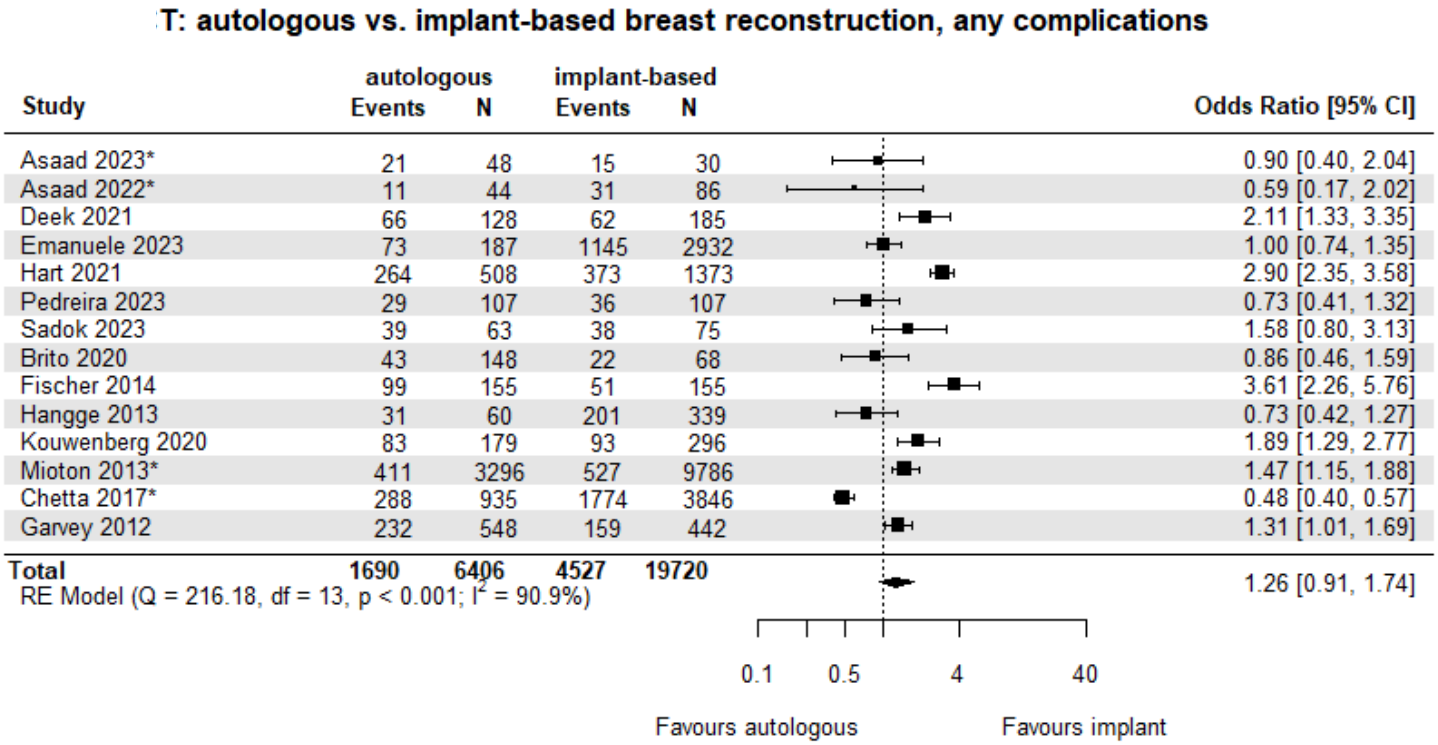
Reference/ Study type	Population	Interventions	Main results	Methodological evaluation
	Follow-up ◆ Autologous: 34.9 months ◆ Implant-based: 27.1 months **Descriptive statistics** ◆ Age (median, range) · Autologous: 46.6 · Implant-based: 48.9 ◆ BMI (mean, SD) · Autologous: 26.9 · Implant-based: 24.3 ◆ Stadium: · NR ◆ Neoadjuvant chemotherapy (% yes) · Autologous: 16 · B Implant-based 13 ◆ Adjuvant chemotherapy (% yes) · NR ◆ Reconstruction type · Autologous: DIEP, TRAM, and the superficial inferior epigastric artery (SIEA) flap · Implant-based: NR ◆ Smoke · Autologous: 6 · Implant-based: 9		◆ Physical well-being · Autologous: 71.4 (15.90) · Implant-based: 67.6 (13.90)	· Assessed more than once: no · Possibly affected by knowledge of outcome status? no ◆ Drop-out rate & reasons reported: no ◆ Outcome: yes · Outcome measure is well-defined, valid and reliable; · No blind outcome assessment, however, this is unlikely to affect the results ◆ Main cofounders taken into account: no. ◆ Confidence intervals reported: no ◆ Selective reporting (comparison with protocol): no

Reference/ Study type	Population	Interventions	Main results	Methodological evaluation
Tallroth 2021 Randomized controlled study	**Inclusion criteria (for analysis):** ◆ patients with prior unilateral mastectomy, but no RT **Exclusion criteria (for analysis):** ◆ insufficient abdominal donor tissue for a DIEP flap reconstruction ◆ earlier abdominal liposuction ◆ previous abdominoplasty ◆ pronounced scars on the chest ◆ shoulder disability ◆ warfarin treatment for atrial fibrillation. **Enrolment period** ◆ April 2012 – January 2018 **Follow-up** ◆ NR **Descriptive statistics** ◆ Age (median, range) · Autologous: 52.3 · Implant-based: 55.8 ◆ BMI (mean, sd) · Autologous: 26.1 · Implant-based: 25.1 ◆ Stadium: · NR ◆ Neoadjuvant chemotherapy (% yes) · NR	**Interventions** A: Autologous · N = 44 B: Implant-based · N = 29 **Analysis** ◆ Fisher exact test + Mann-Whitney tests ◆ No adjustment	**Overall complications (within the first 30 postoperative days)** · Autologous: 16/44 · Implant-based: 2/29 **Breast –Q (Means, SD)** ◆ Satisfaction with breasts · Autologous: 72.1 (17.7) · Implant-based: 63.4 (11.8) ◆ Satisfaction with overall outcome · Autologous: 82.3 (21.4) · Implant-based: 79.4 (14.2) ◆ Physical well-being · Autologous: 79.6 (21.1) · Implant-based: 72.0 (21.5)	**General information** ◆ **Study duration:** April 2012 – January 2018 ◆ Median Follow up/ data cutoff: NR ◆ **ITT:** Yes ◆ **Randomisation:** Yes ◆ **Blinding:** No ◆ **Funding**: None. ◆ **COI**: None ◆ **Other limitations:** None. **Risk of bias considerations (Cochrane Risk of bias tool I; assessment of the review)** ◆ Study type: RCT ◆ Random sequence generation: Unclear ◆ Allocation concealment: Unclear ◆ Blinding of participants: High ◆ Blinding of study personnel: High ◆ Blinding of outcome assessors (objective outcomes): Low ◆ Blinding of outcome assessors (subjective outcomes): Unclear ◆ Incomplete outcome data: Low ◆ Selective outcome reporting: Low ◆ Other bias: Low ◆ Overall: Moderate

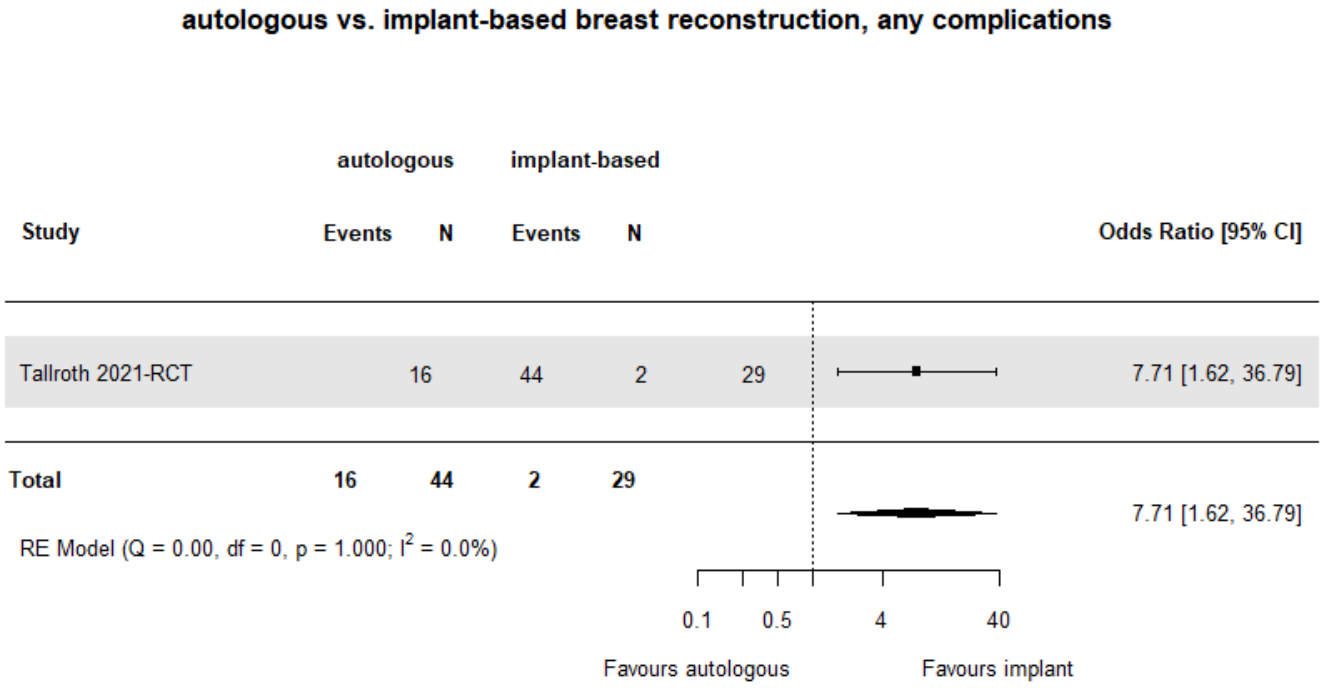
Reference/ Study type	Population	Interventions	Main results	Methodological evaluation
	◆ Adjuvant chemotherapy (% yes) · Autologous: 25 · Implant-based: 13 ◆ Reconstruction type · Autologous: (DIEP) deep inferior epigastric perforator expander prosthesis (EP) · Implant-based: expander prosthesis (EP) ◆ Smoke · Autologous: 4 · Implant-based: 2			

6.1.3 Meta-analysen

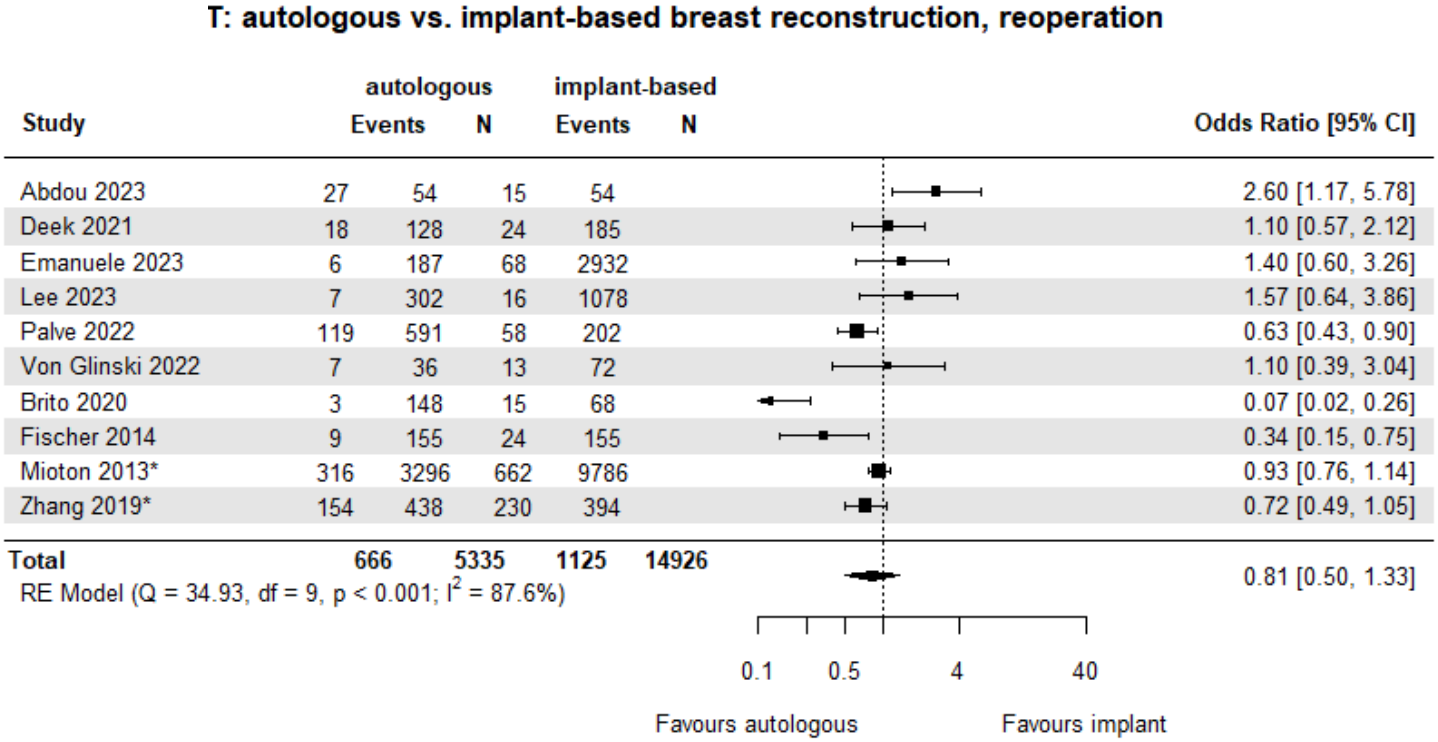
6.1.3.1 Any complications (Data from NRSIs)



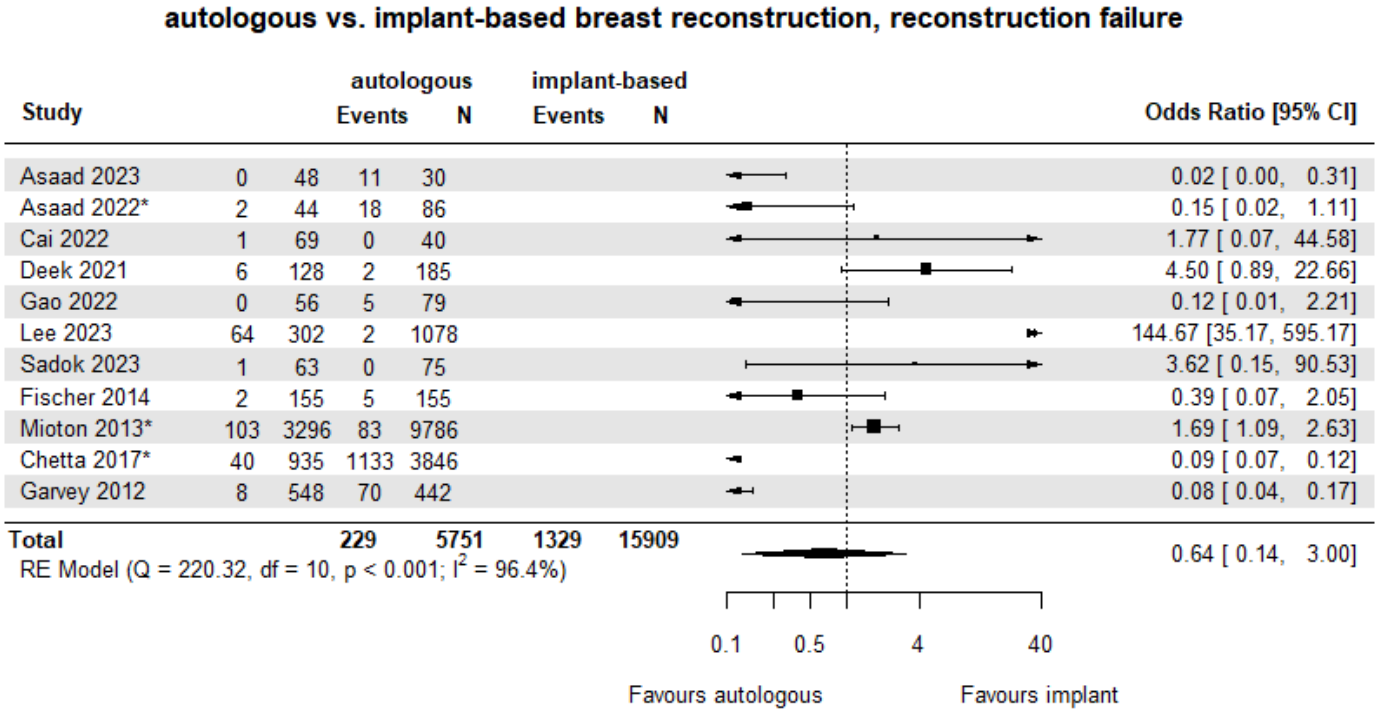
6.1.3.2 Any complications (Data from RCT)



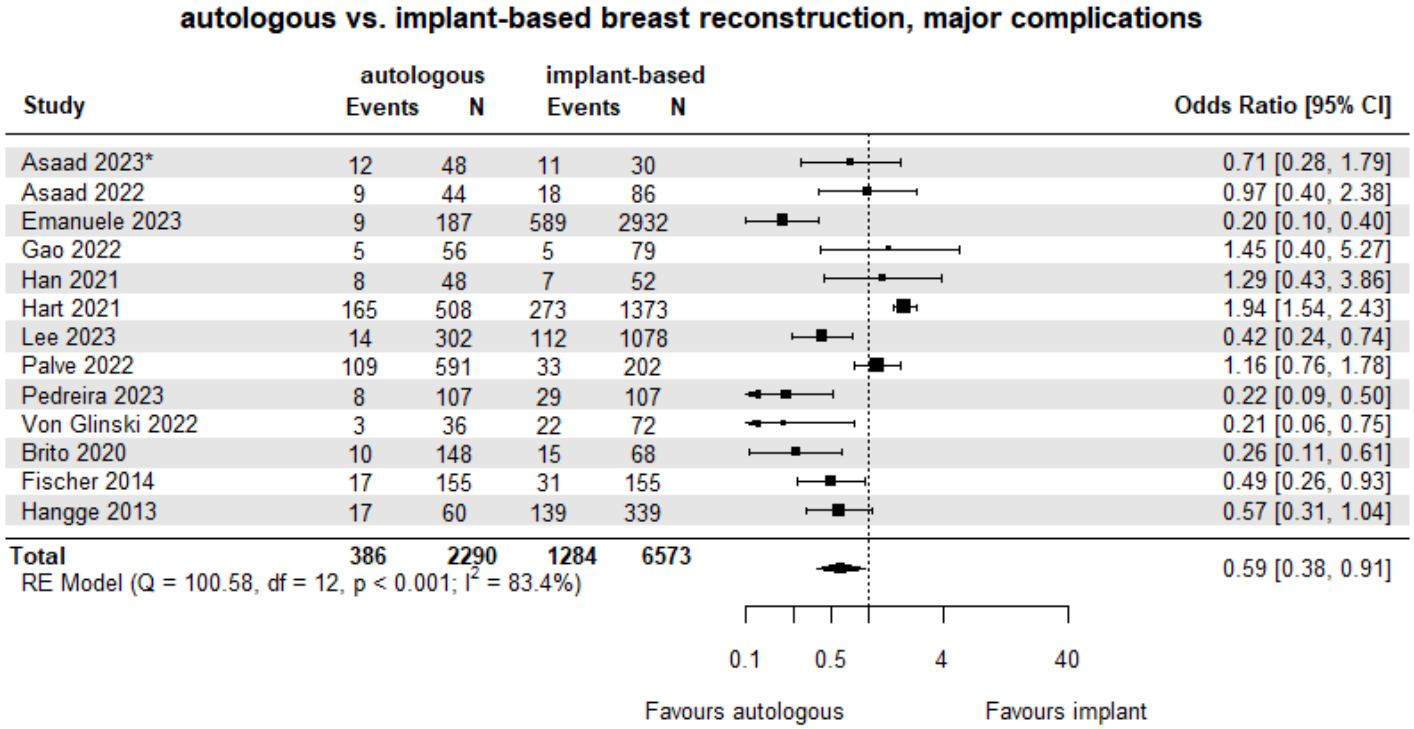
6.1.3.3 Reoperations (Data from NRSIs)



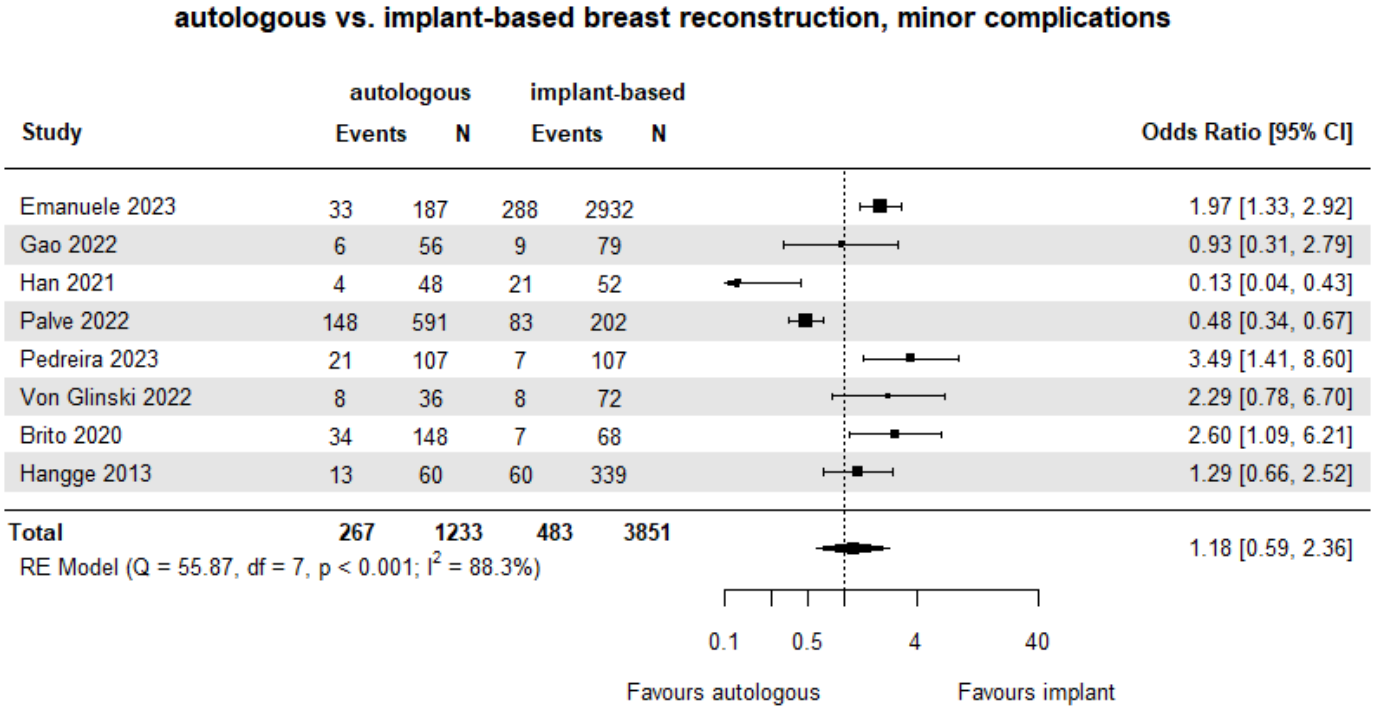
6.1.3.4 Reconstruction failure (Data from NRSIs)



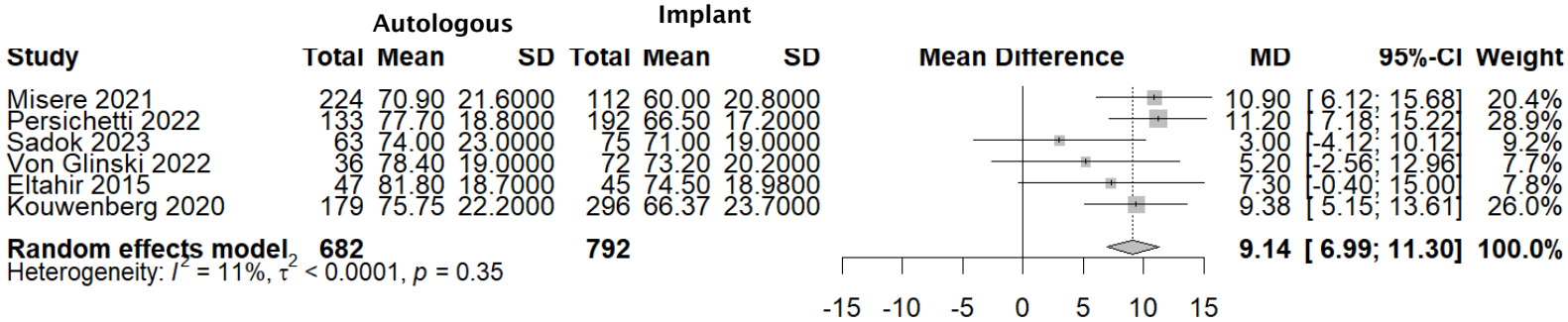
6.1.3.5 Major complications (Data from NRSIs)



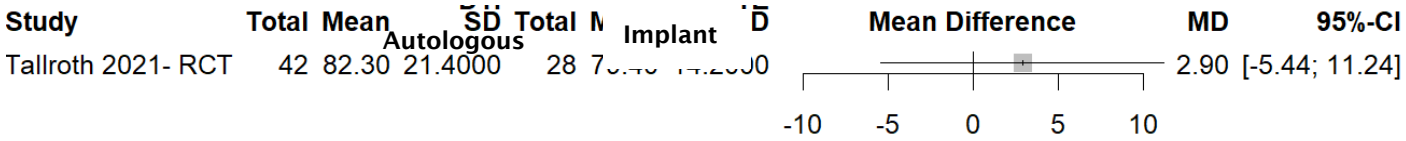
6.1.3.6 Minor complications (Data from NRSIs)



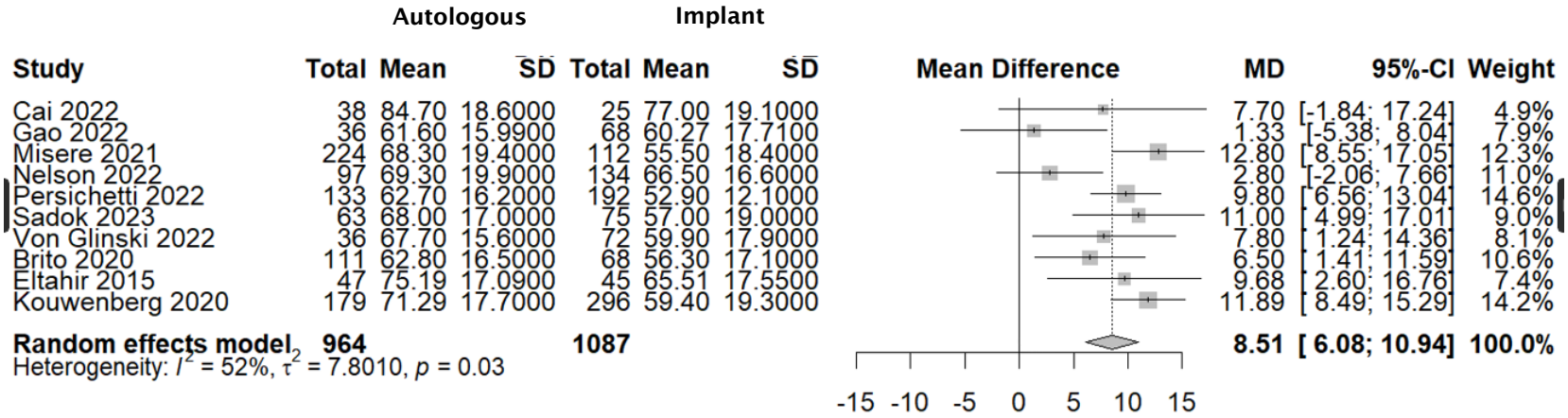
6.1.3.7 Satisfaction with outcome (Data from NRSIs)



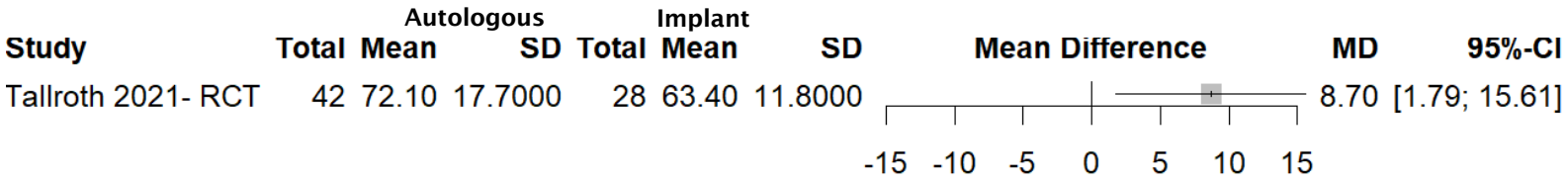
6.1.3.8 Satisfaction with outcome (Data from RCT)



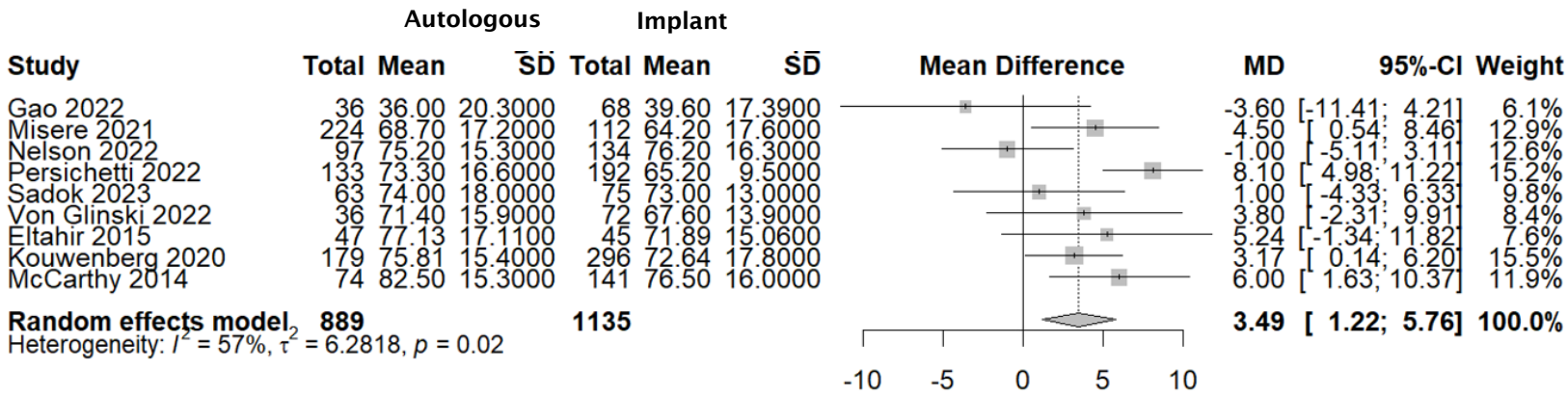
6.1.3.9 Satisfaction with breasts (Data from NRSIs)



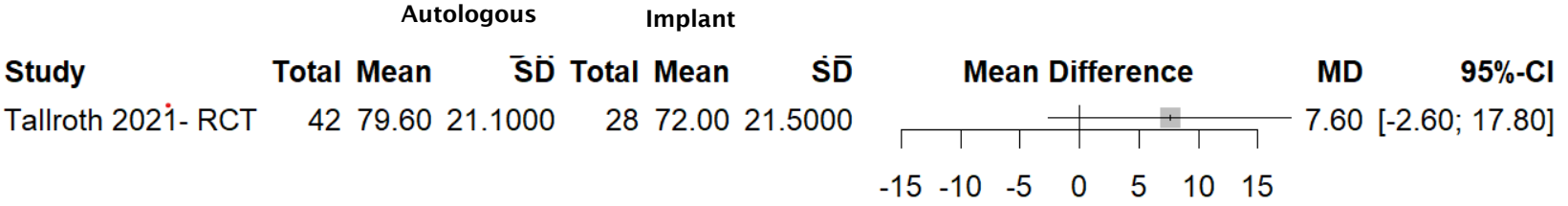
6.1.3.10 Satisfaction with breasts (Data from RCT)



6.1.3.11 Physical well-being (Data from NRSIs)



6.1.3.12 Physical well-being (Data from RCT)



6.1.4 Vertrauen in die Evidenz (nach GRADE)

Summary of findings:

Autologous compared to implant-based reconstruction in women with mastectomy for breast reconstruction

Patient or population: women with mastectomy for breast reconstruction

Intervention: any autologous breast reconstruction

Comparison: any implant-based breast reconstruction

Outcomes	**Anticipated absolute effects**[*] (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with implant-based reconstruction	**Risk with autologous**				
Any complications						
NRSI: Any complications	230 per 1.000	**273 per 1.000** (213 to 341)	**OR 1.26** (0.91 to 1.74)	26126 (14 non-randomised studies)	⊕◯◯◯ Very low[a,b,c]	Autologous breast reconstruction probably reduces the incidence of complications (any) compared to implant-based reconstruction. The evidence from observational studies is very uncertain.
RCT: Any complications	69 per 1.000	**364 per 1.000** (107 to 732)	**OR 7.71** (1.62 to 36.79)	73 (1 RCT)	⊕⊕◯◯ Low[d,e]	
Reoperations						
NRSI: Reoperations	75 per 1.000	**62 per 1.000** (39 to 98)	**OR 0.81** (0.50 to 1.33)	20261 (10 non-randomised studies)	⊕◯◯◯ Very low[a,b,c]	It is uncertain whether autologous compared to implant-based breast reconstruction increases or decreases the incidence of reoperations.
Reconstruction failure						

Summary of findings:						
NRSI: Reconstruction failure	84 per 1.000	**55 per 1.000** (13 to 215)	**OR 0.64** (0.14 to 3.00)	21660 (11 non-randomised studies)	⊕◯◯◯ Very low[a,b,c]	It is uncertain whether autologous compared to implant-based breast reconstruction increases or decreases the incidence of reconstruction failures.
Major complications						
NRSI: Major complications	195 per 1.000	**125 per 1.000** (84 to 181)	**OR 0.59** (0.38 to 0.91)	8863 (13 non-randomised studies)	⊕◯◯◯ Very low[a,b]	It is uncertain whether autologous compared to implant-based breast reconstruction increases or decreases the incidence of major complications.
Minor complications						
NRSI: Minor complications	125 per 1.000	**145 per 1.000** (78 to 253)	**OR 1.18** (0.59 to 2.36)	5084 (8 non-randomised studies)	⊕◯◯◯ Very low[a,b,c]	It is uncertain whether autologous compared to implant-based breast reconstruction increases or decreases the incidence of minor complications.
Satisfaction with outcome (assessed with: BREAST-Q Scale from: 0 to 100)						
NRSI: Satisfaction with outcome	The mean satisfaction with outcome was **70**	MD **9.14 higher** (6.99 higher to 11.3 higher)	-	1474 (6 non-randomised studies)	⊕⊕◯◯ Low[a]	Autologous breast reconstruction may increase the score of satisfaction with outcome compared to implant-based reconstruction.
RCT: Satisfaction with outcome	The mean satisfaction with outcome was **79**	MD **2.9 higher** (5.44 lower to 11.24 higher)	-	70 (1 RCT)	⊕⊕◯◯ Low[d,e]	
Satisfaction with breasts (assessed with: BREAST-Q Scale from: 0 to 100)						
NRSI: Satisfaction with breasts	The mean satisfaction with breasts was **61**	MD **8.51 higher** (6.08 higher to 10.94 higher)	-	2051 (10 non-randomised studies)	⊕⊕◯◯ Low[a]	Autologous breast reconstruction may increase the score of satisfaction with

Summary of findings:						
RCT: Satisfaction with breasts	The mean satisfaction with breasts was **63**	MD **8.7 higher** (1.79 higher to 15.61 higher)	-	70 (1 RCT)	⊕⊕◯◯ Low[d,e]	breasts compared to implant-based reconstruction.
Physical well-being (assessed with: BREAST-Q Scale from: 0 to 100)						
NRSI: Physical well-being	The mean physical well-being was **68**	MD **3.49 higher** (1.22 higher to 5.76 higher)	-	2024 (9 non-randomised studies)	⊕⊕◯◯ Low[a]	Autologous breast reconstruction may increase the score of physical well-being compared to implant-based reconstruction.
RCT: Physical well-being	The mean physical well-being was **72**	MD **7.6 higher** (2.6 lower to 17.8 higher)	-	70 (1 RCT)	⊕⊕◯◯ Low[d,e]	

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: confidence interval; **MD:** mean difference; **OR:** odds ratio

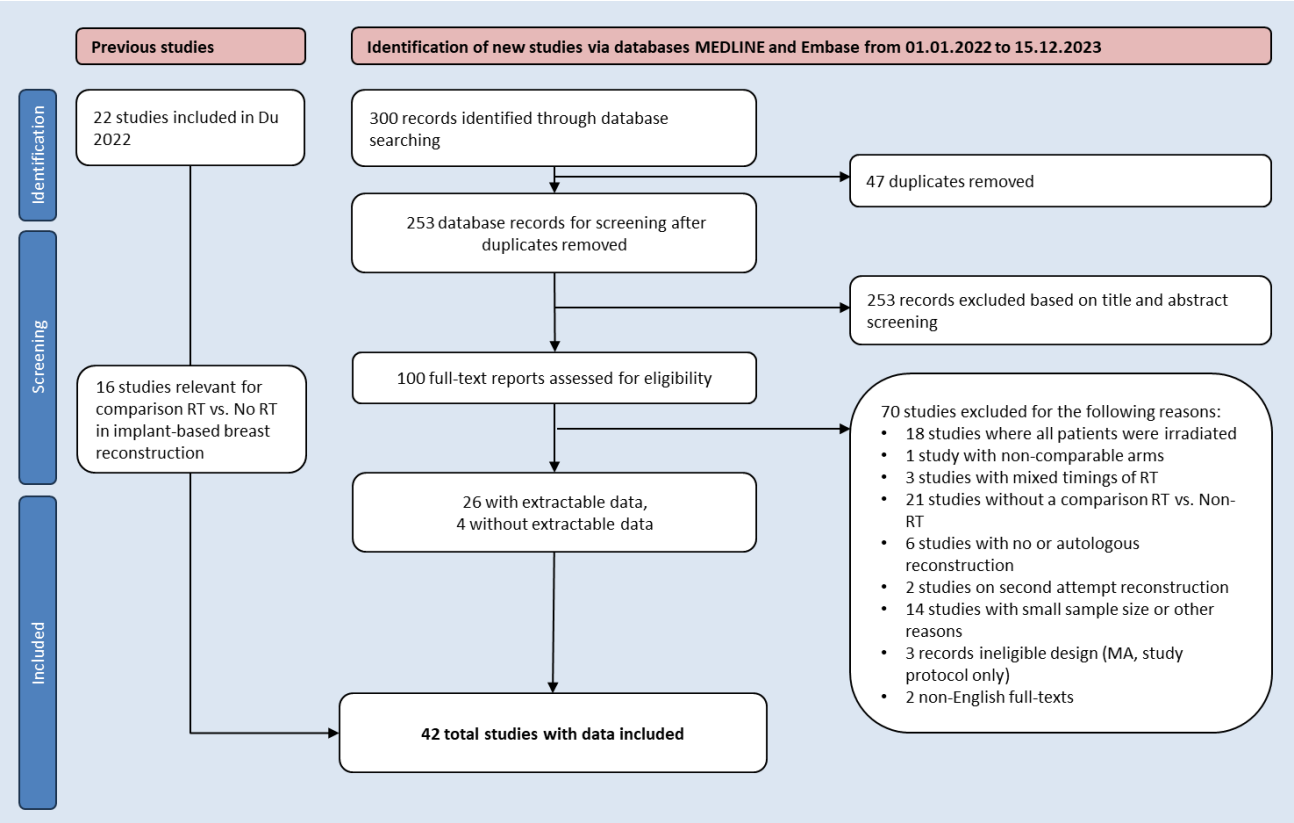
GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

Explanations

a. Downgraded by two levels due to very serious risk of bias: Included studies were observational only, and the majority did not adjust at all for relevant baseline characteristics. Results are thus prone to confounding.
b. Downgraded one level due to serious inconsistency (high heterogeneity).
c. Downgraded by one level due to serious imprecision; the 95% confidence interval includes both effects (in favor of autologous and in favor of implant)
d. Downgraded by one level due to serious risk of bias (unclear allocation concealment, unclear blinding unclear reporting bias)
e. Downgraded by one level due to serious imprecision: large confidence intervals and small sample size & few events.

6.2 PICO 7

6.2.1 PRISMA Flowdiagramm



6.2.2 Evidenztabellen

6.2.2.1 Systematisches Review

6.2.2.1.1 Evidenztabelle systematisches Review Du 2022

Du, F, Liu, R, Zhang, H, Xiao, Y, Long, X, Post-mastectomy adjuvant radiotherapy for direct-to-implant and two-stage implant-based breast reconstruction: A meta-analysis.. J Plast Reconstr Aesthet Surg, 2022. 75 (9)(9): p. 3030-3040., https://pubmed.ncbi.nlm.nih.gov/35961927/.

Reference/ Study type	Review description	Interventions	Study Population	Ergebnisse der untersuchten Endpunkte	Methodological comments	Included publications
Du 2022 Systematisches Review mit Meta-Analyse	**Study design** ◆ Cohort studies, case control studies **Search dates** ◆ 01.01.1995 to 31.12.2021 **Databases** ◆ PubMed, Embase, The Cochrane Library ◆ ((radiation therapy) OR (radiotherapy)) AND ((post*) OR (adjuvant) OR (after)) AND ((implant) OR (expander)) AND (breast) **Inclusion criteria** ◆ immediate breast reconstruction surgery ◆ TE or DTI **Exclusion criteria:**	**Question/ Aim** "This meta-analysis aims to evaluate the outcomes of DTI and TEI procedures followed by PMRT." **Interventions:** A: PMRT B: no PMRT	22 studies published between 2011 and 2022, including 15,345 breasts that received immediate implant-based reconstruction ◆ PMRT: 2847 ◆ No PMRT: 12,498 **Descriptive statistics** (see table 1 of Du 2022) ◆ Age: mean ages between 44.9 and 52 years old ◆ BMI: mean/median BMI values reported to be between 20.6 and 30 kg/m²	**Capsular contractur (Baker grade 3-4)** *Overall pooled results (DTI + TEI):* ◆ 10 studies ◆ PMRT: 158/929 ◆ No PMRT: 126/3817 ◆ Risk ratio 4.48 (95% CI 3.60 to 5.58) in favor of no PMRT *DTI only pooled results* ◆ 5 studies ◆ PMRT: 55/355 ◆ No PMRT: 95/1666 ◆ Risk ratio 3.60 (95% CI 2.62 to 4.96) **Overall complications** Definition: the sum of any recorded complications except capsular contracture of all reconstruction procedures, including seroma, delayed wound	**Risk of bias assessment of studies:** not assessed, reassessed for the current clinical guideline **Overall confidence in results of SR (AMSTAR-2):** ◆ PICO elements: yes ◆ A priori design: partial yes, review question and search strategy ◆ Justification for design: no ◆ Literature search >= 2 databases, search strategy + other sources: · 3 databases · String for PubMed provided · No further resources searched ◆ Selection in duplicate: probably. ◆ Data extraction in duplicate: · Data are collected by one author from each report and independently confirmed by another author.	Included and checked for additional outcomes: ◆ Allué-Cabanuz 2019 ◆ Apte 2020 ◆ Cordeiro 2015 ◆ Hamann 2019 ◆ Hille-Betz 2015 ◆ Korwar 2014 ◆ Loreti 2020 ◆ Masià 2020 ◆ Naoum 2020 ◆ Olsen 2017 ◆ Riggio 2019 ◆ Salzberg 2016 ◆ Seth 2015 ◆ Sinnott 2018 ◆ Spear 2012 ◆ Tejera Hernàndez 2019 **Excluded for this guideline,**

Du, F, Liu, R, Zhang, H, Xiao, Y, Long, X, Post-mastectomy adjuvant radiotherapy for direct-to-implant and two-stage implant-based breast reconstruction: A meta-analysis.. J Plast Reconstr Aesthet Surg, 2022. 75 (9)(9): p. 3030-3040., https://pubmed.ncbi.nlm.nih.gov/35961927/.

- reviews, case reports, and articles with insufficient full text
- breast-conserving therapy
- patients without a history of breast cancer
- patients received radiotherapy before mastectomy
- patients received sole autologous flap reconstruction without implants;
- data of radiotherapy population unavailable, outcomes of different radiation times are not separated

- Reconstruction type (N studies)
  - DTI rep. separately: 7
  - Expander reported separately: 14
  - DTI or expander: 4
  -

healing, implant loss, wound breakdown, revision surgery, reconstruction failure, etc.

Overall pooled results (DTI + TEI):

- 12 studies
- PMRT: 406/1797
- No PMRT: 1247/11045
- Risk ratio 1.67 95% CI 1.52 to 1.85) in favor of no PMRT

DTI only pooled results

- 4 studies
- PMRT: 88/276
- No PMRT: 194/696
- Risk ratio 1.11 (95% CI 0.90 to 1.37)

- List of excluded studies: no
- sufficient detail on studies: partial yes, table 1 provided but not with all necessary information
- RoB assessed: no
- Funding of incl. studies: no
- MA appropriate: partly; overall complications with varying definitions
- RoB considered in MA: NA, no RoB assessment
- RoB in interpretation: NA, no RoB assessment
- Heterogeneity explained: no
- Publication bias investigated: discussed, but not presented
- Sources of CoI: The authors have no conflict of interest to disclose.

Sources of funding

National High Level Hospital Clinical Research Funding (2022-PUMCH-A-209), the National Key R&D Program of China (2020YFE0201600) and the CAMS Innovation Fund for Medical Sciences (No. 2020-I2M- C&T-A-004).

comparison RT on TE versus final implant only:

- Collier 2014
- Dicuonzo 2019
- Lentz 2013
- Nava 2011
- Santosa 2016
- Yoon 2020

Characteristics of the systematic review chosen for this PICO 7.

6.2.2.1.2 Characteristics of studies included in Du 2022 (Table 1)

Authors Years	Country	Enrolment period	N PMRT	N control	Age (mean, range) PMRT/ control	BMI (kg/m², mean, range) PMRT/ control	Follow-up (months, mean, range) PMRT/ control	Reconstruction Type	Outcomes reported
Allué-Cabañuz 2019	Spain	2000 to 2016	71	100	48.4.9.0 (26-87) a	NA	NA	DTI	necrosis, infection, seroma, hematoma, reintervention, capsular contracture III/IV
Apte 2020	UK	February 2012 to July 2017	29	62	50.66 (30-77) *	NA	36 (2-77)	DTI	seroma, delayed wound healing, implant loss, wound breakdown, revision surgery, capsular contracture
Cordeiro 2015	USA	2003 to 2012	304	1468	46.3 + 8.9;46.1: + 10.6b	25.3+5.0; 26.3+5.6b	40.3(1.6-113) :30.1 (0.5-118) b	TEI	TE removal, implant removal
Hamann 2019	Germany	2008 to 2012	26	52	50.2/52.8	NA	17.0 (3.9-61.0)/16.6 (2.7-50.0) a	TEI	Capsular contracture III/IV
Hille-Betz 2015	Germany	2009 -2013	4	57	46*	NA	19.6 (0.4-47.1)*	DTI or TEI	seroma, skin flap necrosis, capsular contracture
Korwar 2014	UK	2006 - 2011	45	47	49.5/52.1[a]	27.3/27.2	23/18 a	DTI or TEI	early implant loss, late implant loss, delayed implant, necrosis, hematoma, seroma, infection, fat necrosis, capsular contracture

Authors Years	Country	Enrolment period	N PMRT	N control	Age (mean, range) PMRT/ control	BMI (kg/m², mean, range) PMRT/ control	Follow-up (months, mean, range) PMRT/ control	Reconstruction Type	Outcomes reported
Loreti 2020	Italy	2013 to 2018	312*	312	49.3*	NA	36 (12-36)*	DTI	Capsular contracture III-IV
Masia 2020	Spain	November 2012 to June 2018	159	1243	52.4*	23.9*	22.7*	DTI or TEI	seroma, dehiscence, hematoma, necrosis, infection, extrusion, RBA, fever, implant rotation, rippling, implant loss, capsular contracture
Naoum 2020	UK	1997 -2017	407	568	49.7/52.4°(DTI); 46.5/49.1°(TEI)	NA	52/50 (DTI); 75/73 (TEI);	DTI, TEI	infection, necrosis, fat necrosis, seroma hematoma, capsular contracture
Olsen 2017	USA	2004 - 2011	34	34	50.4*	NA	3 *	TEI	noninfectious wound complication, surgical site infection
Riggio 2019	Italy	December 2011 to June 2014	4 38	57 DTI 163 TEI	46(23-74) (DTI); 48(27-75) *(TEI); (median)	20.6 (16.6-27.8) *(DTI); 23.0 (16.0-37.6) *(TEI); (median)	26 (median)	DTI, TEI	necrosis, infection, inflammation and seroma, implant damage, exposure, rupture or severe lateral displacement.
Salzberg 2016	USA	December of 2001 to May of 2014	52	763	47	24.4 (4.8; range 16 to 54)	56.4	DTI	capsular contracture

Authors Years	Country	Enrolment period	N PMRT	N control	Age (mean, range) PMRT/ control	BMI (kg/m², mean, range) PMRT/ control	Follow-up (months, mean, range) PMRT/ control	Reconstruction Type	Outcomes reported
Seth 2015	USA	February 1999 to January 2008	208 248	879	48.6*	25.3*	360*	TEI	Exposure, infection, pain/tightness, hematoma, seroma, flap necrosis, ECF (explanation or conversion to flap)
Sinnott 2018	USA	January 2010 to December 2017	21	87	52.7/52.4	30.0/28.9	20.6/18.7	DTI or TEI	Infection, seroma, hematoma, dehiscence, necrosis, capsular contracture, rippling, implant loss
Spear 2012	USA	August of 2004 to June of 2010	56	355	44.9/46.2	25.8/24.3	15.2 (6.0-80.5)	TEI	Capsular contracture III/IV
Tejera Hernandez 2019	Spain	2010 to 2016	23	41	NA	NA	43.9/54.9	TEI	General complications, capsular contracture

Characteristics of the studies included in Du 2022 (only those revelant to PICO 7 are presented). Information taken over and representation adapted from Table 1 of Du 2022.

6.2.2.1.3 Risk of Bias assessment of Studies included in Du 2022 (RoB assessment adapted from SIGN for cohort studies)

Authors Years	Study Design	Bias due to confounding	Selection bias	Assessment reliable: • Assessed more than once: • Possibly affected by knowledge of outcome status?	Attrition Bias	Outcome • well-defined, valid and reliable: • Blind outcome assessment to exposure	CI reported?	Reporting Bias
Allué-Cabañuz 2019	retrospective cohort study	High risk: no adjustment	Unclear, no information provided	yes/no/no	High risk: not reported	Reliable outcome measure; no blind outcome assessment	no	no protocol accessible.
Apte 2020	prospective cohort study	High risk: no adjustment	Low risk: prospective cohort study with consecutive sampling	yes/no/no	High risk: not reported	Reliable outcome measure; no blind outcome assessment	no	no protocol accessible.
Cordeiro 2015	retrospective cohort study	High risk: no adjustment for capsular contracture; moderate risk for reconstruction failure	Low risk: prospective data collection	yes/no/no	High risk: not reported	Reliable outcome measure; no blind outcome assessment	partly (for adjusted OR)	no protocol accessible.
Hamann 2019	prospective cohort study	High risk: no adjustment	High risk: Of 161 eligible patients, 97 patients followed the invitation	yes/no/no	High risk: not reported	Reliable outcome measure; no blind outcome assessment	no	no protocol accessible.
Hille-Betz 2015	retrospective cohort study	High risk: no adjustment	Unclear, no information provided	yes/no/no	High risk: not reported	Reliable outcome measure; no blind outcome assessment	no	no protocol accessible.

Authors Years	Study Design	Bias due to confounding	Selection bias	Assessment reliable: • Assessed more than once: • Possibly affected by knowledge of outcome status?	Attrition Bias	Outcome • well-defined, valid and reliable: • Blind outcome assessment to exposure	CI reported?	Reporting Bias
Korwar 2014	retrospective cohort study	High risk: no adjustment	Low risk: prospective data collection	yes/no/no	High risk: not reported	Reliable outcome measure; no blind outcome assessment	no	no protocol accessible.
Loreti 2020	retrospective cohort study	High risk: no adjustment	Unclear, no information provided	yes/no/no	High risk: not reported	Reliable outcome measure; no blind outcome assessment	no	no protocol accessible.
Masia 2020	retrospective cohort study	High risk: no adjustment	Low risk: "The sole patients excluded from the analysis were those with less than 3 months of follow-up."	yes/no/no	High risk: not reported	Reliable outcome measure; no blind outcome assessment	no	no protocol accessible.
Naoum 2020	retrospective cohort study	High risk: no adjustment	High risk: inclusion criterion "availability of surgical and PMRT notes"	yes/no/no	High risk: not reported	Reliable outcome measure; no blind outcome assessment	no	no protocol accessible.
Olsen 2017	retrospective cohort study	High risk: no adjustment	High risk: only insured participants included ("Medical claims	yes/no/no	High risk: not reported	Reliable outcome measure; no blind outcome assessment	no	no protocol accessible.

Authors Years	Study Design	Bias due to confounding	Selection bias	Assessment reliable: • Assessed more than once: • Possibly affected by knowledge of outcome status?	Attrition Bias	Outcome • well-defined, valid and reliable: • Blind outcome assessment to exposure	CI reported?	Reporting Bias
			were restricted to paid claims.")					
Riggio 2019	retrospective cohort study	moderate risk: adjusted for BMI, expander volume, age	Unclear, no information provided	yes/no/no	High risk: not reported	Reliable outcome measure; no blind outcome assessment	partly (for adjusted OR)	no protocol accessible.
Salzberg 2016	retrospective cohort study	Moderate risk: adjusted for BMI, implant volume	Unclear, no information provided	yes/no/no	High risk: not reported	Reliable outcome measure; no blind outcome assessment	no	no protocol accessible.
Seth 2015	retrospective cohort study	High risk: no adjustment	Unclear, no information provided	yes/no/no	High risk: not reported	Reliable outcome measure; no blind outcome assessment	no	no protocol accessible.
Sinnott 2018	retrospective cohort study	High risk: no adjustment	Unclear, no information provided	yes/no/no	High risk: not reported	Reliable outcome measure; no blind outcome assessment	no	no protocol accessible.
Spear 2012	retrospective cohort study	High risk: no adjustment	Unclear, no information provided	yes/no/no	High risk: not reported	Reliable outcome measure; no blind outcome assessment	no	no protocol accessible.
Tejera Hernandez 2019	retrospective cohort study + prospective QoL data collection	High risk: bias by indication ("It is decided to administer adjuvant radiotherapy to patients with axillary involvement,	Unclear, no information provided	yes/no/no	High risk: not reported	Reliable outcome measure; no blind outcome assessment	no	no protocol accessible.

Authors Years	Study Design	Bias due to confounding	Selection bias	Assessment reliable: • Assessed more than once: • Possibly affected by knowledge of outcome status?	Attrition Bias	Outcome • well-defined, valid and reliable: • Blind outcome assessment to exposure	CI reported?	Reporting Bias
		positive margins or with tumors larger than 5 cm.")						

Risk of bias assessment of studies included in Du 2022 that were eligible for inclusion for PICO 7.

6.2.2.2 Primärstudien – neu identifiziert

Reference/ Study type	Population	Interventions	Main results	Methodological evaluation
Adam 2021 Prospective cohort study	**Inclusion criteria (for analysis):** ◆ Prospectively registered consecutive patients with breast cancer who underwent mastectomy and implant-based IBR **Exclusion criteria (for analysis):** ◆ NR **Enrolment period** ◆ 1 January 2007 to 31 December 2011 **Follow-up**	**Interventions** A: RT after implant · N = 304 B: no RT after implant · N = 386 C: RT before implant · N = 64 · C not considered in analysis **Analysis**	**Implant loss (implant removal due to any reason)** ◆ HR 3.41 (95% CI 2.24 to 5.23) in favour of no PMRT · RT: 73/299 · No RT: 24/388 **Reoperation:** · RT: 63/303 · No RT: 34/384 **Minor complications:** · RT: 86/303 · No RT: 110/384	**General information** ◆ **Follow-up:** Median follow-up 120 (range 1–171) months ◆ **Funding**: JdB is supported by grants from the Swedish Cancer Society and Stockholm County Council together with the Karolinska Institutet (ALF grant). This study was supported by the Percy Falk Foundation. ◆ **CoI**: The authors declare no conflict of interest. **Risk of bias considerations (adapted from SIGN cohort study checklist)**

Reference/ Study type	Population	Interventions	Main results	Methodological evaluation
	◆ Median follow-up 120 (range 1–171) months **Descriptive statistics** ◆ Age (median, range) · RT: 46 (21-74) years · No RT: 50 (24-77) years ◆ BMI (mean, sd) · RT: 24.3 (.8) · No RT: 23.8 (3.6) ◆ Stadium: NR ◆ Adjuvant chemotherapy (% yes) · RT: 22.7% · No RT: 1.8% ◆ Neoadjuvant chemotherapy (% yes) · RT: 57.8% · No RT: 35.7% ◆ Reconstruction type · All direct to implant ◆ Mesh/ADM (%) · No mesh used ◆ Implant position · All subpectoral	◆ univariable and multivariable Cox proportional hazards regression ◆ Adjustment for age, year of reconstruction for outcome implant removal only	**Major complications** · RT: 15/303 · No RT: 21/384 **QoL-outcomes: Breast -Q** ◆ BREAST-Q satisfaction with breasts · Post-score (2020): 52.64 ◆ BREAST-Q Satisfaction with overall outcome · Post-score (2020): 66.66 ◆ BREAST-Q Psychosocial well-being · Post-score (2020): 69.81 ◆ BREAST-Q Sexual well-being · Post-score (2020): 49.21 ◆ BREAST-Q Physical well-being · Post-score (2020): 76.24	◆ Study type: prospective cohort study ◆ Confounding: High risk (Baseline characteristics are not well-balanced across groups, i.e., tumor size, pre- and postoperative chemotherapy; only adjustment for one outcome) ◆ Selection bias into the study: Unclear, no comparison between groups. The response rate was 72.2%. ◆ Intervention · Assessment reliable: yes · Assessed more than once: no · Possibly affected by knowledge of outcome status? no ◆ Drop-out rate & reasons reported: · Similar across groups: ""A responder analysis showed no differences in demographics and tumour characteristics between responders and non-responders, except for a higher proportion of smokers (12.3 versus 19.3 per cent; P=0.045) and of women with breast cancer recurrence (5.6 versus 12.7 per cent; P=0.006) among non-responders." ◆ Outcome · Outcome measure is well-defined, valid and reliable; · No blind outcome assessment, however, this is unlikely to affect the results

Reference/ Study type	Population	Interventions	Main results	Methodological evaluation
				◆ Main cofounders taken into account: no. ◆ Confidence intervals reported: partly. ◆ Selective reporting (comparison with protocol): not protocol provided, not assessable.
Bernini 2022 Retrospective cohort study	**Inclusion criteria (for analysis):** ◆ Therapeutic or prophylactic pre-pectoral IBBR **Exclusion criteria (for analysis):** ◆ NR **Enrolment period** ◆ October 2012 to May 2016 **Follow-up** ◆ 4.0 year median follow up time (mean 3.9 years; range 3–5.5) **Descriptive statistics (reported for overall population)** ◆ Age >55 years: 21% ◆ BMI >25: 21.9% ◆ Stadium: NR ◆ Adjuvant chemotherapy: 11% ◆ Neoadjuvant chemotherapy: 29.7% ◆ Reconstruction type (%) · Tissue expander: 43.8% · DTI: 56.2% ◆ Mesh/ADM: all ◆ Implant position: all prepectoral	**Interventions** A: RT after implant · N = 37 B: no RT after implant · N = 108 (may have received pre-operative RT) **Analysis** ◆ Type of analysis: Frequencies ◆ No adjustment	**Implant loss** (explantation rate due to any reason): ◆ RT: 3/33 ◆ No RT: 4/83 **Overall complications** (acute toxicities: BR failure and surgical complications such as skin-nipple necrosis, seroma, wound dehiscence, surgical site infection, hematoma, and atopic versus graft reaction) ◆ RT: 5/37 ◆ No RT: 14/83 **Mortality** ◆ RT: 2/33 ◆ No RT: 1/83 **Local recurrence** ◆ RT: 2/33 ◆ No RT: 3/83 **Metastatic disease** ◆ RT: 8/33 ◆ No RT: 6/83	**General information** ◆ **Follow-up**: 4.0 year median follow up time (mean 3.9 years; range 3–5.5) ◆ **Funding**: None. ◆ **CoI**: All authors have no conflict of interest to declare. **Risk of bias considerations (adapted from SIGN cohort study checklist)** ◆ Study type: retrospective cohort study ◆ Confounding: High risk (no adjustment or matching of baseline characteristics, no comparison between RT arms provided) ◆ Selection bias into the study: Unclear, no information provided. ◆ Intervention · Assessment reliable: yes · Assessed more than once: no · Possibly affected by knowledge of outcome status? no ◆ Drop-out rate & reasons reported: · Not reported. ◆ Outcome

Reference/ Study type	Population	Interventions	Main results	Methodological evaluation
				· Outcome measure is well-defined, valid and reliable; · No blind outcome assessment, however, this is unlikely to affect the results ◆ Main cofounders taken into account: no. ◆ Confidence intervals reported: no. ◆ Selective reporting (comparison with protocol): no protocol provided, not assessable.
Cagli 2022 retrospective cohort study Study name/registry name	**Inclusion criteria (for analysis):** ◆ diagnosis of ductal or lobular breast cancer or ductal carcinoma in situ; ◆ modified radical mastectomy (MRM) or skin/nipple-sparing mastectomy (S/NSM); ◆ immediate reconstruction with submuscular TE; ◆ no previous breast surgery (either cosmetic either oncological), nor radiation therapy **Exclusion criteria (for analysis):** ◆ previous breast-conserving surgery followed by RT, ◆ previous breast augmentation, ◆ diagnosis of breast sarcoma, prophylactic mastectomy, ◆ immediate autologous reconstruction (ABR), ◆ direct-to-implant (DTI) and prepectoral implants,	**Interventions** A: RT after implant, on tissue expander or final implant (subgroup timing reported) · N = 105 B: no RT after implant · N = 78 **Analysis** ◆ A univariable logistic regression analysis of various patient-related and treatment-related factors for the outcomes implant	**Complications:** ◆ Minor complications: · RT to TE/I: 13/105 · No RT: 7/78 ◆ Major complications: · RT to TE/I: 19/105 · No RT: 13/78 ◆ Seroma · RT to TE/I: 3/105 · No RT: 1/78 ◆ Necrosis · RT to TE/I: 3/105 · No RT: 8/78 ◆ Implant failure · RT to TE/I: 27/105 · No RT: 3/78 ◆ Infections: · RT to TE/I: 9/105	**General information** ◆ **Follow-up:** mean follow-up · TE-PMRT: 4.58 years · PI-PMRT: 7 years · no-PMRT: 5.75 years ◆ **Funding**: No intramural or extramural funding supported this study. ◆ **CoI**: The authors declare that they have no conflict of interest. **Risk of bias considerations (adapted from SIGN cohort study checklist)** ◆ Study type: retrospective cohort study ◆ Confounding: Moderate risk (baseline characteristics are comparable, however, no adjustment in analysis, remaining unobserved confounding possible) ◆ Selection bias into the study: Unclear, no information provided. ◆ Intervention

Reference/ Study type	Population	Interventions	Main results	Methodological evaluation
	◆ delayed reconstruction. **Enrolment period** ◆ between 2010 and 2019 **Follow-up** ◆ between 4.6 and 7 years mean FU depending on the group **Descriptive statistics** ◆ Age (mean, SD, years) · TE-PMRT: 49.4 (9.8) · PI-PMRT: 51.08 (12.1) · no RT: 50.3 (10.6) ◆ BMI (median, range) · TE-PMRT: 25.9 (5.3) · PI-PMRT: 25.3 (4.06) · no RT: 23.5 (3.7) ◆ Stadium · TE-PMRT: ▪ G1: 1.8% ▪ G2: 34.5% ▪ G3: 32.7% ▪ Gx: 31% · PI-PMRT: ▪ G1: 6.1% ▪ G2: 40% ▪ G3: 30.6% ▪ Gx: 24.5% · no RT: ▪ G1: 9% ▪ G2: 43.6%	failure and capsular contracture	· No RT: 3/78 ◆ Capsular contracture · RT to TE/I: 60/105 · No RT: 3/78 ◆ Implant loss: · RT to TE/I: 8/105 · No RT: 2/78 ◆ Reoperation: · RT to TE/I: 11/105 · No RT: 7/78 ◆ Wound complications: · RT to TE/I: 4/105 · No RT: 6/78	· Assessment reliable: yes · Assessed more than once: no · Possibly affected by knowledge of outcome status? No (prospective data collection) ◆ Drop-out rate & reasons reported: · Low risk: no drop-outs ◆ Outcome · Outcome measure is well-defined, valid and reliable; · No blind outcome assessment, however, this is unlikely to affect the results; as the outcomes are standard clinical characteristics ◆ Main cofounders taken into account: oly for two outcomes. ◆ Confidence intervals reported: no (for two outcomes: yes) Selective reporting (comparison with protocol): no protocol provided, not assessable.

Reference/ Study type	Population	Interventions	Main results	Methodological evaluation
	▪ G3: 38.5% ▪ Gx: 9% ◆ Adjuvant chemotherapy (% yes) · TE-PMRT: 58.2% · PI-PMRT: 70% · no RT: 53.9% ◆ Neoadjuvant chemotherapy (% yes) · TE-PMRT: 38.2% · PI-PMRT: 42% · no RT: 7.5% ◆ Reconstruction type: Tissue expander and later implant ◆ Mesh/ADM: no mesh used ◆ Implant position: retropectoral			
Conte 2023 Retrospective cohort study	**Inclusion criteria (for analysis):** ◆ Female at birth ◆ 18 years or older and underwent mastectomy with immediate IBR **Exclusion criteria:** ◆ Patients who did not present to their follow-up visits ◆ Patients who underwent autologous tissue reconstruction using a deep inferior epigastric perforator (DIEP) flap technique were included in demographic data but excluded from the statistical analysis of complications following IBR **Enrolment period**	**Interventions** A: RT after implant-based reconstruction · N = 73 B: no RT after implant · N = 244 **Analysis** ◆ Frequencies, for overall complications multivariable analysis ◆ No adjustment for frequencies, overall	**Complications (breasts):** ◆ overall complications: · RT: 45/72 · No RT: 130/395 ◆ Capsular contracture · RT to TE/I: 26/72 · No RT: 63/395 ◆ Implant loss: · RT to TE/I: 26/72 · No RT: 80/395	**General information** ◆ **Follow-up:** NR ◆ **Funding**: NR ◆ **CoI**: The Authors have no conflicts to interest to declare in relation to this study. **Risk of bias considerations (adapted from SIGN cohort study checklist)** ◆ Study type: retrospective cohort study ◆ Confounding: Moderate risk for overall complications, high risk for capsular contracture, implant loss ◆ Selection bias into the study: Unclear, no information provided. ◆ Intervention

Reference/ Study type	Population	Interventions	Main results	Methodological evaluation
	◆ 1 January 2017 to 31 December 2019 **Follow-up** ◆ NR **Descriptive statistics (reported for complete cohort)** ◆ Age: median 51 (range 19 to 83) years ◆ BMI: median 26.5 (range 16.64 to 48.90) ◆ Stadium: · I: 21% · II: 20% · III: 9% · IV: 1% · prophylactic: 47% · unknown: 2% ◆ Adjuvant chemotherapy: NR ◆ Neoadjuvant chemotherapy: NR ◆ Reconstruction type · DTI: 35% · Tissue expander: 60% ◆ Mesh/ADM (%) · dermal matrix: 75% · no dermal matrix: 25% ◆ Implant position: NR	complications adjusted for age, ethnicity, race, mastectomy type, DTI vs expander reconstruction, use of dermal matrix, neoadjuvant chemotherapy, BMI, smoking, diabetes, autoimmune disease, previous cosmetic breast surgery		· Assessment reliable: yes · Assessed more than once: no · Possibly affected by knowledge of outcome status? No ◆ Drop-out rate & reasons reported: · moderate risk: 34 out of 351 patients were excluded due to lack of follow-up ◆ Outcome · Outcome measure is well-defined, valid and reliable; · No blind outcome assessment, however, this is unlikely to affect the results; as the outcomes are standard clinical characteristics ◆ Main cofounders taken into account: only for overall complications ◆ Confidence intervals reported: no (for overall complications yes) ◆ Selective reporting (comparison with protocol): no protocol provided, not assessable.
Dave 2023 retrospective cohort study	**Inclusion criteria (for analysis):** ◆ PP-IBBR owing to mastectomy for cancer ◆ prophylactic mastectomy for risk reduction	**Interventions** A: RT after implant-based reconstruction · N = 9	**Complications (breasts):** ◆ Minor complications: · RT: 2/9 · No RT: 47/436	**General information** ◆ **Follow-up:** Median follow-up was 21 (range 2–71) months ◆ **Funding**: NR

Reference/ Study type	Population	Interventions	Main results	Methodological evaluation
	◆ prepectoral correction of previous submuscular reconstruction, such as for implant displacement, animation deformity **Exclusion criteria:** ◆ NR **Enrolment period** ◆ June 2013 to March 2019 **Follow-up** ◆ Median follow-up 21 (range 2–71) months **Descriptive statistics (reported for complete cohort)** ◆ Age: mean age 44 (range 20–78) years ◆ BMI: >=30: 10.2% ◆ Stadium: NR ◆ Adjuvant chemotherapy: NR ◆ Neoadjuvant chemotherapy: 6,2% ◆ Reconstruction type: all DTI ◆ Mesh/ADM: 100% ◆ Implant position: 100% prepectoral	B: no RT after implant · N = 436 **Analysis** ◆ Frequencies, for overall complications and implant loss multivariable analysis ◆ No adjustment for frequencies, multivariable analysis adjusted for sentinel node biopsy, axillary clearance, Wise-pattern incision, and adjuvant radiotherapy	◆ Major complications · RT to TE/I: 4/9 · No RT: 23/436 · OR 7.11, 95% CI 1.6 to 31.61 ◆ Overall complications · RT to TE/I: 70/9 · No RT: 80/436 ◆ Implant loss · RT to TE/I: 2/9 · No RT: 13/436 · OR 5.09, 95% CI 0.83 to 31.18	◆ **CoI**: The authors declare no conflict of interest. **Risk of bias considerations (adapted from SIGN cohort study checklist)** ◆ Study type: retrospective cohort study ◆ Confounding: High risk, no adjustment for baseline characteristics ◆ Selection bias into the study: Unclear, no information provided. ◆ Intervention · Assessment reliable: yes · Assessed more than once: no · Possibly affected by knowledge of outcome status? No ◆ Drop-out rate & reasons reported: · High risk: not reported ◆ Outcome · Outcome measure is well-defined, valid and reliable; · No blind outcome assessment, however, this is unlikely to affect the results; as the outcomes are standard clinical characteristics ◆ Main cofounders taken into account: No ◆ Confidence intervals reported: no ◆ Selective reporting (comparison with protocol): no protocol provided, not assessable.
De Boniface 2022	**Inclusion criteria (for analysis):**	**Interventions**	**Complications**	**General information**

Reference/ Study type	Population	Interventions	Main results	Methodological evaluation
retrospective cohort study	◆ primary or recurrent breast cancer ◆ Patients with bilateral disease were registered as two cases if both sides fulfilled the inclusion criteria; otherwise, only the eligible side was registered. **Exclusion criteria (for analysis):** ◆ Risk-reducing mastectomies **Enrolment period** ◆ 1 January 2005 to 31 December 2015 **Follow-up:** ~median 72 months **Descriptive statistics** ◆ Age (median, range) · PMRT: 47 (range 21-78) · no PMRT: 50 (range 21-79) ◆ BMI (median, range): NR ◆ Stadium · PMRT: ▪ T1: 38.6% ▪ T2: 43.7% ▪ T3: 16.9% ▪ missing: 0.7% · no PMRT: ▪ T1: 66.6% ▪ T2: 32.0% ▪ T3: 0.9% ▪ Missing: 0.5% ◆ Neoadjuvant chemotherapy (% yes) · PMRT: 25.8%	A: RT after implant · N = 749 B: no RT after implant · N = 856 **Analysis** ◆ univariable and multivariable logistic regression analyses for implant loss, frequencies for reoperation ◆ implant loss adjusted for low risk: adjusted for ADM, hospital, lymph node dissection, nipple-sparing mastectomy, specimen weight, type of implant, ipsilateral revisional surgery, neoadjuvant chemotherapy, endocrine therapy, smoking, diabetes, antihypertensive meds, immunosuppressive meds, BMI, Age	◆ Reoperation: · RT: 549/749 · No RT: 536/856 ◆ Implant loss (due to complication or patient wish) · RT: 132/631 · No RT: 56/636 · HR: 2.44, 95% CI 1.7 to 3.52	◆ **Follow-up**, median · PMRT: 72 (range 1-190) · no PMRT: 71 (range 1-198) ◆ **Funding**: Swedish Breast Cancer Association (Bröstcancerförbundet). · J.d.B. is supported by a Junior Clinical Investigator Award from the Swedish Cancer Society (CAN 2017/1036). A.L.V.J. is supported by a Research Starting Grant from the Swedish Research Council (2021-01657). · The funding organization had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication. ◆ **CoI**: The authors declare no conflict of interest. **Risk of bias considerations (adapted from SIGN cohort study checklist)** ◆ Study type: retrospective cohort study ◆ Confounding: low risk for implant loss (overall), high risk for reoperation (no adjustment) ◆ Selection bias into the study: Unclear, no information provided. ◆ Intervention

Reference/ Study type	Population	Interventions	Main results	Methodological evaluation
	· no PMRT: 3.6% ◆ Adjuvant chemotherapy · PMRT: 82.8% · no PMRT: 48.2% ◆ Reconstruction type (%) · Permanent: ▪ PMRT: 17.4% ▪ no PMRT: 24.9% · permanent expander: ▪ PMRT: 51.1% ▪ no PMRT: 46.1% · temp. expander ▪ PMRT: 30.4% ▪ no PMRT: 27.3% ◆ Mesh/ADM (%) · PMRT: 3.7% · no PMRT: 4.1% ◆ Implant position (sub, prepectoral?) · complete muscle coverage: ▪ PMRT: 94.7% ▪ no PMRT: 94.7% · partly submuscular ▪ PMRT: 5.3% ▪ no PMRT: 5.3% · prepectoral ▪ PMRT: 0 ▪ no PMRT: 0			· Assessment reliable: yes · Assessed more than once: no · Possibly affected by knowledge of outcome status? No ◆ Drop-out rate & reasons reported: · High risk: not reported ◆ Outcome · Outcome measure is well-defined, valid and reliable; · No blind outcome assessment, however, this is unlikely to affect the results; as the outcomes are standard clinical characteristics ◆ Main cofounders taken into account: yes, for implant loss, no for reoperation ◆ Confidence intervals reported: partly ◆ Selective reporting (comparison with protocol): no protocol provided, not assessable.
Doherty 2023	**Inclusion criteria (for analysis):**	**Interventions** A: RT after implant	**Complications** ◆ Reoperation:	**General information** ◆ **Follow-up range:** 3.7 years to 11.7 years

Reference/ Study type	Population	Interventions	Main results	Methodological evaluation
retrospective cohort study	◆ mastectomy and same day breast reconstruction, for any indication **Exclusion criteria (for analysis):** ◆ non-Ontario residents, ◆ pediatric patients, ◆ those with missing or invalid age, sex, or mastectomy laterality ◆ Patients who had undergone a prior mastectomy, did not have an associated physician billing record, or had an uncertain reconstruction status or approach ◆ For the current study, we additionally excluded patients without immediate breast reconstruction as well as those who died or experienced flap loss or explantation before the start of follow-up period (see exposure definition in the Variable Definitions section). **Enrolment period** ◆ 1 January 2007 to 31 December 2014 **Follow-up:** 3.7 years to 11.7 years **Descriptive statistics** ◆ Age (median, IQR) · RT: median 47.5 (IQR 41.0-55.0) · No RT: median 49.0 (IQR 43.0-56.0) ◆ BMI (median, range): NR ◆ Stadium · Stage 0: ≤5 vs. NR	· N = 378 B: no RT after implant · N = 1964 **Analysis** ◆ Multivariable Cox regression analysis ◆ HR adjusted for patient age, institution teaching status, cancer diagnosis in past year, history of breast-conserving surgery with radiation, reconstruction type, and reoperation within the first 10 months of surgery.	· RT: 216/378 · No RT: 719/1964 · HR 1.82, 95% CI 1.49 to 2.23	◆ **Funding**: Project-specific funding was not obtained for this study, but the project was supported by the Institute for Clinical Evaluative Sciences, Western University, and the Department of Surgery at the Schulich School of Medicine and Dentistry, University of Western Ontario, Canada. ◆ **CoI**: The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper. **Risk of bias considerations (adapted from SIGN cohort study checklist)** ◆ Study type: retrospective cohort study ◆ Confounding: Low risk, adjustment for sufficient factors ◆ Selection bias into the study: Unclear, no information provided. ◆ Intervention · Assessment reliable: yes · Assessed more than once: no · Possibly affected by knowledge of outcome status? No ◆ Drop-out rate & reasons reported: · High risk: not reported ◆ Outcome · Outcome measure is well-defined, valid and reliable;

Reference/ Study type	Population	Interventions	Main results	Methodological evaluation
	· Stage I: 18.9% vs. 57.8% · Stage II: 45.9% vs. 25.3% · Stage III: 31.7% vs. 2.6% · Stage IV: ≤5 vs. ≤5 · Stage not available: 2.4% vs. 11.1% ◆ Neoadjuvant chemotherapy: NR ◆ Adjuvant chemotherapy: NR ◆ Reconstruction type (%) · Flap: 27.2% vs. 31.1% · Implant: 64.6% vs. 59.0% · Implant and flap: 8.2% vs. 9.9% ◆ Mesh/ADM: NR ◆ Implant position: NR			· No blind outcome assessment, however, this is unlikely to affect the results; as the outcomes are standard clinical characteristics ◆ Main cofounders taken into account: yes ◆ Confidence intervals reported: yes ◆ Selective reporting (comparison with protocol): no protocol provided, not assessable.
Dominici 2021 cross-sectional study	**Inclusion criteria (for analysis):** ◆ women diagnosed with primary invasive breast cancer or ductal carcinoma in situ ◆ at 40 years or younger **Exclusion criteria (for analysis):** ◆ only a short-form survey (eg, all patients enrolled in Toronto, n = 91), ◆ deceased or lost to follow-up (n = 411 ◆ confirmed recurrence or who presented with de novo stage IV disease (n = 52) **Enrolment period** ◆ 10 October 2006 to 30 June 2016	**Interventions** A: RT after implant · N = 113 B: no RT after implant · N = 174 **Analysis** ◆ Mean scores	**Quality of Life: Breast-Q** ◆ satisfaction with breasts: · RT: 53 · No RT: 64 ◆ Psychosocial well-being: · RT: 66 · No RT: 72 ◆ Sexual well-being: · RT: 47 · No RT: 52 ◆ Physical well-being: · RT: 77 · No RT: 80	**General information** ◆ **Follow-up:** median of 5.8 years (range, 1.9-10.4 years) from diagnosis ◆ **Funding**: Supported in part by grant SAC1000008 from the Susan G. Komen Foundation (Dr Partridge), grant BCRF17-121 from the Breast Cancer Research Foundation (Dr Partridge), and grant K01HS023680 from the Agency for Healthcare Research and Quality (Dr Rosenberg). ◆ **CoI**: Dr King reported receiving speaker's fees from and serving on an advisory board for Exact Sciences (formerly Genomic Health) and serving as information service faculty and on the

Reference/ Study type	Population	Interventions	Main results	Methodological evaluation
	Follow-up ◆ median of 5.8 years (range, 1.9-10.4 years) from diagnosis **Descriptive statistics** ◆ Age: median 36 years, range 17-40 ◆ BMI (%) · <18.5: 4% · 18.5-24.9: 60% · >=25: 32% ◆ Stadium · 0: 10% · 1: 38% · 2: 39% · 3: 13% ◆ Neoadjuvant chemotherapy: 73% ◆ Adjuvant chemotherapy: NR ◆ Reconstruction type (%) · No Reconstruction: 11% · Implant-based reconstruction: 72% · Autologous reconstruction: 14% · complex reconstruction: 3% · unkown: 0% ◆ Mesh/ADM: NR ◆ Implant position: NR			virtual tumor board for Precisca Cancer outside the submitted work. Dr Peppercorn reported having a spouse who is an employee of GlaxoSmithKline outside the submitted work. Dr Rosenberg reported receiving grants from the Agency for Healthcare Research and Quality, Breast Cancer Research Foundation, and Susan G. Komen Foundation during the conduct of the study. No other disclosures were reported. **Risk of bias considerations (adapted from SIGN cohort study checklist)** ◆ Study type: retrospective cohort study ◆ Confounding: high risk: unclear, as the main comparison was not RT vs. No RT. Unadjusted analyses. ◆ Selection bias into the study: · high risk: enrolled were 1302, 411 were decseased/lost-to-follow-up; 159 non-responders were excluded ◆ Intervention · Assessment reliable: yes · Assessed more than once: no · Possibly affected by knowledge of outcome status? No ◆ Drop-out rate & reasons reported: · moderate risk: 34 out of 351 patients were excluded due to lack of follow-up

Reference/ Study type	Population	Interventions	Main results	Methodological evaluation
				◆ Outcome · Outcome measure is well-defined, valid and reliable; validated questionnaire BRAST-Q · No blind outcome assessment, this may affect the results ◆ Main cofounders taken into account: no ◆ Confidence intervals reported: no ◆ Selective reporting (comparison with protocol): no protocol provided, not assessable.
Emanuele Lisa 2023 retrospective case-control study	**Inclusion criteria (for analysis):** ◆ female patients ◆ age over 18 years at the time of diagnosis ◆ patients who had undergone mastectomy and immediate reconstruction with implant in one or two stages or with autologous flaps with or without adjuvant radiotherapy. **Exclusion criteria (for analysis):** ◆ patients with prior breast or chest wall irradiation ◆ delayed reconstruction ◆ patients lost to follow-up. **Enrolment period** ◆ 2001 to 2020 **Follow-up**	**Interventions** A: RT after implant · N = 1088 B: no RT after implant · N = 1841 **Analysis** ◆ Frequencies ◆ No adjustment.	**Complications** ◆ Reconstruction failure · RT: 48/1088 · No RT: 20/1841 ◆ Implant loss · RT: 194/1088 · No RT: 115/1841 ◆ Reoperation · RT: 270/1088 · No RT: 81/1841 ◆ Overall complications · RT: 662/1088 · No RT: 472/1841 ◆ Minor complications · RT: 209/1088 · No RT: 270/1841 ◆ Major complications	**General information** ◆ **Follow-up**: · DTI: · PMRT: 2.8 years (IQR 2.0-4.0) · no PMRT: 2.4 years (IQR 1.9-3.3) · TE: · PMRT: 2.3 years (IQR 1.5-3.4) · no PMRT: 2.4 years (1.6-3.2) ◆ **Funding**: Humanitas Clinical and Research Center ◆ **CoI**: The authors declare that they have no conLicts of interest. **Risk of bias considerations (adapted from SIGN cohort study checklist)** ◆ Study type: retrospective cohort study ◆ Confounding: high risk: no adjustment for relevant clinical characteristics such

Reference/ Study type	Population	Interventions	Main results	Methodological evaluation
	◆ Between 2 and 3 years, see methodological evaluation **Descriptive statistics** ◆ Age · DTI: ▪ PMRT: median 49 (IQR 43-56) ▪ no PMRT: median 47 (IQR 41-53) · TE: ▪ PMRT: median 49 (IQR 43-57) ▪ no PMRT: median 50 (IQR 44-58) ◆ BMI (%) · DTI: ▪ PMRT: median 22.4 (IQR 20.6-24.2) ▪ no PMRT: median 22.0 (IQR 20.1-23.7) · TE: ▪ PMRT: 23.7 (IQR 21.0-26.6) ▪ no PMRT: 23.2 (IQR 21.1-25.8) ◆ Stadium: NR ◆ Neoadjuvant chemotherapy: · DTI: ▪ PMRT: 32.1% ▪ no PMRT: 20.2% · TE: ▪ PMRT: 25.1% ▪ no PMRT: 10.3%		· RT: 551/1088 · No RT: 229/1841 ◆ Hematoma · RT: 37/1088 · No RT: 60/1841 ◆ Seroma · RT: 133/1066 · No RT: 139/1841 ◆ Necrosis · RT: 61/1088 · No RT: 104 /1841 ◆ Infections · RT: 66/1088 · No RT: 176 /1841	as receipt of chemotherapy or axillary dissection. ◆ Selection bias into the study: Unclear, patients lost to follow-up were excluded, unclear how many these were; case-control study ◆ Intervention · Assessment reliable: yes · Assessed more than once: no · Possibly affected by knowledge of outcome status? Although this is a case-control study, it is unlikely that RT-status was manipulated after data acquisition. ◆ Drop-out rate & reasons reported: · High risk: not reported ◆ Outcome · Outcome measure is well-defined, valid and reliable; · No blind outcome assessment, however, this is unlikely to affect the results; as the outcomes are standard clinical characteristics ◆ Main cofounders taken into account: no ◆ Confidence intervals reported: no ◆ Selective reporting (comparison with protocol): protocol/trial registry entry available, no selective reporting

Reference/ Study type	Population	Interventions	Main results	Methodological evaluation
	◆ Adjuvant chemotherapy: · DTI: ▪ PMRT: 57.4% ▪ no PMRT: 26.4% · TE: ▪ PMRT: 53.3% ▪ no PMRT: 35.3% ◆ Reconstruction type (%) · DTI: 1227 pts ▪ PMRT: 31.9% ▪ no PMRT: 67.9% · TE: 1702 pts ▪ PMRT: 40.9% ▪ no PMRT: 59.1%Mesh/ADM: NR ◆ Mesh/ADM: no mesh used. ◆ Implant position: retropectoral			
Jeon 2023 retrospective cohort study	**Inclusion criteria (for analysis):** ◆ diagnosed with primary breast cancer, who had undergone mastectomy with DTI breast reconstruction **Exclusion criteria (for analysis):** ◆ previous breast surgery, ◆ refusal to sign the consent form, ◆ previous radiotherapy, ◆ follow-up period < 6 months, ◆ missing data for the pertinent variables. **Enrolment period** ◆ August 2011 to June 2021	**Interventions** A: RT after implant · N = 64 B: no RT after implant · N = 176 **Analysis** ◆ Multivariable logistic regression ◆ Adjusted for age, body mass index,	**Complications** ◆ Overall complications · OR 1.906, 95% CI 1.032 to 3.521 ◆ Capsular contracture · OR 3.261, 95% CI 1.576 to 1.155 in favour of no RT	**General information** ◆ **Follow-up:** approximately 20 months ◆ **Funding**: Faculty Research Grant from Yonsei University College of Medicine (6-2018-0062, Kim YS). ◆ **CoI**: The authors declare that they have no competing interests. **Risk of bias considerations (adapted from SIGN cohort study checklist)** ◆ Study type: retrospective cohort study ◆ Confounding: Low risk, adjusted for relevant confounders

Reference/ Study type	Population	Interventions	Main results	Methodological evaluation
	Follow-up · approximately 20 months **Descriptive statistics** ◆ Age: mean 47 years, SD 7.9 ◆ BMI: mean 22.5, SD 3 ◆ Stadium: · 0: 30% · 1: 33.5% · 2: 29.5% · 3: 6.4% · 4: 0.3% ◆ Neoadjuvant chemotherapy: 45% ◆ Adjuvant chemotherapy: 60% ◆ Reconstruction type: all DTI ◆ Mesh/ADM: 100% ADM ◆ Implant position: mostly sub-pectoral	pathologic tumor stage, mastectomy, axillary surgery, implant-based breast reconstruction (size, surface, insertion plane), positive lymph nodes, dissected lymph nodes, neo-adjuvant and adjuvant chemotherapy, Herceptin, hormone, radiotherapy, diabetes mellitus, hypertension, smoking, drainage duration, follow-up duration.		◆ Selection bias into the study: Unclear, patients with missing data were excluded ◆ Intervention · Assessment reliable: yes · Assessed more than once: no · Possibly affected by knowledge of outcome status? No ◆ Drop-out rate & reasons reported: · High risk: not reported ◆ Outcome · Outcome measure is well-defined, valid and reliable; · No blind outcome assessment, however, this is unlikely to affect the results; as the outcomes are standard clinical characteristics ◆ Main cofounders taken into account: yes ◆ Confidence intervals reported: yes ◆ Selective reporting (comparison with protocol): no protocol provided, not assessable.
Koojman 2022 retrospective cohort study	**Inclusion criteria (for analysis):** ◆ therapeutically operated for carcinoma or ductal carcinoma in situ (DCIS) **Exclusion criteria (for analysis):** ◆ prophylactic procedures ◆ two-staged tissue expander/implant,	**Interventions** A: RT after implant · N = 273 B: no RT after implant · N = 739	**Complications** ◆ Implant loss · RT: 16/273 · No RT: 45/739 ◆ Reoperation (surgical reintervention)	**General information** ◆ **Follow-up**: 16 weeks ◆ **Funding**: NR ◆ **CoI**: None declared. **Risk of bias considerations (adapted from SIGN cohort study checklist)**

Reference/ Study type	Population	Interventions	Main results	Methodological evaluation
	◆ RT before mastectomy **Enrolment period** ◆ 1 January 2013 to 31 December 2018 **Follow-up** ◆ 16 weeks **Descriptive statistics** ◆ Age: · PMRT: mean 44.1, SD 11.57 (range 25-72) · no PMRT: mean 48.4, SD 10.91 (range 19-76) ◆ BMI: · PMRT: 24.0 (16.7–43.4; SD 3.72) · no PMRT: 23.5 (16.5–40.4; SD 3.90) ◆ Stadium: NR ◆ Neoadjuvant chemotherapy: · PMRT: 77.5% · no PMRT: 29.7% ◆ Adjuvant chemotherapy: · PMRT: 8.4% · no PMRT: 22.6% ◆ Reconstruction type: all DTI ◆ Mesh/ADM: 100% ADM (alloderm) ◆ Implant position: all sub-pectoral	**Analysis** ◆ Frequencies ◆ No adjustment.	· RT: 56/273 · No RT: 182/739 ◆ Hematoma · RT: 14/273 · No RT: 27/739 ◆ Seroma · RT: 0/273 · No RT: 3/739 ◆ Necrosis · RT: 28/273 · No RT: 123 /739 ◆ Infections · RT: 14/273 · No RT: 29/739	◆ Study type: retrospective cohort study ◆ Confounding: high risk: no adjustment despite considerable differences in baseline characteristics, such as previous and adjuvant chemotherapy, carcinoma, etc. ◆ Selection bias into the study: low risk: prospective data collection, reasons for exclusions provided ◆ Intervention · Assessment reliable: yes · Assessed more than once: no · Possibly affected by knowledge of outcome status? No ◆ Drop-out rate & reasons reported: · Low risk: no drop-outs ◆ Outcome · Outcome measure is well-defined, valid and reliable; · No blind outcome assessment, however, this is unlikely to affect the results; as the outcomes are standard clinical characteristics ◆ Main cofounders taken into account: No ◆ Confidence intervals reported: no ◆ Selective reporting (comparison with protocol): no protocol provided, not assessable.

Reference/ Study type	Population	Interventions	Main results	Methodological evaluation
Lee 2023 retrospective cohort study	**Inclusion criteria (for analysis):** ◆ Patients who had undergone DIEP flap surgery (DIEP flap group) or two-stage TE/I for breast reconstruction (TE/I group) **Exclusion criteria (for analysis):** ◆ other reconstruction modalities, such as latissimus dorsi myocutaneous or direct-to-implant flaps, which were rarely adopted in our institution during the study period ◆ those who did not complete both stages during the follow-up period owing to causes unrelated to complications; ◆ those who underwent the second stage of exchange-to-implant in another clinic; ◆ those who had planned conversion to autologous tissue reconstruction following tissue expander insertion; ◆ those who had been lost to follow-up within 2 years postoperatively. **Enrolment period** ◆ 2012 to 2017 **Follow-up** ◆ Minimum 24 months **Descriptive statistics**	**Interventions** A: RT after implant · N = 223 B: no RT after implant · N = 939 **Analysis** ◆ Frequencies, Multivariable Cox regression analysis ◆ Adjusted for age, BMI, diabetes, hypertension, smoking status, type of mastectomy, weight of the mastectomy specimen, neoadjuvant chemotherapy, adjuvant chemotherapy, and adjuvant radiotherapy	**Complications** ◆ Major complications · RT: 42/223 · No RT: 70/939 · HR 2.612, 95% CI 1.78 to 3.832	**General information** ◆ **Follow-up:** 24 months ◆ **Funding**: NR ◆ **CoI**: The authors declare no competing interests. **Risk of bias considerations (adapted from SIGN cohort study checklist)** ◆ Study type: retrospective cohort study ◆ Confounding: moderate: multivariable model, PICO of publication DIEP vs. TE, so no baseline table 1 for our question. ◆ Selection bias into the study: Unclear, no information provided. ◆ Intervention · Assessment reliable: yes · Assessed more than once: no · Possibly affected by knowledge of outcome status? No ◆ Drop-out rate & reasons reported: · High risk: not reported ◆ Outcome · Outcome measure is well-defined, valid and reliable; · No blind outcome assessment, however, this is unlikely to affect the results; as the outcomes are standard clinical characteristics ◆ Main cofounders taken into account: yes ◆ Confidence intervals reported: yes

Reference/ Study type	Population	Interventions	Main results	Methodological evaluation
	◆ Age: mean 44.1 years (range, 18–66 years) ◆ BMI: mean 22.5 kg/m2 (range, 15.1–39.8) ◆ Stadium: NR ◆ Neoadjuvant chemotherapy: 8% ◆ Adjuvant chemotherapy: 36% ◆ Reconstruction type: all tissue expander and later implant ◆ Mesh/ADM: 100% NR ◆ Implant position: NR			◆ Selective reporting (comparison with protocol): no protocol provided, not assessable.
Lin 2023 retrospective cohort study	**Inclusion criteria (for analysis):** ◆ therapeutically operated for carcinoma or ductal carcinoma in situ (DCIS) **Exclusion criteria (for analysis):** ◆ prophylactic procedures ◆ two-staged tissue expander/implant, ◆ RT before mastectomy **Enrolment period** ◆ 1 January 2013 to 31 December 2018 **Follow-up** ◆ 16 weeks **Descriptive statistics** ◆ Age: mean age 47.7 years (range, 18 to 80 years) ◆ BMI: mean 24.3 kg/m2 (range, 15.4 to 43.7 kg/m2) ◆ Stadium: NR	**Interventions** A: RT after implant · N = 360 B: no RT after implant · N = 2675 **Analysis** ◆ Multivariable logistic regression analysis ◆ Adjusted for age, BMI, diabetes, smoking, preoperative RT, neoadjuvant chemotherapy, reconstruction type, pocket technique, incision type	**Complications** ◆ Major complications · OR 1.457, 95% CI 0.986 to 2.153 ◆ Necrosis · OR 0.969, 95% CI 0.283 to 3.316	**General information** ◆ **Follow-up:** minimum 24 months ◆ **Funding**: NR ◆ **CoI**: Dr. Liao had consulting contracts with Abbvie/Allergan, the Musculoskeletal Transplant Foundation, and Integra, but he is explicitly not a speaker nor does he represent any industry entities. Dr. Austen is a founder of Cytrellis, Durvena, and AuraGen, which was acquired by Sientra, and owns stock in Sientra. Dr. Colwell will receive royalties from Wolters Kluwer as the Plastic Surgery section editor for UpToDate. The remaining authors have no financial disclosures to report. **Risk of bias considerations (adapted from SIGN cohort study checklist)** ◆ Study type: retrospective cohort study

Reference/ Study type	Population	Interventions	Main results	Methodological evaluation
	◆ Neoadjuvant chemotherapy: 13% ◆ Adjuvant chemotherapy: 25% ◆ Reconstruction type: · DTI: 2043 · TE: 992 ◆ Mesh/ADM: 100% ADM (alloderm) ◆ Implant position: all sub-pectoral			◆ Confounding: Moderate risk: multivariable model, PICO does not correspond, unclear which covariates stayed in the model ◆ Selection bias into the study: Unclear, no information provided. ◆ Intervention · Assessment reliable: yes · Assessed more than once: no · Possibly affected by knowledge of outcome status? No ◆ Drop-out rate & reasons reported: · High risk: not reported ◆ Outcome · Outcome measure is well-defined, valid and reliable; · No blind outcome assessment, however, this is unlikely to affect the results; as the outcomes are standard clinical characteristics ◆ Main cofounders taken into account: partly ◆ Confidence intervals reported: yes ◆ Selective reporting (comparison with protocol): no protocol provided, not assessable.
Martins 2023	**Inclusion criteria (for analysis):** ◆ female gender,	**Interventions** A: RT after implant	**Complications** ◆ Capsular contracture	**General information** ◆ **Follow-up:** mean 24 (SD 15)

Reference/ Study type	Population	Interventions	Main results	Methodological evaluation
retrospective cohort study	◆ those aged above 18 years, ◆ direct-to-implant submuscular breast reconstruction with an ADM sling with Native® biological matrix **Exclusion criteria (for analysis):** ◆ other types of breast reconstruction, ◆ submuscular reconstruction with tissue expanders ◆ less than one month of follow-up. ◆ Patients with advanced disease at the initial diagnosis, as it represents a contraindication for immediate reconstruction **Enrolment period** ◆ October 2016 to March 2020 **Follow-up** ◆ mean 24 (SD 15) **Descriptive statistics** ◆ Age: mean 45.9 (SD 9.1) ◆ BMI: mean 23.4 (SD 3.3) ◆ Stadium: NR ◆ Neoadjuvant chemotherapy: 14% ◆ Adjuvant chemotherapy: 37% ◆ Reconstruction type: all DTI ◆ Mesh/ADM: ADM Native biological matrix ◆ Implant position: all sub-pectoral	· N = 21 B: no RT after implant · N = 105 **Analysis** ◆ Frequencies ◆ RR reported, unclear adjustment	· RT: 11/21 · No RT: 2/105	◆ **Funding**: NR ◆ **CoI**: The authors have declared that no competing interests exist. **Risk of bias considerations (adapted from SIGN cohort study checklist)** ◆ Study type: retrospective cohort study ◆ Confounding: moderate risk: multivariable model, main PICO does not correspond, unclear which covariates stayed in the model ◆ Selection bias into the study: Unclear, no information provided. ◆ Intervention · Assessment reliable: yes · Assessed more than once: no · Possibly affected by knowledge of outcome status? No ◆ Drop-out rate & reasons reported: · High risk: not reported ◆ Outcome · Outcome measure is well-defined, valid and reliable; · No blind outcome assessment, however, this is unlikely to affect the results; as the outcomes are standard clinical characteristics ◆ Main cofounders taken into account: no ◆ Confidence intervals reported: yes

Reference/ Study type	Population	Interventions	Main results	Methodological evaluation
				◆ Selective reporting (comparison with protocol): no protocol provided, not assessable.
Naoum 2022 retrospective cohort study	**Inclusion criteria (for analysis):** primary tumor treated with mastectomy and immediate two stages (TE/I) reconstruction **Exclusion criteria (for analysis):** ◆ bilateral breast cancer, ◆ inflammatory breast cancer, ◆ local failure cases treated with mastectomy and reconstruction, ◆ patients who received radiation after lumpectomy and electively underwent mastectomy with reconstruction ◆ patients who underwent direct-to-implant immediate reconstruction. **Enrolment period** ◆ 2000 to 2019 **Follow-up** ◆ RTE: 84.3 (46.6, 115.7) ◆ RTI: 45.5 (30.7, 68.5) ◆ no PMRT: 101.5 (58.8, 136.4) **Descriptive statistics** ◆ Age (median, IQR) · RTE: 46.3 (40.5, 51.8) · RTI: 44.1 (38.9, 49.9)	**Interventions** A: RT after implant · N = 309 B: no RT after implant · N = 352 **Analysis** ◆ Logistic regression for RT on tissue expander and final implant separately reported, otherwise frequencies ◆ Adjusted for expander/implant coverage, smoking, and BMI, and compared RTI and RTE to no PMRT	**Complications** ◆ Infections: · RT: 64/309 · No RT: 45/352 · For RT on tissue expander: OR 2.17 (95% CI 1.35-3.47) · For RT on final implant: OR 1.38 (95% CI 0.69-2.76) ◆ Capsular contracture · RT: 47/309 · No RT: 17/352 · For RT on tissue expander: OR 3.4 (95% CI 1.77 to 6.54) · For RT on final implant: OR 5.22 (95% CI 2.4 to 11.4) ◆ Implant loss ("overall failure": removal of implant for any complications regardless replacement) · RT: 115/309 · No RT: 77/352 · For RT on tissue expander: OR 2.72 (95% CI 1.82 to 4.05) · For RT on final implant: OR 1.76 (95% CI 1.0 to 3.1)	**General information** ◆ **Follow-up**, median, range · RTE: 84.3 (46.6, 115.7) · RTI: 45.5 (30.7, 68.5) · no PMRT: 101.5 (58.8, 136.4) ◆ **Funding**: NR ◆ **CoI**: Alphonse Taghian has the following Grants No. R01CA139118 (A.G.T.) and P50CA08393 (A.G.T.) from the National Cancer Institute, the Adele McKinnon Research Fund for Breast Cancer-Related Lymphedema (A.G.T.), the Olayan-Xefos Family Fund for Breast Cancer Research (A.G.T.), and the Heinz Family Foundation (A.G.T.). **Risk of bias considerations (adapted from SIGN cohort study checklist)** ◆ Study type: retrospective cohort study ◆ Confounding: moderate risk: multivariable model, but not all relevant covariates considered ◆ Selection bias into the study: Unclear, no information provided. ◆ Intervention · Assessment reliable: yes · Assessed more than once: no

Reference/ Study type	Population	Interventions	Main results	Methodological evaluation
	· no PMRT: 48.2 (42.5, 54.2) ◆ BMI (median, IQR) · RTE: 24.4 (21.6, 28.5) · RTI: 24.9 (21.8, 27.8) · no PMRT: 23.6 (21.3, 26.7) ◆ Stadium · T0: ▪ RTE: 6.4% ▪ RTI: 4.5% ▪ no PMRT: 18.2% · T1: ▪ RTE: 34.5% ▪ RTI: 34.8% ▪ no PMRT: 65.6% · T2: ▪ RTE: 45% ▪ RTI: 47.2% ▪ no PMRT: 15.6% · T3: ▪ RTE: 13.2% ▪ RTI: 13.5% ▪ no PMRT: 0.6% · T4: ▪ RTE: 0.9% ▪ RTI: 0% ▪ no PMRT: 0% ◆ Neoadjuvant chemotherapy (% yes) · RTE: 28.6% · RTI: 21.3% · no PMRT: 4.3% ◆ Adjuvant chemotherapy (%yes)		◆ Implant loss ("absolute failure": expander or implant total loss) · RT: 28/309 · No RT: 13/352 · For RT on tissue expander: OR 2.55 (95% CI 1.18-5.52) · For RT on final implant: 2.93 (95% CI 1.13-7.6)	· Possibly affected by knowledge of outcome status? No ◆ Drop-out rate & reasons reported: · High risk: not reported ◆ Outcome · Outcome measure is well-defined, valid and reliable; · No blind outcome assessment, however, this is unlikely to affect the results; as the outcomes are standard clinical characteristics ◆ Main cofounders taken into account: partly ◆ Confidence intervals reported: no (for subgroups TE versus implant RT yes) ◆ Selective reporting (comparison with protocol): no protocol provided, not assessable.

Reference/ Study type	Population	Interventions	Main results	Methodological evaluation
	· RTE: 63.6% · RTI: 68.5% · no PMRT: 35.9% ◆ Reconstruction type (%) · tissue-expander and implant replacing ◆ Mesh/ADM (%) · Alloderm: ▪ RTE: 40.1% ▪ RTI: 41% ▪ no PMRT: 23.9% · other mesh: ▪ RTE: 6.9% ▪ RTI: 15.7% ▪ no PMRT: 7.8% ◆ Implant position: all subpectoral			
Nelson 2022 retrospective cohort study	**Inclusion criteria (for analysis):** ◆ Implant-based reconstruction **Exclusion criteria (for analysis):** ◆ Patients <18 years ◆ autologous breast reconstruction, ◆ without BREAST-Q data at ≥1 year following reconstruction **Enrolment period** ◆ January 2010 and June 2017 **Follow-up** ◆ 3 years of follow up	**Interventions** A: RT after implant · TE: N = 290 · TI: N = 228 B: no RT after implant · N = 2175 **Analysis** ◆ Frequencies, means, SD	**Complications:** ◆ Implant loss (implant removal): · RT: 24/518 · No RT: 44/2175 ◆ Implant exchange (2) · RT: 112/518 · No RT: 578/2175 ◆ Capsular contracture (Grade 3-4) · RT: 154/518 · No RT: 161/2175 ◆ Wound complication (wound dehiscence)	**General information** ◆ **Follow-up**: 3 years of follow up ◆ **Funding**: This research was funded in part through the NIH/NCI Cancer Center Support Grant P30 CA008748 ◆ **CoI**: Andrea Pusic is a codeveloper of the BREAST-Q, which is owned by Memorial Sloan Kettering Cancer Center. She receives a portion of the licensing fees (royalty payments) when the BREAST-Q is used in industry-sponsored clinical trials. Joseph Dayan is a consultant for Stryker. Babak Mehrara is a consultant for

Reference/ Study type	Population	Interventions	Main results	Methodological evaluation
	Descriptive statistics ◆ Age (mean, SD) · RTE: 48.6 (10.0) · RTI: 47.3 (9.8) · no RT: 49.5 (10.0) ◆ BMI (mean, SD) · RTE: 26.2 (5.3) · RTI: 25.5 (5.1) · no RT: 25.11 (5.1) ◆ Stadium · NR ◆ Neoadjuvant chemotherapy (% yes) · RTE: 34.1% · RTI: 4.4% · no RT: 5.8% ◆ Adjuvant chemotherapy (% yes) · RTE: 36.6% · RTI: 80.7% · no RT: 33.5% ◆ Reconstruction type: tissue expander and implant replacement ◆ Mesh/ADM: NR ◆ Implant position: NR		· RT: 4/518 · No RT: 10/2175 **Breast-Q (mean, SD)** ◆ satisfaction with breasts, year 1 · RT-TE: 56.5 (18.2) · RT-I: 56.8 (18.1) · No RT: 66.5 (18.1) ◆ Satisfaction with breasts, year 2 · RT-TE: 57.2 (20.3) · RT-I: 56.4 (17.4) · No RT: 66.3 (17.4) ◆ Satisfaction with breasts, year 3 · RT-TE: 57.6 (16.7) · RT-I: 56.7 (17.8) · No RT: 65.5 (18.7) ◆ Physical well-being, year 1 · RT-TE: 67.7 (16.9) · RT-I: 65.7 (16.1) · No RT: 75.5 (15.3) ◆ Physical well-being, year 2 · RT-TE: 69.0 (19.4) · RT-I: 67.7 (16.3) · No RT: 77.1 (15.2) ◆ Physical well-being, year 3 · RT-TE: 69.9 (17.6) · RT-I: 70.4 (13.8) · No RT: 77.2 (15.9)	PureTech Corporation. The remaining authors declare no conflicts of interest. **Risk of bias considerations (adapted from SIGN cohort study checklist)** ◆ Study type: retrospective cohort study ◆ Confounding: High risk: no adjustment ◆ Selection bias into the study: low risk: prospective data collection ◆ Intervention · Assessment reliable: yes · Assessed more than once: no · Possibly affected by knowledge of outcome status? No ◆ Drop-out rate & reasons reported: · Unclear: not reported per group ◆ Outcome · Outcome measure is well-defined, valid and reliable; · No blind outcome assessment, however, this is unlikely to affect the results; as the outcomes are standard clinical characteristics ◆ Main cofounders taken into account: no ◆ Confidence intervals reported: no ◆ Selective reporting (comparison with protocol): no protocol provided, not assessable.

Reference/ Study type	Population	Interventions	Main results	Methodological evaluation
Ostapenko 2023 retrospective cohort study	**Inclusion criteria (for analysis):** ◆ Histologically proven BC, ◆ age > 18 years, ◆ female sex, ◆ NSM following prepectoral IBBR **Exclusion criteria (for analysis):** ◆ Other IBBR techniques, ◆ other mastectomy techniques, ◆ lost to follow-up **Enrolment period** ◆ March 2017 to November 2021 **Follow-up** · PMRT: 31.44± 12.37 · no PMRT: 30.91 ± 13.21 **Descriptive statistics** ◆ Age (mean, SD) · PMRT: 44.65 ± 11.58 · no PMRT: 46.51 ± 12.45 ◆ BMI (median, range) · NR ◆ Stadium · PMRT: ▪ pTis: 10.7% ▪ pT1: 39.3% ▪ pT2: 32.1% ▪ pT3: 17.9% ▪ No tumor: 0%	**Interventions** A: RT after implant · N = 28 B: no RT after implant · N = 70 **Analysis** ◆ Frequencies, means, SD ◆ No adjustment	**Complications:** ◆ Overall complications · RT: 9/28 · No RT: 16/70 ◆ Hematoma · RT: 0/28 · No RT: 16/70 ◆ Necrosis · RT: 2/28 · No RT: 2/70 ◆ Seroma · RT: 1/28 · No RT: 2/70 ◆ Infections: · RT: 2/28 · No RT: 3/70 ◆ Implant loss · RT: 3/28 · No RT: 1/70 ◆ Capsular contracture · RT: 5/28 · No RT: 3/70 ◆ Local recurrence: · RT: 2/28 · No RT: 3/70 **Breast-Q (mean, SD**	**General information** ◆ **Follow-up**, mean, SD · PMRT: 31.44± 12.37 · no PMRT: 30.91 ± 13.21 ◆ **Funding**: The authors received no financial support for the research, authorship and publication of this article. ◆ **CoI**: Dr. F.F. has received personal honoraries and educational grants from Pfizer, Novartis, Roche, Astra Zeneca, Springer, Medtronic and Bondimed. The remaining authors have no financial interests to declare in relation to the content of this article. **Risk of bias considerations (adapted from SIGN cohort study checklist)** ◆ Study type: retrospective cohort study ◆ Confounding: high risk: no adjustment, although relevant baseline characteristics differ between groups ("patients in the RT group compared to non-RT differed significantly in the rate of axillary lymph node dissection (17.1% vs. 50%; p=0.001), neoadjuvant (p\.0001) and adjuvant chemotherapy (p\.0001), final tumor stage, and lymph node stage." ◆ Selection bias into the study: Unclear, no information provided. ◆ Intervention · Assessment reliable: yes

Reference/ Study type	Population	Interventions	Main results	Methodological evaluation
	· no PMRT: ▪ pTis: 18.6% ▪ pT1: 64.3% ▪ pT2: 8.6% ▪ pT3: 0% ▪ No tumor: 8.5% ◆ Neoadjuvant chemotherapy (% yes) · PMRT: 82.1% · no PMRT: 25.7% ◆ Adjuvant chemotherapy (% yes) · PMRT: 67.9% · no PMRT: 18.6% ◆ Reconstruction type (%) · Single-Stage: ▪ PMRT: 85.71% ▪ no PMRT: 84.3% · Two Stage: ▪ PMRT: 14.3% ▪ no PMRT: 15.7% ◆ Mesh/ADM: NR ◆ Implant position: all prepectoral		◆ Satisfaction with overall outcome: · RT: 72.53 (21.43) · No RT: 77.28 (21.31) ◆ Psychosocial well-being: · RT: 78.73 (17.39) · No RT: 79.22 (15.56) ◆ Sexual well-being: · RT: 61.38 (22.72) · No RT: 70.26 (22.78) ◆ Physical well-being: · RT: 57.94 (30.08) · No RT: 58.89 (25.21)	· Assessed more than once: no · Possibly affected by knowledge of outcome status? No ◆ Drop-out rate & reasons reported: · High risk: not reported. ◆ Outcome · Outcome measure is well-defined, valid and reliable; · No blind outcome assessment, however, this is unlikely to affect the results; as the outcomes are standard clinical characteristics ◆ Main cofounders taken into account: no ◆ Confidence intervals reported: no ◆ Selective reporting (comparison with protocol): no protocol provided, not assessable.
Pires 2023 retrospective cohort study	**Inclusion criteria (for analysis):** ◆ consecutive patients undergoing mastectomy ◆ with concurrent prepectoral tissue expander placement **Exclusion criteria (for analysis):** ◆ Patients from May 2021 to July 2021 were excluded from the analyses to	**Interventions** A: RT after implant · N = 50 B: no RT after implant · N = 196	**Complications:** ◆ Infections (any infection) · OR 0.7 (95% CI 0.28 to 1.76) ◆ Implant loss (explantation, 2) · OR 1.08 (95% CI 0.03 to 33.69) ◆ Reoperation (return to operating room)	**General information** ◆ **Follow-up:** at least 3 months ◆ **Funding**: University of Utah Population Health Research Foundation, with funding in part from the National Center for Research Resources and the National Center for Advancing Translational Sciences, National Institutes of Health, through grant UL1TR002538 (formerly

Reference/ Study type	Population	Interventions	Main results	Methodological evaluation
	account for a 3-month learning curve in which surgeons adjusted their practices to include increasing the initial tissue expander fill volume, and increasing drain time to at least 14 days. **Enrolment period** ◆ August 2020 to January 2022 **Follow-up** ◆ at least 3 months **Descriptive statistics** ◆ Age: median 47 years ◆ BMI: mean 26.3 ◆ Stadium: NR ◆ Neoadjuvant chemotherapy: 35% ◆ Adjuvant chemotherapy: 35% ◆ Reconstruction type: all tissue expander and implant replacing ◆ Mesh/ADM: 50% with mesh ◆ Implant position: all pre-pectoral	**Analysis** ◆ Logistic regression ◆ Adjusted for age, body mass index, history of diabetes, tobacco use, neoadjuvant chemotherapy, and postoperative radiotherapy	· OR 1.34 (95% CI 0..36 to 4.9)	5UL1TR001067-05, 8UL1TR000105, and UL1RR025764 ◆ **CoI**: The authors have no financial interest to disclose in relation to the content of this study. **Risk of bias considerations (adapted from SIGN cohort study checklist)** ◆ Study type: retrospective cohort study ◆ Confounding: moderate risk: probably adjusted for the listed covariates ◆ Selection bias into the study: Unclear, no information provided. ◆ Intervention · Assessment reliable: yes · Assessed more than once: no · Possibly affected by knowledge of outcome status? No ◆ Drop-out rate & reasons reported: · High risk: not reported ◆ Outcome · Outcome measure is well-defined, valid and reliable; · No blind outcome assessment, however, this is unlikely to affect the results; as the outcomes are standard clinical characteristics ◆ Main cofounders taken into account: partly ◆ Confidence intervals reported: yes

Reference/ Study type	Population	Interventions	Main results	Methodological evaluation
				• Selective reporting (comparison with protocol): no protocol provided, not assessable.
Polotto 2023 retrospective cohort study	**Inclusion criteria (for analysis):** • oncologic or risk-reducing nipple or skin-sparing mastectomy • direct-to-implant ADM-assisted PPBR • age ≥18 and ≤85 years, • TNM stage <IV, • not active smokers in the last 3 preoperative weeks, • ≤1 significant comorbidity (ie, diabetes, obesity, connective tissue disease) **Exclusion criteria (for analysis):** • undergone previous breast, mantle field or total body radiation therapy • patients with <6 months of FU • 2-stage PPBR or other typology of reconstruction planned **Enrolment period** • January 2015 to December 2020 **Follow-up** • PMRT: 28.5 (range 10.6 to 73.2) • no PMRT: 30.4 (range 8.3 to 84) **Descriptive statistics**	**Interventions** A: RT after implant · N = 84 B: no RT after implant · N = 401 **Analysis** • Frequencies, nonparametric tests (Mann-Whitney's U-test, Kruskal-Wallis test) • No adjustment	**Complications** • Overall complications · RT: 18/84 · No RT: 45/401 • Hematoma · RT: 0/84 · No RT: 1/401 • Seroma · RT: 6/84 · No RT: 15/401 • Infections · RT: 1/84 · No RT: 8/401 • Capsular contracture · RT: 7/84 · No RT: 1/401 • Necrosis · RT: 0/84 · No RT: 6/401 • Wound complications (dehiscence) · RT: 0/84 · No RT: 0/401	**General information** • **Follow-up**, median, range: · PMRT: 28.5 (range 10.6 to 73.2) · no PMRT: 30.4 (range 8.3 to 84) • **Funding**: This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors. • **CoI**: The authors have stated that they have no conflicts of interest. **Risk of bias considerations (adapted from SIGN cohort study checklist)** • Study type: retrospective cohort study • Confounding: High risk: no adjustment • Selection bias into the study: Unclear, no information provided. • Intervention · Assessment reliable: yes · Assessed more than once: no · Possibly affected by knowledge of outcome status? No • Drop-out rate & reasons reported: · High risk: not reported • Outcome

Reference/ Study type	Population	Interventions	Main results	Methodological evaluation
	◆ Age (median, range) · PMRT: 54.0 (11.0) · no PMRT: 55.1 (11.5) ◆ BMI (median, range) · PMRT: 23.3 (3.4) · no PMRT: 23.1 (3.4) ◆ Stadium: NR ◆ Neoadjuvant chemotherapy (% yes) · PMRT: 33.3% · no PMRT: 14.9% ◆ Adjuvant chemotherapy (% yes) · PMRT: 70.2% · no PMRT: 27.3% ◆ Reconstruction type (%): all direct-to-implant ◆ Mesh/ADM: 100% with mesh ◆ Implant position: all prepectoral		◆ Implant loss · RT: 4/84 · No RT: 14/401	· Outcome measure is well-defined, valid and reliable; · No blind outcome assessment, however, this is unlikely to affect the results; as the outcomes are standard clinical characteristics ◆ Main cofounders taken into account: no ◆ Confidence intervals reported: no ◆ Selective reporting (comparison with protocol): no protocol provided, not assessable.
Safran 2022 retrospective cohort study	**Inclusion criteria (for analysis):** ◆ unilateral or bilateral direct-to-implant prepectoral breast reconstruction following mastectomy **Exclusion criteria (for analysis):** ◆ patient preference, ◆ previously failed implantbased reconstruction, ◆ delayed reconstruction, ◆ autologous-based reconstruction	**Interventions** A: RT after implant · N = 81 B: no RT after implant · N = 253 **Analysis** ◆ Multivariable logistic regression analysis	**Complications** ◆ Capsular contracture · OR 7.195, p = 0.007	**General information** ◆ **Follow-up:** 30.5 months ◆ **Funding**: No funding was received for this work. ◆ **CoI**: Dr. Dionisopoulos received travel support from Allergan/Lifecell for educational conferences. The remaining authors have no financial interests to declare.

Reference/ Study type	Population	Interventions	Main results	Methodological evaluation
	Enrolment period ◆ June 2016 to June 2019 **Follow-up** · 30.5 months **Descriptive statistics** ◆ Age: mean 48.4 years (range, 19 to 83 years) ◆ BMI: mean 25.89 kg/m2 (range, 18.2 to 53.9 kg/m2) ◆ Stadium: NR ◆ Neoadjuvant chemotherapy: 35.1% ◆ Adjuvant chemotherapy: NR ◆ Reconstruction type: all DTI ◆ Mesh/ADM: 74.9% with mesh ◆ Implant position: all pre-pectoral	◆ Adjusted for Age, BMI, diabetes, smoker, skin-sparing mastectomy, midlateral, wise pattern, implant size, ADM, days drain inserted, pocket infection, seroma, hematoma, minor complications		**Risk of bias considerations (adapted from SIGN cohort study checklist)** ◆ Study type: retrospective cohort study ◆ Confounding: high risk: adjustment for other complications as well, which may be on the causal pathway instead of confounder ◆ Selection bias into the study: Unclear, no information provided. ◆ Intervention · Assessment reliable: yes · Assessed more than once: no · Possibly affected by knowledge of outcome status? No ◆ Drop-out rate & reasons reported: · High risk: not reported ◆ Outcome · Outcome measure is well-defined, valid and reliable; · No blind outcome assessment, however, this is unlikely to affect the results; as the outcomes are standard clinical characteristics ◆ Main cofounders taken into account: only for overall complications ◆ Confidence intervals reported: p-value used for calculation of CI ◆ Selective reporting (comparison with protocol): no protocol provided, not assessable.

Reference/ Study type	Population	Interventions	Main results	Methodological evaluation
Saksornai 2023 Retrospective cohort study	**Inclusion criteria (for analysis):** ◆ women ◆ aged >18 years ◆ mastectomy and immediate breast reconstruction using a one-stage, direct-to-implant (DTI) approach, autologous-based reconstruction, or a combination of both techniques **Exclusion criteria (for analysis):** ◆ palliative surgery, ◆ cosmetic surgery (transgender patients), ◆ reconstruction with a pedicled omental flap **Enrolment period** ◆ January 2008 to December 2018 **Follow-up (mean, SD)** ◆ PMRT: 53.42, SD 36.96 ◆ no PMRT: 54.17, SD 34.98 **Descriptive statistics** ◆ Age (mean, SD) · PMRT: 44.81 (8.96) · no PMRT: 45.27 (7.41) ◆ BMI (mean, SD) · PMRT: 22.31 (3.56) · no PMRT: 22.02 (3.24) ◆ Stadium:	**Interventions** A: RT after implant · N = 38 B: no RT after implant · N = 48 **Analysis** ◆ Frequencies ◆ No adjustment	**Complications** ◆ Overall complications · RT: 23/42 · No RT: 19/52 ◆ Capsular contracture (grade 3-4) · RT: 16/38 · No RT: 7/48 ◆ Extrusion · RT: 1/42 · No RT: 0/48	**General information** ◆ **Follow-up**, mean, SD · PMRT: 53.42±36.96 · no PMRT: 54.17±34.98 ◆ **Funding**: This research was supported by grants for the Development of New Faculty Staff and the Ratchadaphiseksomphot Endowment Fund. ◆ **CoI**: The authors have no conflicts of interest to declare. **Risk of bias considerations (adapted from SIGN cohort study checklist)** ◆ Study type: retrospective cohort study ◆ Confounding: High risk, no adjustment ◆ Selection bias into the study: Unclear, no information provided. ◆ Intervention · Assessment reliable: yes · Assessed more than once: no · Possibly affected by knowledge of outcome status? No ◆ Drop-out rate & reasons reported: · High risk: not reported ◆ Outcome · Outcome measure is well-defined, valid and reliable; · No blind outcome assessment, however, this is unlikely to affect the

Reference/ Study type	Population	Interventions	Main results	Methodological evaluation
	· 0: ▪ PMRT: 1.5% ▪ no PMRT: 16.7 · I: ▪ PMRT: 17.6% ▪ no PMRT: 37.9 · II: ▪ PMRT: 38.2% ▪ no PMRT: 31.8% · III: ▪ PMRT: 32.4% ▪ no PMRT: 3% · IV: ▪ PMRT: 1.5% ▪ no PMRT: 0% · NA ▪ PMRT: 8.8% ▪ no PMRT: 10.6% ◆ Neoadjuvant chemotherapy: NR ◆ Adjuvant chemotherapy (% yes) · PMRT: 79.4% · no PMRT: 51.5% ◆ Reconstruction type (%): · Implant: ▪ PMRT: 61.8% ▪ no PMRT: 78.8% · Autologous: ▪ PMRT: 38.2% ▪ no PMRT: 21.2% · Combined approach: ▪ PMRT: 25% ▪ no PMRT: 33%			results; as the outcomes are standard clinical characteristics ◆ Main cofounders taken into account: no ◆ Confidence intervals reported: no ◆ Selective reporting (comparison with protocol): no protocol provided, not assessable.

Reference/ Study type	Population	Interventions	Main results	Methodological evaluation
	◆ Mesh/ADM: NR ◆ Implant position: · Prepectoral: ▪ PMRT: 19% ▪ no PMRT: 30.8% · Subpectoral: ▪ PMRT: 81% ▪ no PMRT: 69.2%			
Sewart 2022 prospective cohort study ISRCTN37664281	**Inclusion criteria (for analysis):** ◆ IBBR using any technique ◆ subpectoral reconstructions with and without mesh, and pre-pectoral techniques ◆ Patients undergoing neoadjuvant chemotherapy or endocrine therapy before IBBR were eligible for inclusion. **Exclusion criteria (for analysis):** ◆ delayed reconstruction ◆ implant in combination with an autologous flap. **Enrolment period** ◆ 1 February 2014 to 30 June 2016 **Follow-up** ◆ 18 months **Descriptive statistics**	**Interventions** A: RT after implant · N = 214 B: no RT after implant · N = 514 **Analysis** ◆ Frequencies, means, SDs ◆ No adjustment	**Complications** ◆ Infections (at 3 months) · RT: 62/214 · No RT: 115/516 ◆ Implant loss (at 3 months) · RT: 13/214 · No RT: 26/516 ◆ Reoperation (at 3 months) · RT: 35/214 · No RT: 84/516 ◆ Hospitalisation (readmission at 3 months) · RT: 38/214 · No RT: 77/516 **Breast-Q** (median, IWR, range; not used in analysis), 18 months post-score ◆ Satisfaction with breasts: · RT: 49 (41–62; 0–100)	**General information** ◆ **Follow-up:** 18 months ◆ **Funding**: NR ◆ **CoI**: NR **Risk of bias considerations (adapted from SIGN cohort study checklist)** ◆ Study type: retrospective cohort study ◆ Confounding: High risk, no adjustment ◆ Selection bias into the study: Unclear, no information provided. ◆ Intervention · Assessment reliable: yes · Assessed more than once: no · Possibly affected by knowledge of outcome status? No ◆ Drop-out rate & reasons reported: · High risk: not reported ◆ Outcome

Reference/ Study type	Population	Interventions	Main results	Methodological evaluation
	◆ Age (median, IQR, range) · PMRT: 50 (44–58; 28–80) · no PMRT: 52 (47–60.5; 16–83) ◆ BMI (median, IQR, range) · PMRT: 24.9 (22.9–28.4; 16.4–41) · no PMRT: 24.5 (22.3–28; 16.8–42.6) ◆ Stadium · NR ◆ Neoadjuvant chemotherapy (% yes) · PMRT: 22% · no PMRT: 6% ◆ Adjuvant chemotherapy (% yes) · PMRT: 77% · no PMRT: 7% ◆ Reconstruction type (%) · Single-stage reconstruction: ▪ PMRT: 77% ▪ no PMRT: 80% · Two-stage reconstruction: ▪ PMRT: 23% ▪ no PMRT: 20% · Different approach per breast: ▪ PMRT: 1% ▪ no PMRT: 1% ◆ Mesh/ADM (%) · Biological mesh: ▪ PMRT: 52% ▪ no PMRT: 58%		· No RT: 61 (49–73; 0–100) ◆ Satisfaction with overall outcome: · RT: 67 (51–75; 0–100) · No RT: 75 (61–86; 0–100) ◆ Psychosocial well-being: · RT: 61.5 (48–79; 0–100) · No RT: 67 (52–86; 0–100) ◆ Sexual well-being: · RT: 41 (26–57; 0–100) · No RT: 45 (33–60; 0–100) ◆ Physical well-being: · RT: 68 (60–81; 13–100) · No RT: 77 (66–85; 18–100)	· Outcome measure is well-defined, valid and reliable; · No blind outcome assessment, however, this is unlikely to affect the results; as the outcomes are standard clinical characteristics ◆ Main cofounders taken into account: only for overall complications ◆ Confidence intervals reported: no (for overall complications yes) ◆ Selective reporting (comparison with protocol): study was registered and planned satisfaction with care, complications and health-related quality of life (BREAST-Q)

Reference/ Study type	Population	Interventions	Main results	Methodological evaluation
	◆ Implant position: mostly sub-pectoral			
Stuart 2021 retrospective cohort study	**Inclusion criteria (for analysis):** ◆ immediate breast reconstruction after mastectomy ◆ alloplastic ◆ staged breast reconstruction **Exclusion criteria (for analysis):** ◆ NR **Enrolment period** ◆ 2009-2013 **Follow-up** ◆ Minimum 24 months **Descriptive statistics** ◆ Age (mean, range) · PMRT: 48.6 (25–74) · no PMRT: 51.6 (32–78) ◆ BMI (median, range) · PMRT: 27.7 (17.9–41.1) · no PMRT: 26.5 (16.2–43.2) ◆ Stadium · In situ: ▪ PMRT: 7.8% ▪ no PMRT: 16.7% · I–IIB: ▪ PMRT: 48.5%	**Interventions** A: RT after implant · N = 167 B: no RT after implant · N = 84 **Analysis** ◆ Frequencies ◆ No adjustment	**Complications** ◆ Overall complications (early): · RT: 40/167 · No RT: 26/84 ◆ Seroma · RT: 45/167 · No RT: 14/84 ◆ Hematoma · RT: 0/167 · No RT: 2/84 ◆ Infections (local infection): · RT: 9/167 · No RT: 9/84 ◆ Necrosis (partial necrosis): · RT: 8/167 · No RT: 4/84 ◆ Wound complications (total dehiscence, >1/3) · RT: 1/167 · No RT: 0/84 ◆ Reoperation (second surgical intervention) · RT: 25/167 · No RT: 11/84 ◆ Impant loss	**General information** ◆ **Follow-up:** minimum follow-up of 24 months ◆ **Funding**: This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors. ◆ **CoI**: None of the authors has a financial interest in any of the products, devices, or drugs mentioned in this manuscript. S.R.S., C.L.G.C., E.M., T.C.S.C., T.T.F., G.N.M., H.A.C. — none declared; A.M.M is a Member of the Medical Advisory Board, Establishment Labs. **Risk of bias considerations (adapted from SIGN cohort study checklist)** ◆ Study type: retrospective cohort study ◆ Confounding: high risk: no adjustment, although baseline characteristics differ, i.e., stage, chemotherapy, etc. ◆ Selection bias into the study: Unclear, no information provided. ◆ Intervention · Assessment reliable: yes · Assessed more than once: no · Possibly affected by knowledge of outcome status? No

Reference/ Study type	Population	Interventions	Main results	Methodological evaluation
	▪ no PMRT: 72.6% · III: ▪ PMRT: 44.3% ▪ no PMRT: 10.7% ◆ Neoadjuvant chemotherapy (% yes) · PMRT: 46.7% · no PMRT: 14.3% ◆ Adjuvant chemotherapy (% yes) · PMRT: 40.7% · no PMRT: 46.4% Reconstruction type: tissue expander with later implant placement ◆ Mesh/ADM (%): none ◆ Implant position: all sub-pectoral		· RT: 16/167 · No RT: 9/84 ◆ Extrusion · RT: 1/167 · No RT: 0/84 ◆ Capsular contracture (severe) · RT: 6/167 · No RT: 2/84	◆ Drop-out rate & reasons reported: · High risk: not reported ◆ Outcome · Outcome measure is well-defined, valid and reliable; · No blind outcome assessment, however, this is unlikely to affect the results; as the outcomes are standard clinical characteristics ◆ Main cofounders taken into account: only for overall complications ◆ Confidence intervals reported: no (for overall complications yes) ◆ Selective reporting (comparison with protocol): no protocol provided, not assessable.
Sun 2022 retrospective cohort study	**Inclusion criteria (for analysis):** ◆ Women with breast ductal carcinoma in situ (DCIS) or clinical stage I–III invasive breast cancer ◆ mastectomy and breast reconstruction with or without PMRT **Exclusion criterira** ◆ loss to follow-up or deceased ◆ incomplete expander-implant replacement ◆ implant removal for reasons unrelated to surgery	**Interventions** A: RT after implant · N = 59 B: no RT after implant · N = 221 **Analysis** ◆ Univariable and multivariate logistic regression analyses for reconstruction	**Complications** ◆ Overall complications · RT: 30/59 · No RT: 73/221 · OR 2.0 (95% CI 1.065 to 3.754) ◆ Necrosis · RT: 2/59 · No RT: 3/221 ◆ Bleeding: · RT: 4/59	**General information** ◆ **Follow-up:** · PMRT: 37.2 · no PMRT: 51.3 ◆ **Funding**: None. ◆ **CoI**: The authors have no conflicts of interest to declare. **Risk of bias considerations (adapted from SIGN cohort study checklist)** ◆ Study type: retrospective cohort study

Reference/ Study type	Population	Interventions	Main results	Methodological evaluation
	◆ completed postoperative adjuvant RT in other medical institutions ◆ presented with benign tumors. **Enrolment period** ◆ January 2012 to June 2020 **Follow-up** · PMRT: 37.2 months · no PMRT: 51.3 months **Descriptive statistics** ◆ Age (mean, SD) · PMRT: 36.71 (9.19) · no PMRT: 40.54 (8.03) ◆ BMI (mean, SD) · PMRT: 21.53 (2.45) · no PMRT: 21.51 (2.38) ◆ Stadium · 0: ▪ PMRT: 0% ▪ no PMRT: 45% · IA: ▪ PMRT: 1.7% ▪ no PMRT: 31% · IB: ▪ PMRT: 3.4% ▪ no PMRT: 0% · IIA: ▪ PMRT: 16.9% ▪ no PMRT: 37.0% · IIB:	failure and overall complications ◆ Multivariable analysis adjusted for age, BMI, personal history, history, adjuvant therapy, reconstruction type, and implant volume	· No RT: 9/221 ◆ Wound complications (incision dehiscence) · RT: 9/59 · No RT: 15/221 ◆ Seroma · RT: 2/59 · No RT: 5/221 ◆ Hematoma · RT: 0/59 · No RT: 1/221 ◆ Infections: · RT: 13/59 · No RT: 21/221 ◆ Reconstruction failure · RT: 11/59 · No RT: 19/221 · OR: 2.44 (95% CI 1.01 to 5.91)	◆ Confounding: high risk for most outcomes: no adjustment, although baseline characteristics differ, i.e., stage, chemotherapy, etc.; moderate risk for reconstruction failure and overall complications ◆ Selection bias into the study: Unclear, no information provided. ◆ Intervention · Assessment reliable: yes · Assessed more than once: no · Possibly affected by knowledge of outcome status? No ◆ Drop-out rate & reasons reported: · unclear: drop-out rate reported, but not per group ◆ Outcome · Outcome measure is well-defined, valid and reliable; · No blind outcome assessment, however, this is unlikely to affect the results; as the outcomes are standard clinical characteristics ◆ Main cofounders taken into account: only for overall complications and reconstruction failure ◆ Confidence intervals reported: no (for overall complications and reconstruction failure yes)

Reference/ Study type	Population	Interventions	Main results	Methodological evaluation
	▪ PMRT: 25.4% ▪ no PMRT: 9.7% · IIIA: ▪ PMRT: 45.8% ▪ no PMRT: 1.4% · IIIB&C: ▪ PMRT: 6.8% ▪ no PMRT: 0% ◆ Neoadjuvant chemotherapy (% yes) · PMRT: 39% · no PMRT: 12.5% ◆ Adjuvant chemotherapy (% yes) · PMRT: 100% · no PMRT: 76.9% ◆ Reconstruction type (%) · 1-stage: ▪ PMRT: 25.4% ▪ no PMRT: 61.5% · 2-stage: ▪ PMRT: 74.6% ▪ no PMRT: 38.5% ◆ Mesh/ADM: no mesh used ◆ Implant position: all subpectoral			◆ Selective reporting (comparison with protocol): no protocol provided, not assessable.
Wang 2022 retrospective cohort study	**Inclusion criteria (for analysis):** ◆ mastectomy and immediate reconstruction with tissue expanders **Exclusion criteria (for analysis):** ◆ NR	**Interventions** A: RT after implant · N = 57 B: no RT after implant · N = 472	**Complications** ◆ Infections · RT: 20/57 · No RT: 60/472 · OR 2.458 (95% CI 1.277 to 4.731)	**General information** ◆ **Follow-up**: NR ◆ **Funding**: NR ◆ **CoI**: NR **Risk of bias considerations (adapted from SIGN cohort study checklist)**

Reference/ Study type	Population	Interventions	Main results	Methodological evaluation
	Enrolment period ◆ July 2011 to May 2021 **Follow-up:** NR **Descriptive statistics** ◆ Age: mean: 50 years (range, 22–83 years) ◆ BMI: mean 24.5 kg/m2 (range, 16.3–63.3 kg/m2) ◆ Stadium: NR ◆ Neoadjuvant chemotherapy: 20.5% ◆ Adjuvant chemotherapy: 28.3% ◆ Reconstruction type: all tissue expander and implant replacement ◆ Mesh/ADM: NR ◆ Implant position: · prepectoral: 42.7% · dual-plane: 54% · subpectoral: 3.2%	**Analysis** ◆ multivariable logistic regression analysis ◆ probably adjusted for active smoking, adjuvant chemotherapy, and mastectomy skin flap necrosis		◆ Study type: retrospective cohort study ◆ Confounding: high risk: adjustment, however, very few factors ◆ Selection bias into the study: Unclear, no information provided. ◆ Intervention · Assessment reliable: yes · Assessed more than once: no · Possibly affected by knowledge of outcome status? No ◆ Drop-out rate & reasons reported: · High risk: not reported ◆ Outcome · Outcome measure is well-defined, valid and reliable; · No blind outcome assessment, however, this is unlikely to affect the results; as the outcomes are standard clinical characteristics ◆ Main cofounders taken into account: for reconstruction failure and overall complications only ◆ Confidence intervals reported: no (for overall complications yes) ◆ Selective reporting (comparison with protocol): no protocol provided, not assessable.
Yin 2022	**Inclusion criteria (for analysis):**	**Interventions** A: RT after implant	**Complications** ◆ Major complications (Surgical-site infection, wound	**General information** ◆ **Follow-up**: NR

Reference/ Study type	Population	Interventions	Main results	Methodological evaluation
retrospective cohort study	◆ age 18 years or older and documentation of direct-to-implant breast reconstruction. **Exclusion criteria (for analysis):** ◆ metastatic breast cancer, ◆ two-stage expander-implant breast reconstruction, ◆ bilateral breast reconstruction, ◆ reconstruction after polyacrylamide hydrogel removal ◆ implant removal because of locoregional cancer relapse or cosmetic complaints, ◆ use of implant during revision surgery **Enrolment period** ◆ 2014 to 2019 **Follow-up:** NR **Descriptive statistics (for overall group)** ◆ Age: >40 years: 52% ◆ BMI: >24kg/m²: 28% ◆ Stadium: · benign: 4% · 0: 16% · I: 36% · IIA: 36% · IIB: 11% · III: 4% ◆ Neoadjuvant chemotherapy: 3.5% ◆ Adjuvant chemotherapy: 13%	· N = 130 B: no RT after implant · N = 897 **Analysis** ◆ multivariable logistic regression analysis ◆ adjusted for year of surgery and laterality, implant size, adjuvant targeted therapy	dehiscence, and mastectomy flap necrosis requireing rehospitalisation or reoperation) at 3 months · RT: 21/130 · No RT: 69/897 · OR 1.91 (95% CI 1.01 to 3.62)	◆ **Funding**: This work was supported by a Tianjin the Belt and Road Technological Innovation and Cooperation Grant (no. 18PTZWHZ00050) to the Sino-Russian Joint Research Center for Oncoplastic Breast Surgery. ◆ **CoI**: NR **Risk of bias considerations (adapted from SIGN cohort study checklist)** ◆ Study type: retrospective cohort study ◆ Confounding: moderate risk: adjustment for year, laterality, implant size, adjuvant targeted therapy ◆ Selection bias into the study: Unclear, no information provided. ◆ Intervention · Assessment reliable: yes · Assessed more than once: no · Possibly affected by knowledge of outcome status? No ◆ Drop-out rate & reasons reported: · High risk: not reported ◆ Outcome · Outcome measure is well-defined, valid and reliable; · No blind outcome assessment, however, this is unlikely to affect the results; as the outcomes are standard clinical characteristics ◆ Main cofounders taken into account: yes

Reference/ Study type	Population	Interventions	Main results	Methodological evaluation
	◆ Reconstruction type: all DTI, · immediate: 92.4% · delayed: 7.6% ◆ Mesh/ADM: 20% with Mesh ◆ Implant position: pectoralis muscle			◆ Confidence intervals reported: yes ◆ Selective reporting (comparison with protocol): no protocol provided, not assessable.

Characteristics of included studies of studies identified after the search date in Du 2022.

6.2.3 Meta-analysen

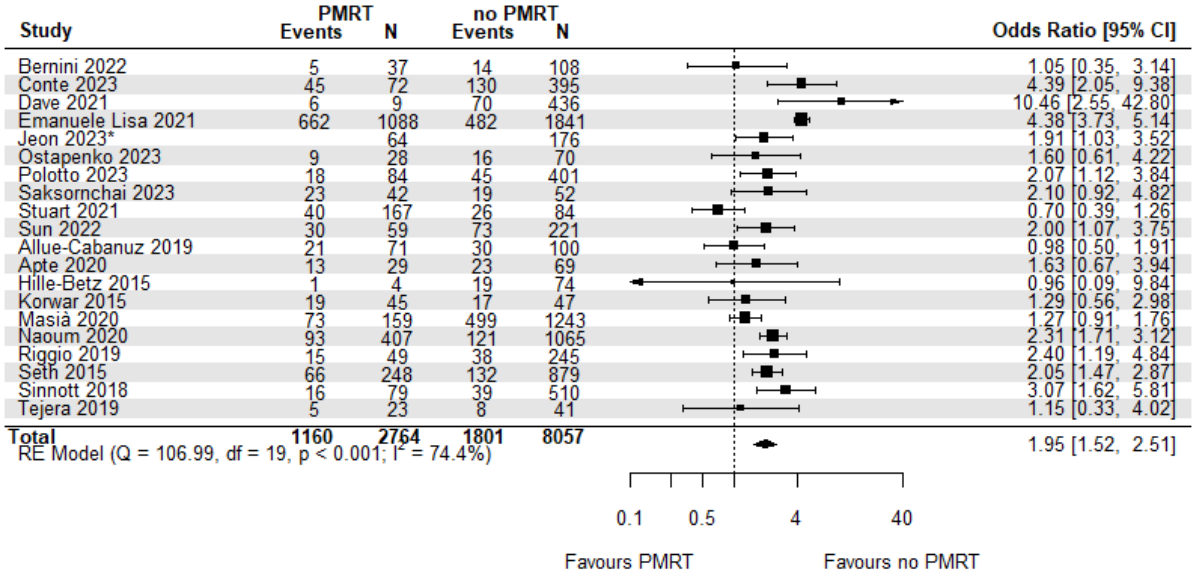
Erklärungen: Mit * markierte Studien haben einen adjustierten Effektschätzer berichtet, der hier verwendet wurde.

6.2.3.1 Overall complications

From the systematic review Du 2022 and additionally identified studies; varying definitions across studies. The following studies in the meta-analysis in Du 2022 were not meta-analysed:

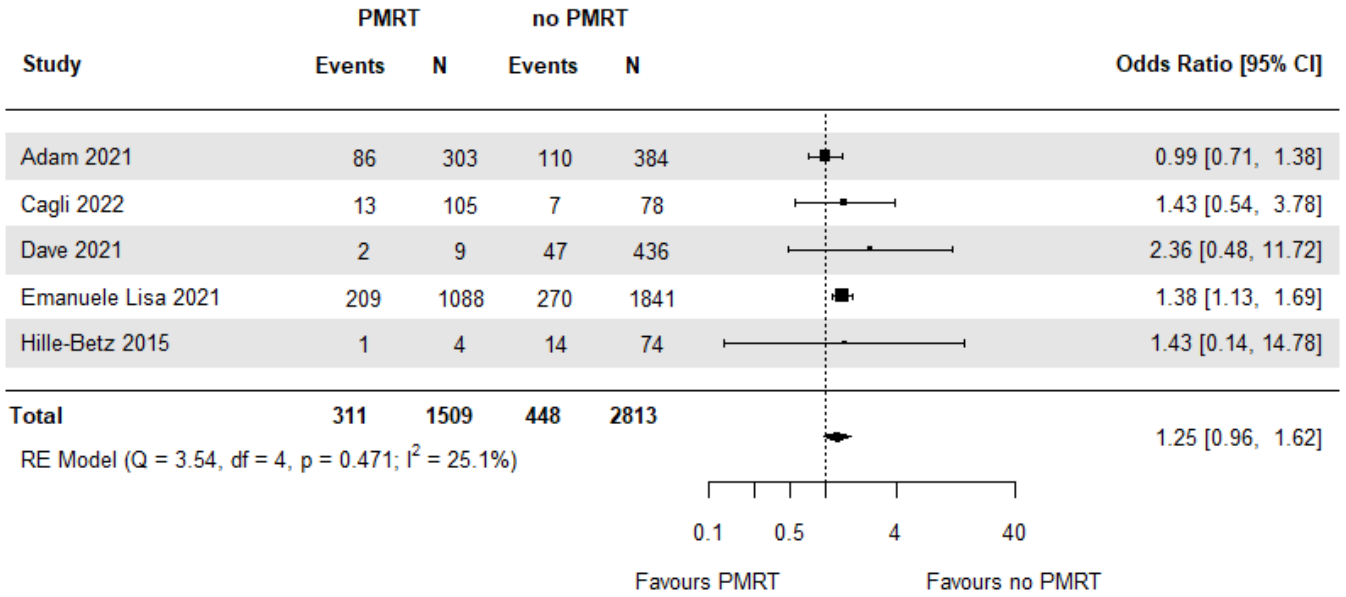
- Cordeiro: The "Overall complications" summarized in Du 2022 equal the outcome reconstruction failure without any further combinations, we therefore analysed this in the respective meta-analysis.
- Olsen: We could not replicate the data extraction.

PMRT compared to no PMRT for implant-based breast reconstruction, overall complications



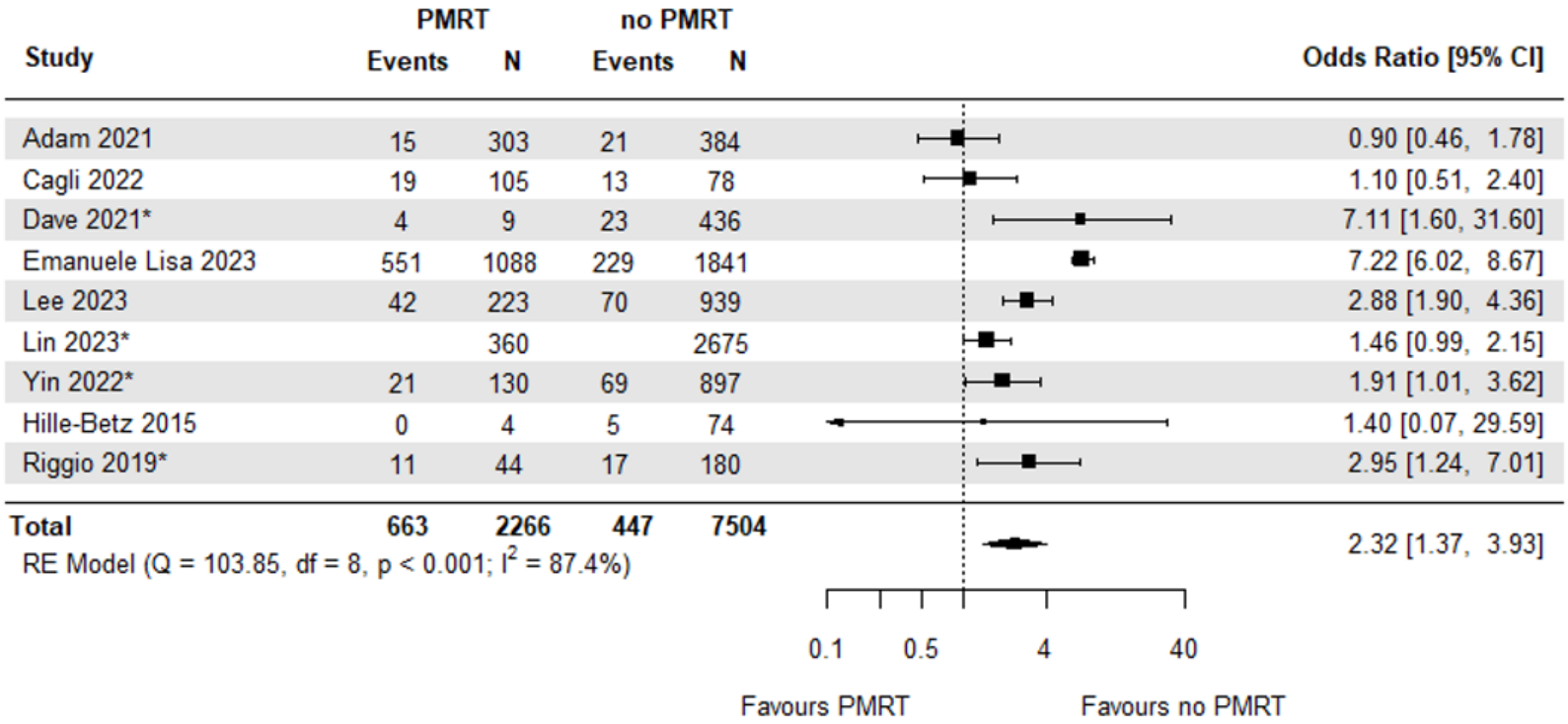
6.2.3.2 Minor complications

PMRT compared to no PMRT for implant-based breast reconstruction, minor complications



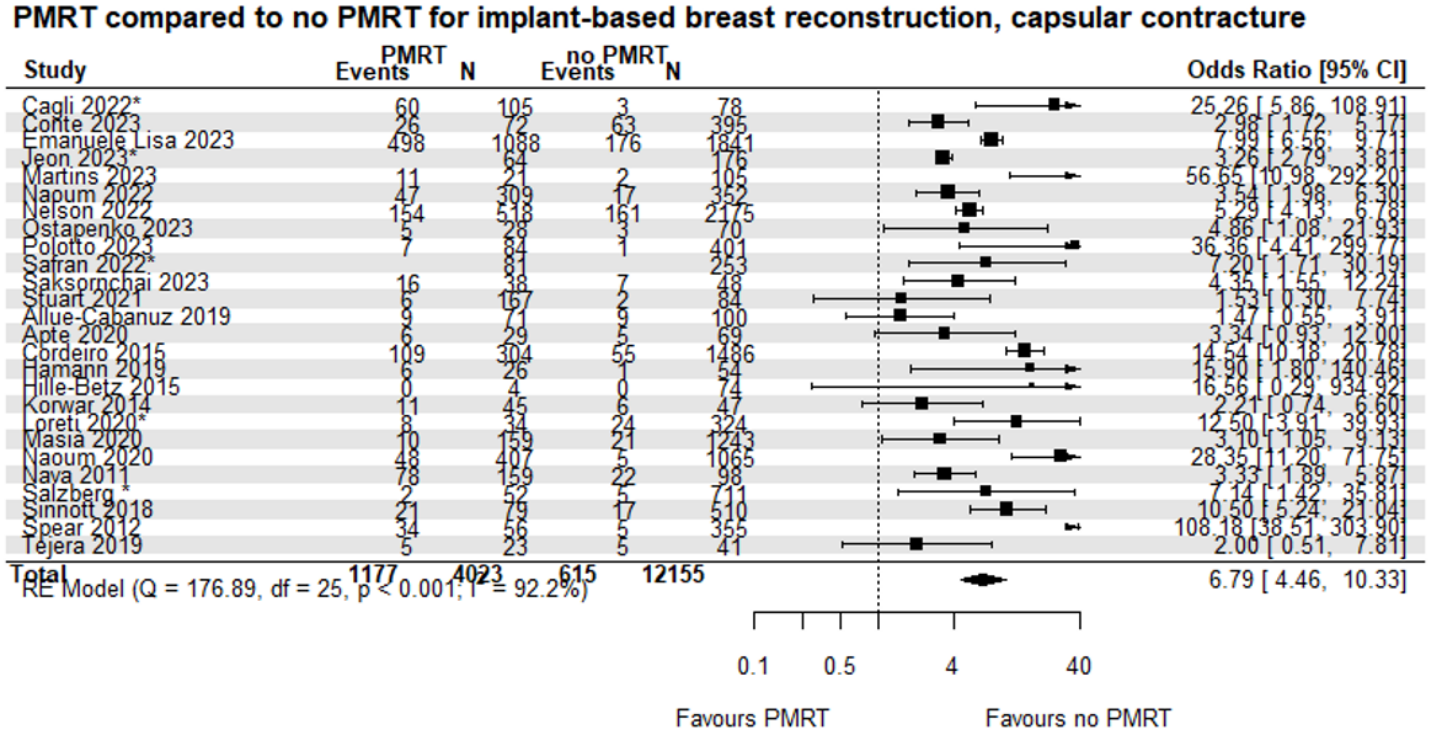
6.2.3.3 Major complications

PMRT compared to no PMRT for implant-based breast reconstruction, major complications



6.2.3.4 Capsular contracture

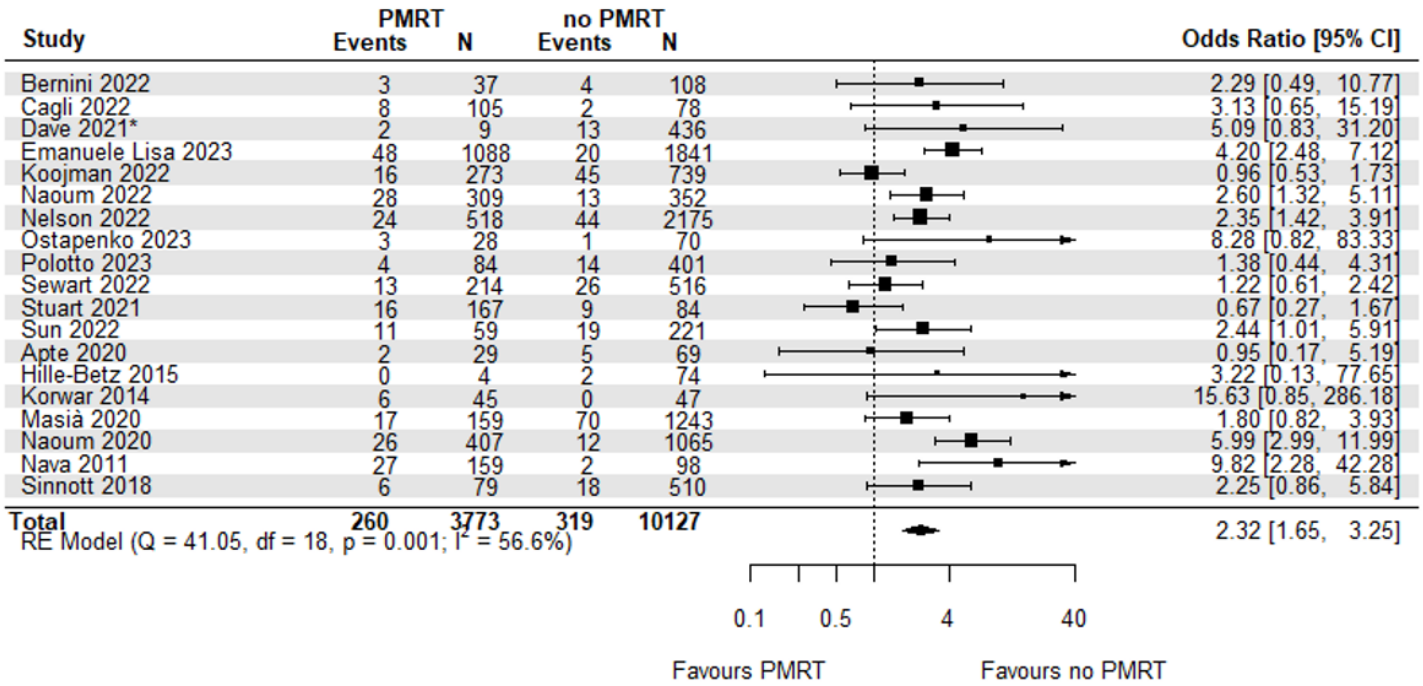
From the systematic review Du 2022 and additionally identified studies; usually Baker grade 3-4



6.2.3.5 Implant loss (absolute failure)

Studies varied in their definition of implant loss. This analysis represents studies that reported “implant loss” without further definition or with a narrow definition, i.e., reconstruction failure due to complications, in some studies also called absolute failure.

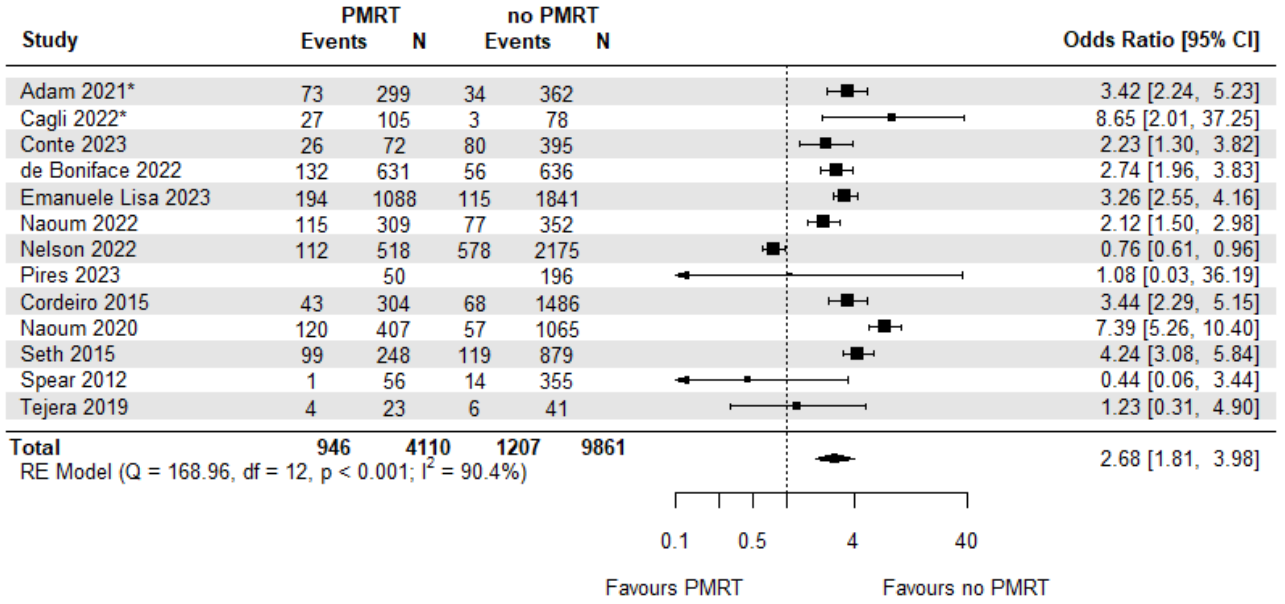
RT compared to no PMRT for implant-based breast reconstruction, implant loss (absolute failure)



6.2.3.6 Implant loss (any reason)

This analysis includes those studies that defined implant loss or reconstruction failure as due to complications or patient wish, in some studies also called overall failure. Studies without explicit definition were instead included in analysis implant loss (narrow definition).

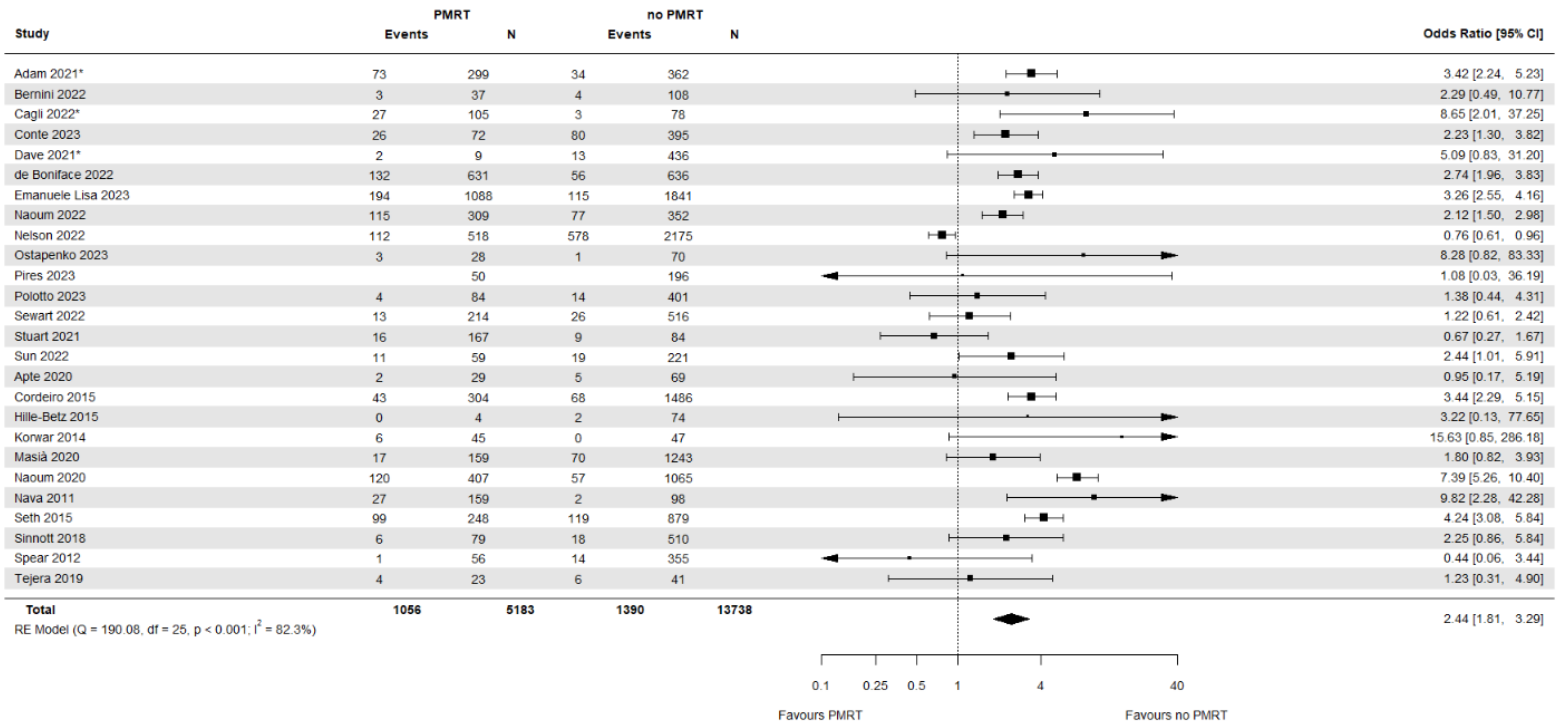
MRT compared to no PMRT for implant-based breast reconstruction, implant loss (any reason)



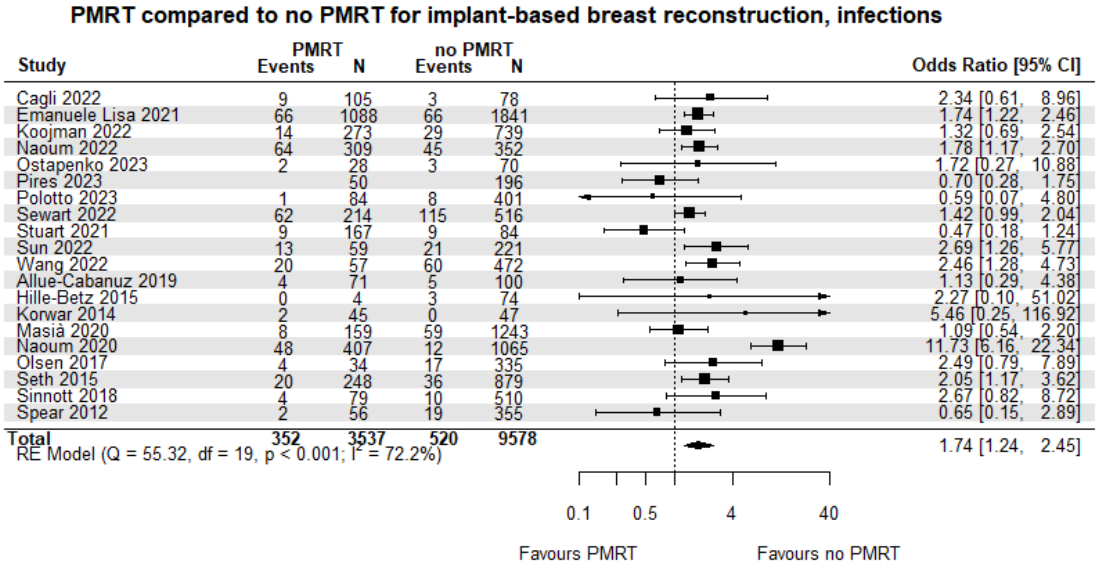
6.2.3.7 Implant loss (any reason/patient wish)

This meta-analysis includes all studies that reported implant loss, with the broadest definition available per study. We chose hierarchically implant loss / reconstruction failure due to complications or patient wish, if this was not reported, we used a narrower definition (i.e., due to complications) or no definition (simply reported as “implant loss”).

PMRT vs. no PMRT for implant-based breast reconstruction, implant loss (any reason, patient wish)



6.2.3.8 Infections

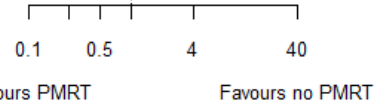


6.2.3.9 Reoperation

PMRT compared to no PMRT for implant-based breast reconstruction, reoperation

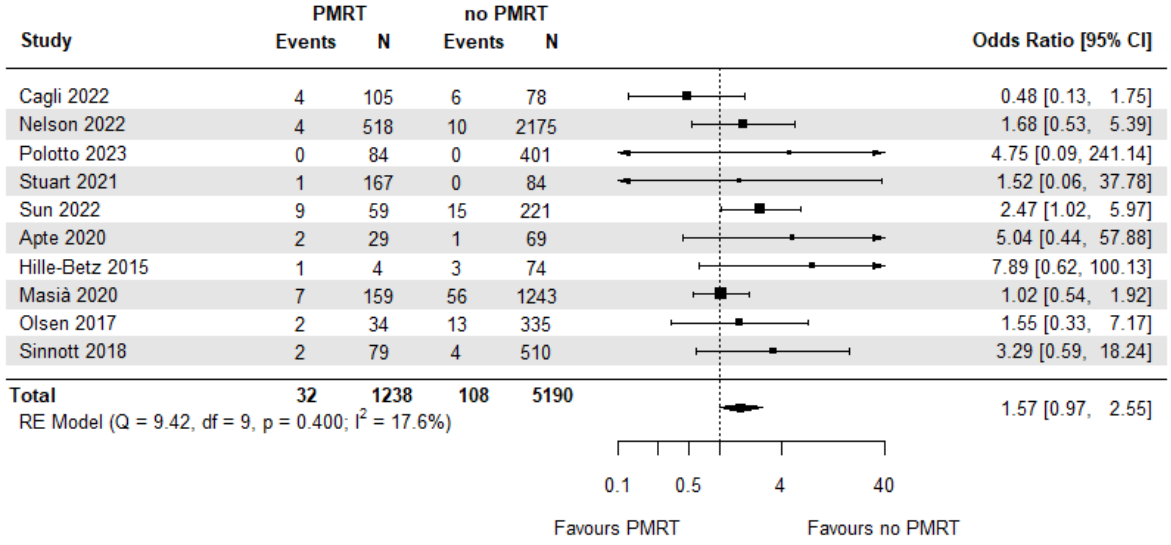
Study	PMRT Events	PMRT N	no PMRT Events	no PMRT N	Odds Ratio [95% CI]
Adam 2021	63	303	30	384	3.10 [1.95, 4.93]
Cagli 2022	11	105	7	78	1.19 [0.44, 3.22]
de Boniface 2022	549	749	536	856	1.64 [1.32, 2.03]
Doherty 2023*	216	378	719	1964	2.31 [1.85, 2.89]
Emanuele Lisa 2021	270	1088	81	1841	7.17 [5.52, 9.32]
Koojman 2022	56	273	182	739	0.79 [0.56, 1.11]
Pires 2023		50		196	1.34 [0.36, 4.94]
Sewart 2022	35	214	84	516	1.01 [0.65, 1.55]
Stuart 2021	25	167	11	84	0.65 [0.31, 1.38]
Allue-Cabanuz 2019	3	71	4	100	1.06 [0.23, 4.88]
Apte 2020	5	29	9	69	1.39 [0.42, 4.57]
Total	**1233**	**3427**	**1663**	**6827**	1.62 [1.02, 2.57]

RE Model (Q = 148.77, df = 10, p < 0.001; I^2 = 92.3%)

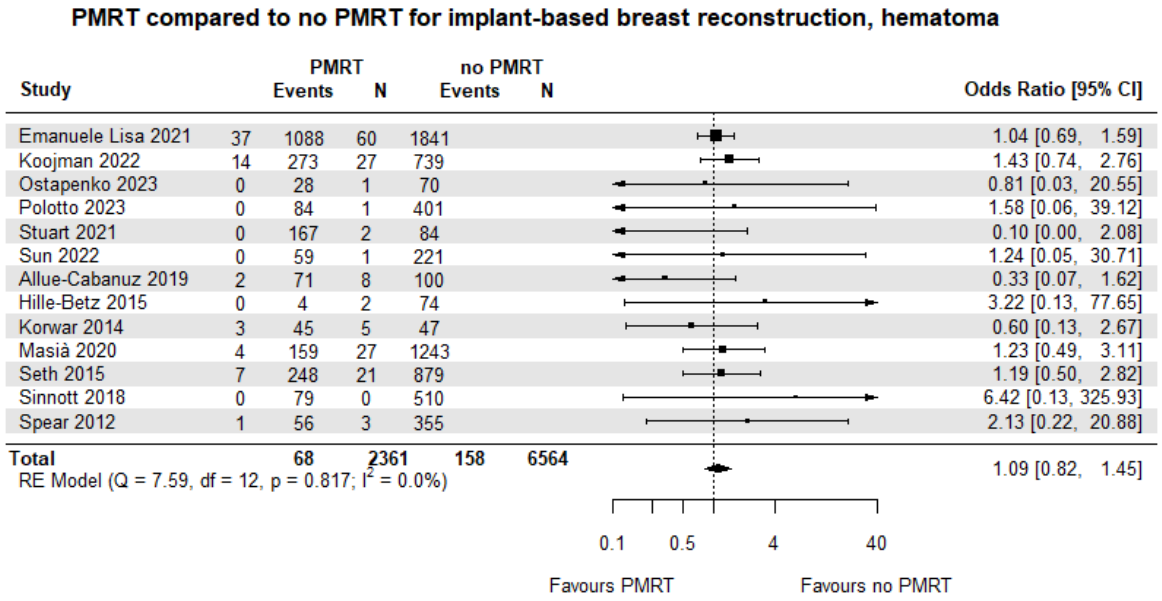


6.2.3.10 Wound complications

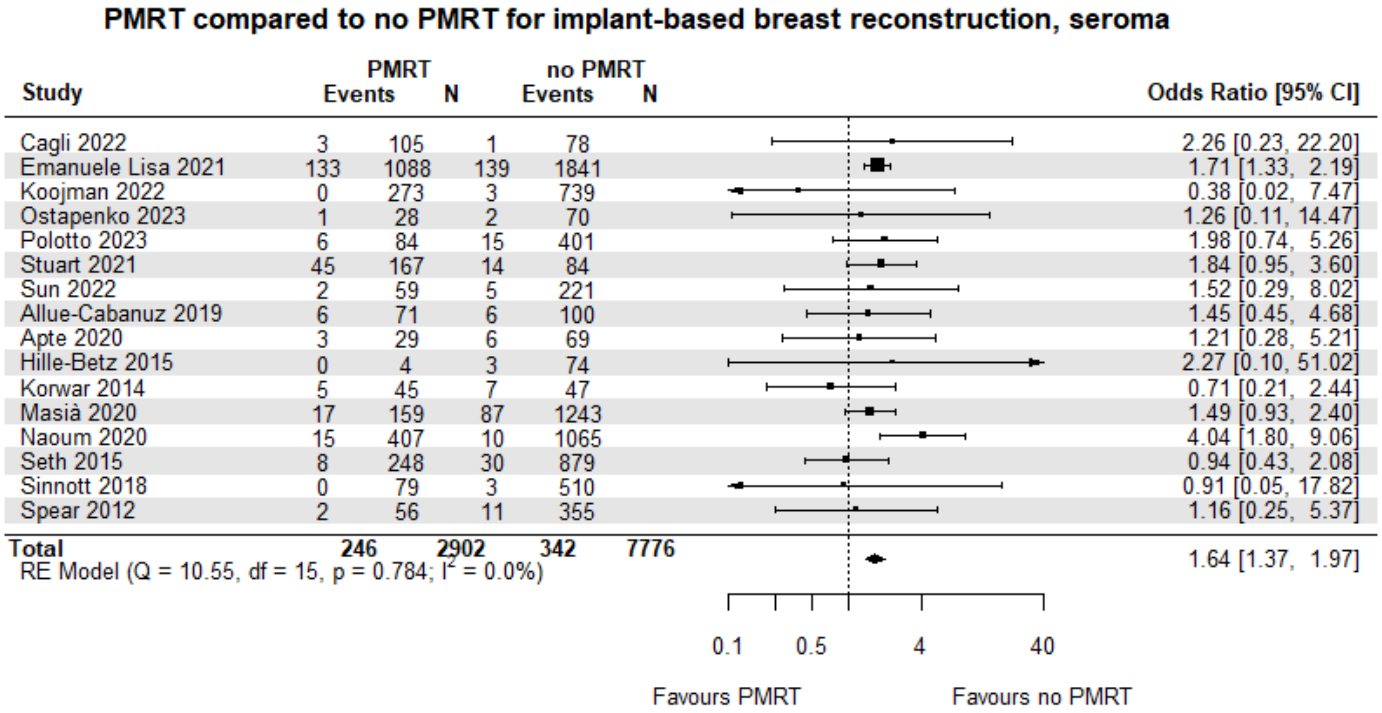
PMRT compared to no PMRT for implant-based breast reconstruction, wound complications



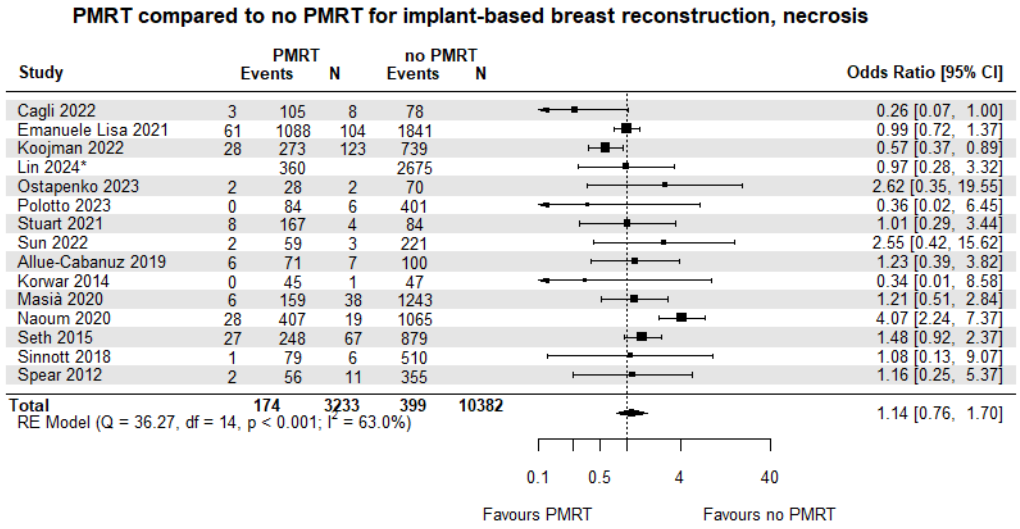
6.2.3.11 Hematoma



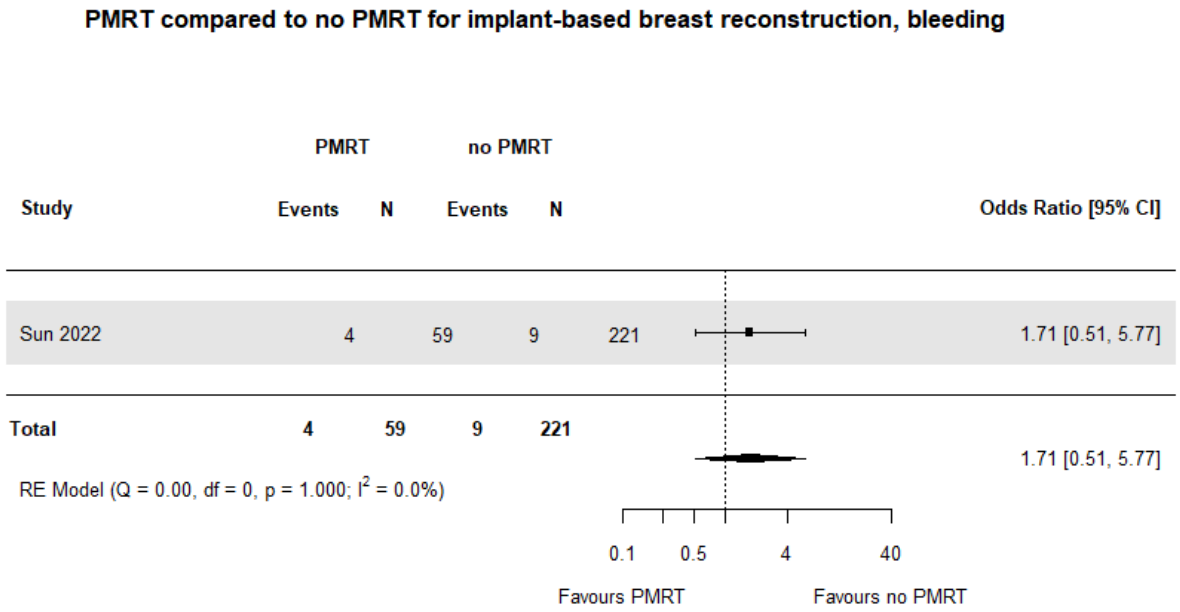
6.2.3.12 Seroma



6.2.3.13 Necrosis

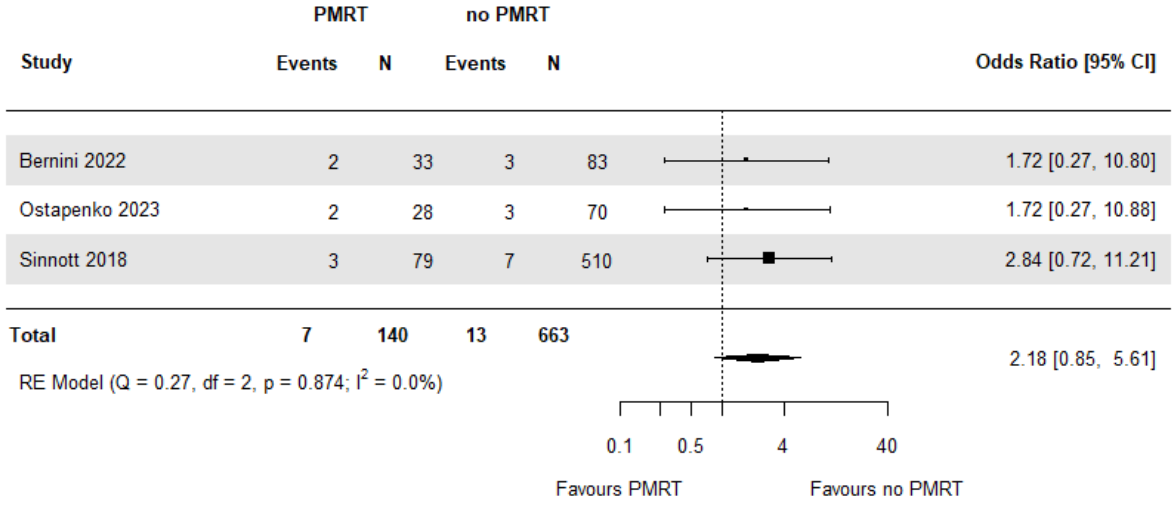


6.2.3.14 Bleeding

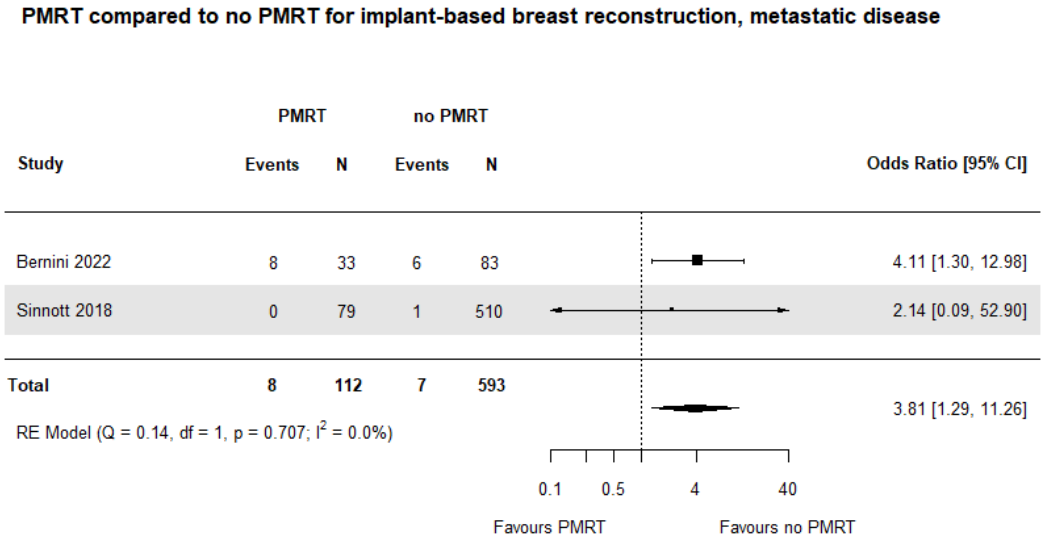


6.2.3.15 Local recurrence

PMRT compared to no PMRT for implant-based breast reconstruction, local recurrence



6.2.3.16 Metastatic disease

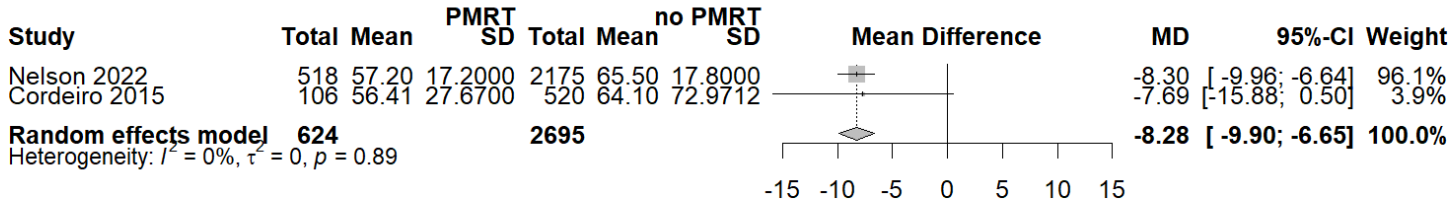


6.2.3.17 BREAST-Q dimensions, only measurements from 2 years onwards after reconstruction (according to median follow-up or time point of QoL measurement)

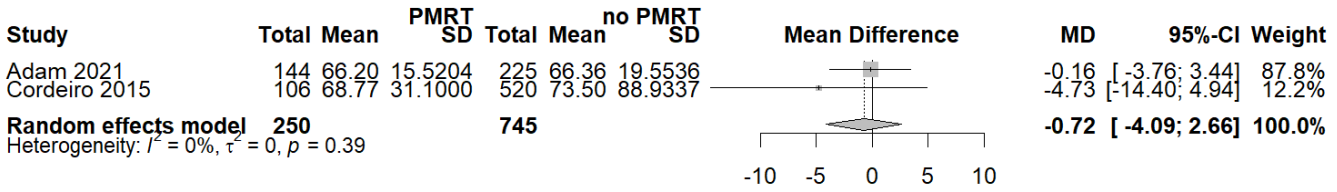
Notes: In Cordeiro 2022 and Nelson 2022, BREAST-Q scores were reported separately for groups with radiation on tissue expander and final implant. For the analysis in this report, groups were combined using this resource / formula by Cochrane (Practical 2 on how to include multi-arm studies in meta-analysis) by Emma Axon.

Cordeiro 2022 probably reported standard errors instead of standard deviations. We converted these to standard deviation before use in MA.

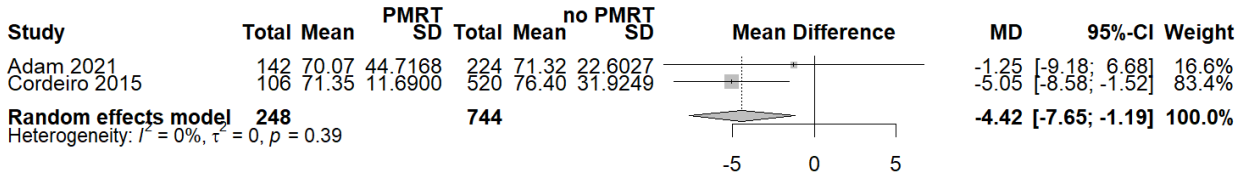
6.2.3.17.1 Satisfaction with breast



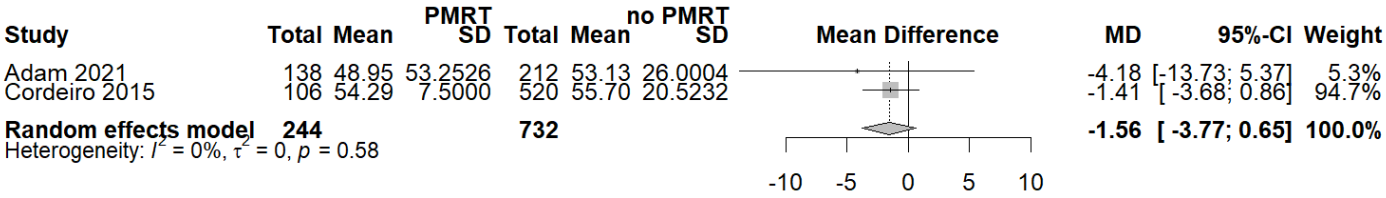
6.2.3.17.2 Satisfaction with overall outcome



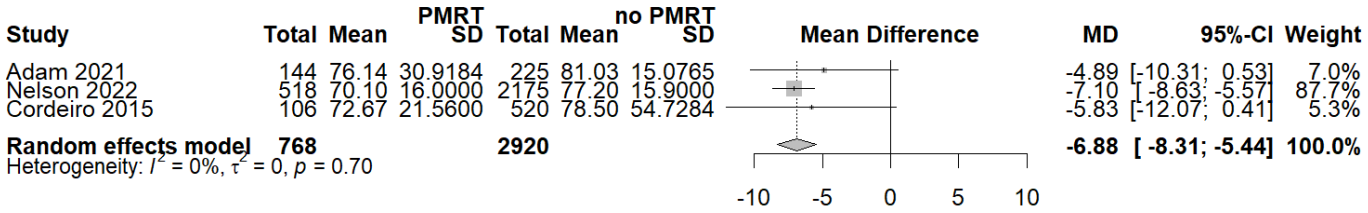
6.2.3.17.3 Psychosocial well-being



6.2.3.17.4 Sexual well-being



6.2.3.17.5 Physical well-being



6.2.4 Vertrauen in die Evidenz (nach GRADE)

Summary of findings:

Radiotherapy compared to no radiotherapy for implant-based breast reconstruction after reconstruction

Patient or population: implant-based breast reconstruction

Intervention: radiotherapy after implant-based breast reconstruction

Comparison: no radiotherapy after implant-based breast reconstruction

Summary of findings:

Outcomes	**Anticipated absolute effects*** (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with no radiotherapy	**Risk with radiotherapy**				
Overall complications	224 per 1 000	**360 per 1 000** (304 to 419)	**OR 1.95** (1.52 to 2.51)	10821 (20 non-randomised studies)	⊕◯◯◯ Very low[a,b]	Radiotherapy after implant-based breast reconstruction may increase the incidence of overall complications but the evidence is very uncertain.
Minor complications	159 per 1 000	**191 per 1 000** (154 to 235)	**OR 1.25** (0.96 to 1.62)	4322 (5 non-randomised studies)	⊕◯◯◯ Very low[a,c]	Radiotherapy after implant-based breast reconstruction may increase the incidence of minor complications but the evidence is very uncertain.
Major complications	60 per 1 000	**128 per 1 000** (80 to 199)	**OR 2.32** (1.37 to 3.93)	9770 (9 non-randomised studies)	⊕⊕◯◯ Low[a,b,d]	Radiotherapy after implant-based breast reconstruction may increase the incidence of major complcations.
Capsular contracture	97 per 1 000	**421 per 1 000** (323 to 526)	**OR 6.79** (4.46 to 10.33)	16178 (26 non-randomised studies)	⊕⊕⊕⊕ High[a,e]	Radiotherapy after implant-based breast reconstruction results in large increase in capsular contracture.
Implant loss (absolute failure)	31 per 1 000	**70 per 1 000** (51 to 96)	**OR 2.32** (1.65 to 3.25)	13900 (19 non-randomised studies)	⊕⊕⊕◯ Moderate[a,d]	Radiotherapy after implant-based breast reconstruction likely increases implant loss (narrow definition).
Implant loss (implant removal due to any reason)	96 per 1 000	**221 per 1 000** (161 to 297)	**OR 2.68** (1.81 to 3.98)	13971 (13 non-randomised studies)	⊕⊕◯◯ Low[a,d,f]	Radiotherapy after implant-based breast reconstruction may increase the incidence of implant loss – overall failure.
Implant loss (any reason / patient wish)	101 per 1 000	**215 per 1 000** (169 to 270)	**OR 2.44** (1.81 to 3.29)	18921 (26 non-randomised studies)	⊕⊕◯◯ Low[a,d,f]	Radiotherapy after implant-based breast reconstruction likely increases implant loss (narrow definition).

Summary of findings:						
Infections	54 per 1 000	**91 per 1 000** (66 to 123)	**OR 1.74** (1.24 to 2.45)	13115 (20 non-randomised studies)	⊕◯◯◯ Very low[a,f]	Radiotherapy after implant-based breast reconstruction may increase the incidence of infections but the evidence is very uncertain.
Reoperation	244 per 1 000	**343 per 1 000** (247 to 453)	**OR 1.62** (1.02 to 2.57)	10254 (11 non-randomised studies)	⊕◯◯◯ Very low[a,f]	Radiotherapy after implant-based breast reconstruction may increase the incidence of reoperation but the evidence is very uncertain.
Wound complications (Dehiscence)	21 per 1 000	**32 per 1 000** (20 to 51)	**OR 1.57** (0.97 to 2.55)	6428 (10 non-randomised studies)	⊕◯◯◯ Very low[a,c]	It is uncertain whether radiotherapy after implant-based breast reconstruction increases or decreases the incidence of wound complications.
Hematoma	24 per 1 000	**26 per 1 000** (20 to 35)	**OR 1.09** (0.82 to 1.45)	8925 (13 non-randomised studies)	⊕⊕◯◯ Low[a]	Radiotherapy after implant-based reconstruction may have little to no effect on hematoma.
Seroma	44 per 1 000	**70 per 1 000** (59 to 83)	**OR 1.64** (1.37 to 1.97)	10678 (16 non-randomised studies)	⊕⊕◯◯ Low[a]	Radiotherapy after implant-based breast reconstruction may increase the incidence of seroma.
Necrosis	38 per 1 000	**44 per 1 000** (29 to 64)	**OR 1.14** (0.76 to 1.70)	13615 (15 non-randomised studies)	⊕⊕◯◯ Low[a]	Radiotherapy after implant-based reconstruction may have little to no effect on seroma.
Bleeding	41 per 1 000	**68 per 1 000** (21 to 197)	**OR 1.71** (0.51 to 5.77)	280 (1 non-randomised study)	⊕◯◯◯ Very low[a,c]	It is uncertain whether radiotherapy after implant-based breast reconstruction increases or decreases the incidence of bleeding.
Local recurrence	20 per 1 000	**42 per 1 000** (17 to 101)	**OR 2.18** (0.85 to 5.61)	803 (3 non-randomised studies)	⊕◯◯◯ Very low[a,c]	It is uncertain whether radiotherapy after implant-based breast reconstruction

Summary of findings:						
						increases or decreases the incidence of recurrence.
Metastatic disease	12 per 1 000	**44 per 1 000** (15 to 119)	**OR 3.81** (1.29 to 11.26)	705 (2 non-randomised studies)	⊕◯◯◯ Very low[a, g]	It is uncertain whether radiotherapy after implant-based breast reconstruction increases or decreases the incidence of metastatic disease.
Satisfaction with breast assessed with: BREAST-Q > 2 years follow-up	The mean satisfaction with breast was **65**	MD **8.28 lower** (9.9 lower to 6.65 lower)	-	3319 (2 non-randomised studies)	⊕⊕◯◯ Low[a]	Radiotherapy after implant-based breast reconstruction may result in a reduction in satisfaction with breast, measured with the BREAST-Q questionnaire.
Satistfaction with overall outcome assessed with: BREAST-Q > 2 years follow-up	The mean satistfaction with overall outcome was **70**	MD **0.72 lower** (4.09 lower to 2.66 higher)	-	995 (2 non-randomised studies)	⊕⊕◯◯ Low[a]	Radiotherapy after implant-based breast reconstruction may have little to no effect on satisfaction with overall outccome, measured with the BREAST-Q questionnaire.
Psychosocial well-being assessed with: BREAST-Q > 2 years follow-up	The mean psychosocial well-being was **74**	MD **4.42 lower** (7.65 lower to 1.19 lower)	-	992 (2 non-randomised studies)	⊕⊕◯◯ Low[a]	Radiotherapy after implant-based breast reconstruction may result in a reduction in psychosocial well-being, measured with the BREAST-Q questionnaire.
Sexual well-being assessed with: BREAST-Q > 2 years follow-up	The mean sexual well-being was **54**	MD **1.56 lower** (3.77 lower to 0.65 higher)	-	976 (2 non-randomised studies)	⊕◯◯◯ Very low[a,c]	It is uncertain whether radiotherapy after implant-based breast reconstruction results in a reduction in sexual well-being, measured with the BREAST-Q questionnaire.
Physical well-being assessed with: BREAST-Q > 2 years follow-up	The mean physical well-being was **78**	MD **6.88 lower** (8.31 lower to 5.44 lower)	-	3688 (3 non-randomised studies)	⊕⊕◯◯ Low[a]	Radiotherapy after implant-based breast reconstruction may result in a reduction in physical well-being, measured with the BREAST-Q questionnaire.

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

Summary of findings:

CI: confidence interval; **OR:** odds ratio

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

Explanations

a. Downgraded by two levels due to very serious risk of bias: Included studies were observational only, and the majority did not adjust at all for relevant baseline characteristics. Results are thus prone to confounding / bias by indication - those receiving radiotherapy were probably at higher stage or higher likelihood of disease progression.

b. Downgraded by one level due to serious inconsistency: Outcome definitions varied between studies. In addition, heterogeneity is high.

c. Downgraded by one level due to serious imprecision; the 95% confidence interval includes both favorable and unfavorable effect of radiotherapy after reconstruction.

d. Upgraded by one level due to large effect (OR > 2).

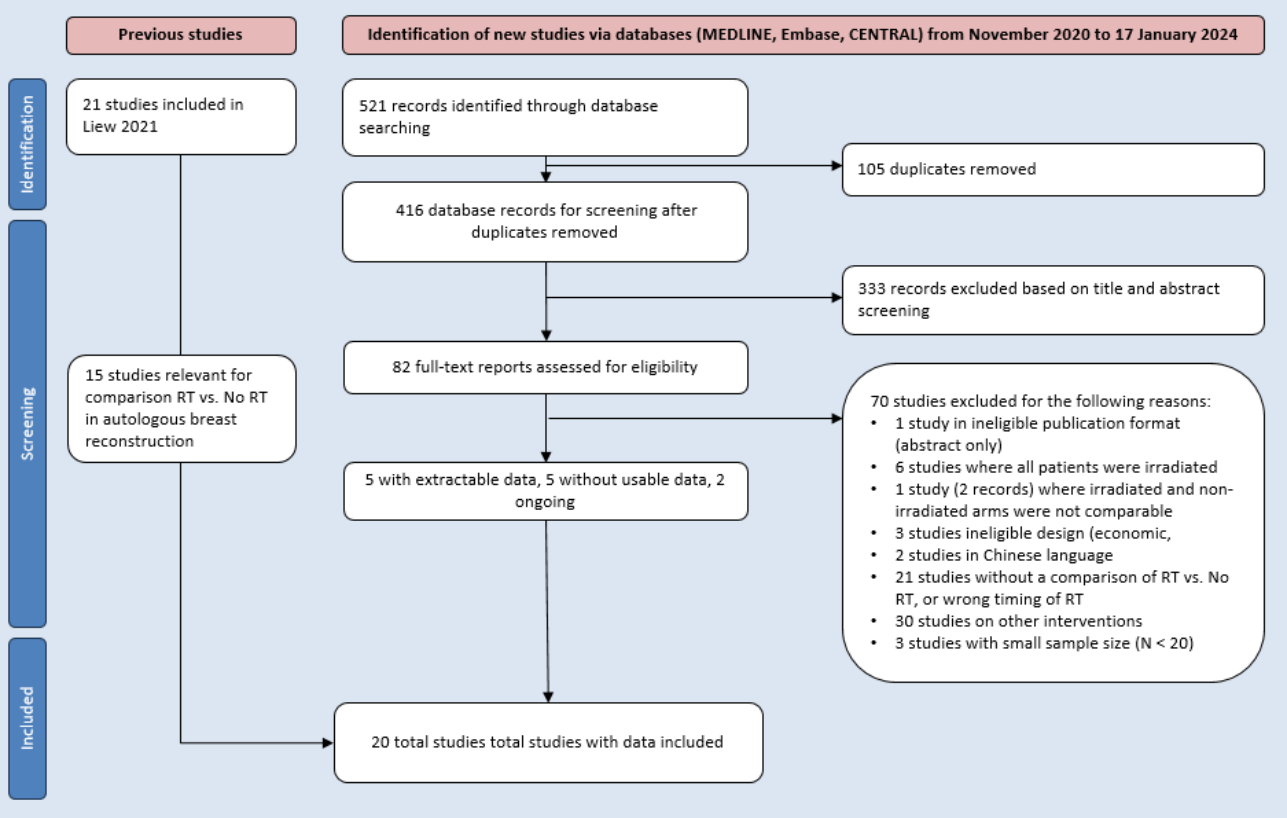
e. Upgraded by two levels due to very large effect (OR > 5).

f. Downgraded by one level due to serious inconsistency: Heterogeneity is high.

g. Downgraded by one level due to serious imprecision, small sample size and number of events.

6.3 PICO 9

6.3.1 PRISMA Flowdiagramm



6.3.2 Evidenztabellen

6.3.2.1 Systematisches Review

6.3.2.1.1 Evidenztabelle systematisches Review Liew 2021

Liew B, Southall C, Kanapathy M, Nikkhah D. Does post-mastectomy radiation therapy worsen outcomes in immediate autologous breast flap reconstruction? A systematic review and meta-analysis. J Plast Reconstr Aesthet Surg. 2021 Dec;74(12):3260-3280. doi: 10.1016/j.bjps.2021.08.005. Epub 2021 Aug 28. PMID: 34565703.

Reference/ Study type	Review description	Interventions	Study Population	Ergebnisse der untersuchten Endpunkte	Methodological comments	Included publications
Liew 2021 Systematisches Review mit Metaanalyse	**Study design** ◆ Cohort studies, prospective studies, retrospective studies **Search dates** ◆ Searched from inception until 19.11.2020 **Databases** ◆ MEDLINE (OvidSP) ◆ EMBASE (OvidSP) ◆ Cochrane CENTRAL **Inclusion criteria** ◆ Primary data from prospective and retrospective comparative studies ◆ Human studies ◆ Studies that include data on autologous flap reconstruction	**Question/ Aim** "The aim of this review is to systematically analyze the existing literature to compare the clinical, aesthetic and patient-reported outcomes in immediately reconstructed autologous flaps exposed to PMRT with the outcomes of flaps with no radiation exposure."	21 studies on 3817 pts with autologous breast reconstruction and a total of 3934 flaps ◆ PMRT: 939 ◆ no PMRT: 2462 ◆ PMRT and delayed reconstruction: 416 **Descriptive statistics** ◆ NR	**Fat necrosis** ◆ 12 studies ◆ PMRT: 81/485 ◆ No PMRT: 157/1577 ◆ RR: 1.91[1.45, 2.52] ◆ p < 0.00001 **Contracture or volume loss** ◆ 4 studies ◆ PMRT: 32/307 ◆ No PMRT: 45/671 ◆ RR: 1.62 [1.06, 2.48] ◆ p < 0.00001 **Revisional operations** ◆ 10 studies ◆ PMRT: 111/436 ◆ No PMRT: 248/1036 ◆ RR: 0.95 [0.80, 1.13] ◆ p = 0.54	**Risk of bias assessment of studies**: ROBINS-I tool *"Using the ROBINS-I tool, it was found that thirteen studies were at moderate risk of bias and eight studies were at serious risk of bias."* **Overall confidence in results of SR (AMSTAR-2):** ◆ PICO elements: yes ◆ A priori design: partial yes ◆ Justification for design: no ◆ Literature search >= 2 databases, search strategy + other sources: partial yes ◆ Selection in duplicate: yes ◆ Data extraction in duplicate: yes ◆ List of excluded studies: no ◆ sufficient detail on studies: partial yes ◆ RoB assessed: yes ◆ Funding of incl. studies: no ◆ MA appropriate: no	Included and checked for additional outcomes: ◆ Williams 1997 ◆ Tran 2000 ◆ Rogers 2000 ◆ Spear 2005 ◆ Carlson 2008 ◆ Chatterjee 2009 ◆ Lee 2010 ◆ Mirzabeigi 2013 ◆ Taghizadeh 2015 ◆ Cooke 2017 ◆ He 2017 ◆ Pont 2017 ◆ Berthet 2018 ◆ Myung 2018 ◆ O'Connell 2018 ◆ Steele 2018 Excluded for this guideline, included only implant-based

Liew B, Southall C, Kanapathy M, Nikkhah D. Does post-mastectomy radiation therapy worsen outcomes in immediate autologous breast flap reconstruction? A systematic review and meta-analysis. J Plast Reconstr Aesthet Surg. 2021 Dec;74(12):3260-3280. doi: 10.1016/j.bjps.2021.08.005. Epub 2021 Aug 28. PMID: 34565703.

Exclusion criteria

- Review, technique, case report or case series articles
- Studies not published in English
- Studies with less than one-year follow-up
- Studies with less than ten patients in each group
- Studies that do not stratify results by type of reconstruction (autologous vs implant-based) and/or timing of reconstruction (immediate vs delayed)
- Studies focused solely on chest wall irradiation prior to breast reconstruction
- Studies focused solely on the elderly (> 65 years) or on obese patients
- Studies with no relevant extractable reconstruction data:
  - Berry 2010
  - Adesiyun 2011
  - Billig 2017
  - Terao 2017
  - Dewael 2019

- RoB considered in MA: yes
- Heterogeneity explained: yes
- Publication bias investigated: no
- Sources of CoI: yes

Sources of funding

No funding was received for this work.

Characteristics of the systematic review chosen for this PICO 9.

6.3.2.1.2 Characteristics of studies included in Liew 2021 (in Table 2)

Authors (year)	Study design (all cohorts)	No. of patients (R = IBR and PMRT; U = IBR only; D = PMRT and DBR)	Mean age (years)	No. of flaps	Flap type	Mean radiation dose (Gy)	Follow-up duration
Williams 1997	Retrospective	R: 19 U: 572	NK	NK	TRAM	50.3 or 49.9	NK
Tran 2000	Retrospective	R: 14 U: 14	NK	R: 14 U: 14	FTRAM, PTRAM	50.99	1 yr;M3 yrs
Rogers 2002	Retrospective	R: 30 U: 30	R: 48.2 U: 48.2	R: 32 U: 37	DIEP	50.5	R: 19.9 mos U: 17.4 mos
Spear 2005	Retrospective	R: 34 U: 78	R: 44.5 U: 49.4	R: 38 U: 91	PTRAM	NK	NK
Carlson 2008	Retrospective	R: 25 U: 128 D: 15	R: 48.9 U: 48.5 D: 44.1	R:25 U: 149 D: 15	PTRAM	NK	NK
Chatterjee 2009	Prospective	R: 22 U: 46	R: 51 U: 53	R: 22 U: 46	DIEP	40, 45 or 50	R: Mdn 4.5 yrs U: Mdn 3 yrs
Berry 2010	Retrospective	R: 78 U: 274	NK	NK	LD, FTRAM, PTRAM, DIEP	NK	NK
Lee 2010	Retrospective	R: 36 U: 371 D: 43	NK	R: 36 U: 371 D: 43	LD, FTRAM, PTRAM, DIEP, SIEA, SGAP	NK	R: Mdn 63.6 mos U: Mdn 56.8 mos D: Mdn 28.3 mos

Authors (year)	Study design (all cohorts)	No. of patients (R = IBR and PMRT; U = IBR only; D = PMRT and DBR)	Mean age (years)	No. of flaps	Flap type	Mean radiation dose (Gy)	Follow-up duration
Adesiyun 2011	Retrospective	R: 35 D: 43	NK	NK	LD, PTRAM, FTRAM, DIEP, SGAP, MSFT	50.4 (45-50.4)	R: Mdn 63.6 mos D: Mdn 28.3 mos
Mirzabeigt 2013	Retrospective	R: 46 U: 113	R: 47.0 U: 52.0	R: 46 U: 113	DIEP, MSFT, SIEA, SGAP, IGAP	NK	R: 17.8 mos U: 13.1 mos
Taghizadeh 2015	Prospective	R: 50 U: 62	R: 47.5 U: 47.1	R: 61 U: 95	DIEP	40 or 50	R: M 33.3 mos U: M 32.9 mos
Billig 2017	Prospective	R: 108 D: 67	NK	NK	FTRAM, DIEP, SIEA	50.4	>1 year
Cooke 2017	Prospective	R: 64 U: 61	R: 51.2 U: 53.2	R: 64 U: 61	DIEP, SIEA	50 or 50.4	>1 year
He 2017	Retrospective	R: 61 U: 278 D: 31	NK	NK	PTRAM, DIEP	40-50.4	year
Pont 2017	Prospective	R: 77 U: 87	R: 48.2 U: 49.7	R: 81 U: 109	DIEP, MSFT, SIEA	50	NK
Terao 2017	Retrospective	R: 38 D: 20	R: 53 D: 49	R: 38 D:20	TRAM, LD	NK	NK
Berthet 2018	Retrospective	R: 29 U: 58	R: 50.9 U: 49.7	R: 29 U: 58	LD	NK	NK

Authors (year)	Study design (all cohorts)	No. of patients (R = IBR and PMRT; U = IBR only; D = PMRT and DBR)	Mean age (years)	No. of flaps	Flap type	Mean radiation dose (Gy)	Follow-up duration
Myung 2018	Retrospective	R: 21 U: 21	R: 46.7 U: 47.1	R: 21 U: 21	FTRAM, DIEP	50	> 18 mos
O' Connell 2018	Retrospective	R: 28 U: 80 D: 38	R: 57.8 U: 56.8 D: 54.3a	R: 28 U: 80 D: 38	DIEP	40	R: Mdn 27.5 mos U: Mdn 48.7 mos
Steele 2018	Retrospective	R: 104 U: 189 D: 119	R: 48 U: 51 D: 50	NK	DIEP, FTRAM, PTRAM, ELD	NK	NK
Dewael 2019	Retrospective	R: 20 D: 40	R: 46.3 D: 46.1	R: 20 D: 40	DIEP, SGAP,	50	R: M 7.5 yrs D: M 8.5 yrs

Characteristics of the studies included in Liew 2021 that were eligible for inclusion for PICO 9.

6.3.2.1.3 Risk of Bias assessment of Studies included in Liew 2021 (using ROBINS-I Cochrane Tool)



Study	D1	D2	D3	D4	D5	D6	D7	Overall
Williams et al. (1997)	−	+	+	+	+	×	+	−
Tran et al. (2000)	+	+	+	+	+	−	+	−
Rogers et al. (2002)	−	+	+	+	+	−	+	−
Spear et al. (2005)	−	+	+	+	+	−	+	−
Carlson et al. (2008)	−	+	+	+	−	+	+	−
Chatterjee et al. (2009)	−	+	+	+	+	+	+	−
Berry et al. (2010)	−	+	+	+	+	+	+	−
Lee et al. (2010)	−	+	+	+	+	×	+	×
Adesiyun et al. (2011)	−	+	+	+	+	×	+	×
Mirzabeigi et al. (2013)	−	+	+	+	+	−	+	−
Taghizadeh et al. (2015)	−	+	+	+	+	+	+	−
Billig et al. (2017)	−	+	+	+	+	×	+	×
Cooke et al. (2017)	−	+	+	+	+	×	+	×
He et al. (2017)	−	+	+	+	−	+	+	−
Pont et al. (2017)	−	+	+	+	+	×	+	×
Terao et al. (2017)	−	+	+	+	+	−	+	−
Berthet et al. (2018)	−	+	+	+	+	×	+	×
Myung et al. (2018)	−	+	+	+	+	+	+	−
O' Connell et al. (2018)	−	+	+	+	+	×	×	×
Steele et al. (2018)	−	+	+	+	−	×	+	×
Dewael et al. (2019)	−	+	+	+	+	−	+	−

Risk of Bias Domains
Pre-Intervention
D1: Bias due to confounding
D2: Bias in selection of participants into the study
At Intervention
D3: Bias in classification of interventions
Post-Intervention
D4: Bias due to deviation from intended interventions
D5: Bias due to missing data
D6: Bias in measurement of outcome
D7: Bias in selection of the reported result

Judgement
Critical risk of bias
Serious risk of bias
Moderate risk of bias
Low risk of bias
No information

Caption of Figure 3 from: Liew et al. Does post-mastectomy radiation therapy worsen outcomes in immediate autologous breast flap reconstruction? A systematic review and meta-analysis. J Plast Reconstr Aesthet Surg. 2021 Dec;74(12):3260-3280. doi: 10.1016/j.bjps.2021.08.005. (open access source: https://pubmed.ncbi.nlm.nih.gov/34565703/).

6.3.2.2 Primärstudien – neu identifiziert

Reference/ Study type	Population	Interventions	Main results	Methodological evaluation
Hsieh 2023 Retrospective cohort study	**Inclusion criteria (for analysis):** ◆ Immediate breast reconstruction **Exclusion criteria (for analysis):** ◆ Recurrence ◆ Previous radiation therapy ◆ Lost to follow-up **Enrolment period** ◆ July 2008 – December 2018 **Follow-up** ◆ RT: 5.2 ±2.48 years (range 2.4–10.5) ◆ no RT: 5.73 ±2.73 years (range 2.3–12.8) **Descriptive statistics** ◆ Age (median, range) · RT: 40.0 ± 7.5 (29-53) · No RT: 45.5 ± 8.3 (24 - 65) ◆ BMI (median, range) · RT: 24.5 ± 3.7 (19.5 - 32.0) <30: 13 (92.9%) >30: 2 (13.3%) · No RT: 24.2 ± 4.2 (17.3 - 40.1) <30: 78 (92.9%) >30: 6 (7.1%) ◆ Stadium (TNM)	**Interventions** A: RT after autologous reconstruction · N = 15 B: no RT after autologous reconstruction · N = 86 **Analysis** ◆ frequencies & mean ± standard deviation (range) ◆ No matching ◆ No adjustment	**Heamatoma required evacuation (< 30 days)** · RT: 1/15 · No RT: 0/86 **Infections (< 30 days)** · RT: 0/15 · No RT: 0/86 **Wound required surgical intervention (> 30 days)** · RT: 0/15 · No RT: 1/86 **Fat necrosis required surgical intervention (< 30 days):** · RT: 0/15 · No RT: 3/86 **NAC necrosis (< 30 days)** · RT: 0/15 · No RT: 0/86 Local recurrence · RT: 0/15 · No RT: 0/86 **QoL-outcomes: Breast –Q (mean, SD)** Psychosocial well-being: · RT: 66.2 (20.1) · No RT: 75.1 (17.3)	**General information** ◆ **Follow-up**: mean 5 years ◆ **Funding:** This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors. ◆ **CoI**: The authors declare that they have no conflict of interest. **Risk of bias considerations (adapted from SIGN cohort study checklist)** ◆ Study type: restrospective cohort study ◆ Confounding: probably (high risk risk) ◆ Rate of participation/Exclusions reported (selection bias into the study): yes (low risk) ◆ Exposure/Intervention · Assessment reliable: yes · Assessed more than once: no · Possibly affected by knowledge of outcome status: no (low risk due to retrospective data collection and no possible influence) ◆ Drop-out rate & reasons reported: not reported ◆ Outcome · Outcome measure is well-defined, valid and reliable: yes · Blind outcome assessment to exposure: (→If not, Knowledge of exposure status likely to influence the outcome: no (low risk due to

Reference/ Study type	Population	Interventions	Main results	Methodological evaluation
	· RT: Stage 0 (DCIS): 0 (0.0%), Stage I: 2 (13.3%), Stage II: 5 (33.3%), Stage III: 8 (53.3%) · No RT: Stage 0 (DCIS): 21 (24.4%), Stage I: 28 (32.6%), Stage II: 37 (43.0%), Stage III: 0 (0.0%) ◆ Chemotherapy (% yes) (previous) · RT: 6 (40.0%) · No RT: 7 (8.1%) ◆ Reconstruction type (flap type) (%) · RT: DIEP (73.3%), PAP (13.3%), Free ms-TRAM (13.3%) · No RT: DIEP (87.2%), PAP (7.0%), Free ms-TRAM (5.8%)		Physical well-being (chest): · RT: 60.1 (20.3) · No RT: 73.9 (17.3) Physical well-being (donor site): · RT: 73.2 (28.6) · No RT: 78.3 (18.4) Sexual well-being: · RT: 44.1 (18.3) · No RT: 50.8 (22.4) Satisfaction with breast: · RT: 60.1 (10.4) · No RT: 65.1 (14.8) Satisfaction with surgeon: · RT: 95.2 (9.6) · No RT: 92.8 (13.5) Satisfaction with information from surgeon: · RT: 74.0 (15.1) · No RT: 74.8 (18.3) Satisfaction with medical team: · RT: 97.3 (5.5) · No RT: 93.1 (14.5) Satisfaction with other staff: · RT: 93.9 (13.0)	retrospective data collection and no possible influence) ◆ Main cofounders taken into account: no ◆ Confidence intervals reported: no ◆ Selective reporting (comparison with protocol): no protocol found **Other limitations or comments**: retrospective design

Reference/ Study type	Population	Interventions	Main results	Methodological evaluation
			· No RT: 89.7 (17.1) **Aesthetics (mean, SD)** Breast shape of reconstructive site: · RT: 4.0 (0.3) · No RT: 4.12 (0.5) Symmetry of inframammary fold: · RT: 4.3 (0.5) · No RT: 4.1 (0.6) Symmetry of volume: · RT: 4.0 (0.5) · No RT: 4.0 (0.5) Symmetry of shape: · RT: 3.7 (0.5) · No RT: 3.9 (0.6) Overall outcomes: · RT: 3.9 (0.4) · No RT: 4.1 (0.5)	
Jagsi 2018 Prospective multicenter cohort study	**Inclusion criteria (for analysis):** ◆ female sex ◆ age 18 years or older, ◆ undergoing first-time, immediate, or delayed reconstruction following mastectomy. **Exclusion criteria (for analysis):**	**Interventions** A: RT after autologous reconstruction · N = 236	**Hematoma** ◆ One year post-op: · RT: 9/236 · No RT: 27/407 ◆ Two years post-op: · RT: 8/199 · No RT: 21/332	**General information** ◆ **Follow-up**: NR (at least 2 years) ◆ **Funding**: This work was supported by the National Institutes of Health/National Cancer Institute (grant number R01 CA152192). ALP was supported, in part, by National Institutes of Health/National Cancer Institute Cancer Center Support (grant number P30 CA008748),

Reference/ Study type	Population	Interventions	Main results	Methodological evaluation
	◆ patients treated with prophylactic mastectomy (without cancer diagnosis) ◆ women who had received radiotherapy prior to mastectomy ◆ patients who received bilateral reconstruction with autologous reconstruction techniques on one side and implant-based reconstruction techniques on the other ◆ those who received two-staged crossover of procedure types ◆ those who received immediate reconstruction after mastectomy of one breast but delayed reconstruction of the other **Enrolment period** ◆ 2012 – 2015 **Follow-up** ◆ NR (at least 2 years) **Descriptive statistics (reported only for combined for autologous and implant-based reconstructions)** ◆ Age (years, %) · RT: <30: 19/622 (3.1%); 30-39: 99/622 (15.9%); 40-49: 211/622 (33.9%); 50-59: 191/622 (30.7%); ≥60: 102/622 (16.4%) · No RT: <30: 24/1625 (1.5%); 30-39: 181/1625 (11.1%); 40-49: 586/1625 (36.1%); 50-59: 542/1625 (33.4%); ≥60: 292/1625 (18.0%)	B: no RT after autologous reconstruction · N = 407 **Analysis** ◆ Frequencies; mixed-effects logistic regression model ◆ No matching ◆ Adjusted for Baseline value of the corresponding outcome variable, clinical and demographic characteristics and between-enter variability by including sites (e.g., reconstruction timing, age, extent of disease, bilateral vs unilateral reconstruction, chemotherapy receipt, nodal	**Wound dehiscence** ◆ One-year post-op: · RT: 12/236 · No RT: 8/407 ◆ Two years post-op: · RT: 11/199 · No RT: 8/332 **Wound infection requiring oral antibiotics** ◆ One-year post-op: · RT; 4/236 · No RT: 7/407 ◆ Two years post-op: · RT: 3/199 · No RT: 5/332 **Wound infection requiring IV antibiotics** ◆ One-year post-op: · RT: 5/236 · No RT: 3/407 ◆ Two years post-op: · RT: 3/199 · No RT: 3/332 **Wound infection requiring surgical repair** ◆ One-year post-op: · RT: 5/236	funded by the National Cancer Institute (grant number 1RO1 CA152192). ◆ **CoI**: NR **Risk of bias considerations (adapted from SIGN cohort study checklist)** ◆ Study type: prospective multicenter cohort study ◆ Confounding: adjusted for but still possible (moderate risk) ◆ Rate of participation/Exclusions reported (selection bias into the study): yes ◆ Exposure/Intervention · Assessment reliable: yes · Assessed more than once: yes · Possibly affected by knowledge of outcome status: possible (no blinding; due to prospective design influence on subjective outcomes like QoL especially problematic) ◆ Drop-out rate & reasons reported: not reported ◆ Outcome · Outcome measure is well-defined, valid and reliable: yes · Blind outcome assessment to exposure: (→If not, Knowledge of exposure status likely to influence the outcome: possible (no blinding) ◆ Main cofounders taken into account: yes (for outcome any complication and major complication) ◆ Confidence intervals reported: no

Reference/ Study type	Population	Interventions	Main results	Methodological evaluation
	◆ BMI (median, range) · RT: <30: 431/622 (69.3%); ≥30: 191/622 (30.7%) · No RT: <30: 1251/1625 (77.0%); ≥30: 374/1625 (23.0%) ◆ Stadium · RT: NR · No RT: NR ◆ Chemotherapy (% yes) · RT: 585/622 (94.1%) · No RT: 588/1625 (36.2%) ◆ Reconstruction type (flap type) (%) · RT: NR · No RT: NR	management, body mass index, smoking, diabetes, race, ethnicity, education, employment, income, and hospital site)	· No RT: 4/407 ◆ Two years post-op: · RT: 3/199 · No RT: 3/332 **Chronic fat necrosis** ◆ One-year post-op: · RT: 11/236 · No RT: 33/407 ◆ Two years post-op: · RT: 14/199 · No RT: 29/332 **Total flap loss** ◆ One-year post-op: · RT: 1/236 · No RT: 8/407 ◆ Two years post-op: · RT: 1/199 · No RT: 6/332 **QoL-outcomes: Breast –Q (mean, SD)** Satisfaction with breast: ◆ One-year post-op: · RT: 63.9 (16.9) · No RT: 68.5 (17.5) ◆ Two years post-op: · RT: 65.1 (18.2) · No RT: 69 (17.8)	◆ Selective reporting (comparison with protocol): no protocol found **Other limitations or comments**: NA

Reference/ Study type	Population	Interventions	Main results	Methodological evaluation
			Satisfaction with outcome: ◆ One-year post-op: · RT: 71.8 (21.6) · No RT: 74.3 (20.3) ◆ Two years post-op: · RT: 70.1 (22.9) · No RT: 73.6 (20) Psychosocial well-being: ◆ One-year post-op: · RT: 70.4 (18.6) · No RT: 75.4 (19.6) ◆ Two years post-op: · RT: 71.8 (19.4) · No RT: 77.7 (18.9) Physical well-being: ◆ One-year post-op: · RT: 71.2 (13.9) · No RT: 76.3 (15.8) ◆ Two years post-op: · RT: 72 (15.3) · No RT: 77.2 (15.1)	
Emanuele, 2023 retrospective case-control	**Inclusion criteria (for analysis):** ◆ female patients ◆ age over 18 years at the time of diagnosis	**Interventions**	**Complications** ◆ **Hematoma:** · RT: 7/79	**General information** ◆ **Follow-up**: average: 2 years ◆ **Funding**: The authors declare that they have no conLicts of interest.

Reference/ Study type	Population	Interventions	Main results	Methodological evaluation
multicenter study	◆ patients who had undergone mastectomy and immediate reconstruction with implant in one or two stages or with autologous flaps with or without adjuvant radiotherapy **Exclusion criteria (for analysis):** ◆ prior breast or chest wall irradiation ◆ delayed reconstruction ◆ patients lost to follow-up **Enrolment period** ◆ 2001 – 8th April 2020 **Follow-up** ◆ Average: 2 years **Descriptive statistics** ◆ Age (median, range) · RT: 50 (45-59) · No RT: 50.5 (45-56) ◆ BMI (median, range) · RT: 26.5 (24.0 - 28.4) ≥30: 11 (15.3%) · No RT: 25.0 (23.0 - 27.1) ≥30: 9 (9.2%) ◆ Stadium · RT: NR · No RT: NR ◆ Chemotherapy (% yes) · RT: 25 (31.7%)	A: RT after autologous reconstruction · N = 79 B: no RT after autologous reconstruction · N = 108 **Analysis** ◆ multivariable hierarchical logistic regression analyses ◆ No matching ◆ adjusted for age, the BMI, smoking habits, diabetes, other autoimmune diseases, type of chemotherapy, axillary dissection, and type of surgical procedure	· No RT: 7/108 ◆ **Early infection (< 30 days):** · RT: 4/79 · No RT: 2/108 ◆ **Late infection (≥ 30 days):** · RT: 2/79 · No RT: 1/108 ◆ **Early and late infection:** · RT: 0/79 · No RT: 0/108 ◆ **Skin necrosis:** · RT: 18/79 · No RT: 10/108 ◆ **Liponecrosis:** · RT: 9/79 · No RT: 10/108 ◆ **Partial flap necrosis:** · RT: 10/79 · No RT: 6/108 ◆ **Full-thickness flap necrosis:** · RT: 3/79 · No RT: 2/108 ◆ **Reintervention:** · RT: 3/79 · No RT: 3/108	◆ **CoI**: NR **Risk of bias considerations (adapted from SIGN cohort study checklist)** ◆ Study type: retrospective case-control multicenter study ◆ Confounding: probably (high risk risk) ◆ Rate of participation/Exclusions reported (selection bias into the study): yes ◆ Exposure/Intervention · Assessment reliable: yes · Assessed more than once: no · Possibly affected by knowledge of outcome status: no (low risk due to retrospective data collection and no possible influence) ◆ Drop-out rate & reasons reported: no problems ◆ Outcome · Outcome measure is well-defined, valid and reliable: yes · Blind outcome assessment to exposure: (→If not, Knowledge of exposure status likely to influence the outcome: no (low risk due to retrospective data collection and no possible influence) ◆ Main confounders taken into account: unclear (no adjusted data reported per outcome) ◆ Confidence intervals reported: no ◆ Selective reporting (comparison with protocol): registration number available NCT04783818

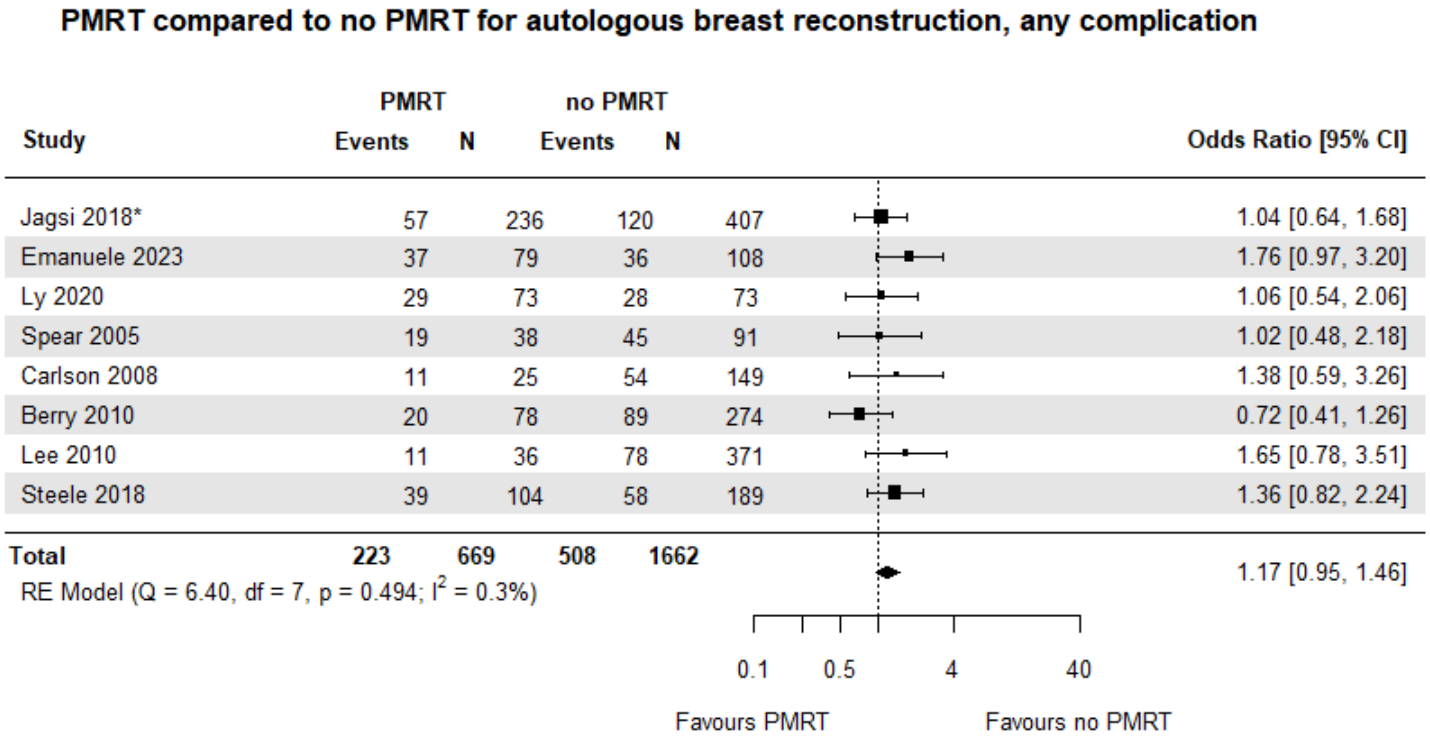
Reference/ Study type	Population	Interventions	Main results	Methodological evaluation
	· No RT: 18 (16.6%) ◆ Reconstruction type (flap type) (%) · RT: NR · No RT: NR			**Other limitations or comments**: retrospective design
Ly, 2020 Retrospective cohort study	**Inclusion criteria (for analysis):** ◆ Immediate bilateral breast reconstruction with abdominally based free-flaps followed by unilateral PMRT **Exclusion criteria (for analysis):** ◆ Prior breast radiation ◆ Implant-based rechonstruction ◆ Flap loss prior to radiation ◆ Follow-up less than 6 months ◆ Incomplete radiation data **Enrolment period** ◆ 2007 – 2017 **Follow-up** ◆ mean: 58.9 ± 29.3 **Descriptive statistics (reported for complete cohort)** ◆ Age (mean, SD): 48.9 ± 9.0 ◆ BMI (median, range): · normal (18.5–24.9): 14 (19.2%) · overweight (25–29.9): 29 (39.7%) · obese (≥30): 30 (41.1%)	**Interventions** A: RT after autologous reconstruction · N = 29 B: No RT after autologous reconstruction · N = 28 **Analysis** ◆ frequencies, proportions and poisson regression ◆ No matching ◆ No adjustment	**Complications:** ◆ Wound infection: · RT: 0/29 · No RT: 2/28 ◆ Fat necrosis or oil cysts: · RT: 21/29 · No RT: 23/28 ◆ Delayed wound healing or dehiscence: · RT: 1/29 · No RT: 4/28 ◆ Partial or total flap loss: · RT: 0/29 · No RT: 0/28 ◆ Revision surgeries: · RT: 31/29 · No RT: 30/28	**General information** ◆ **Follow-up**: mean: 58.9 ± 29.3 ◆ Funding: NR ◆ **CoI**: The authors declare no potential conflict of interest. **Risk of bias considerations (adapted from SIGN cohort study checklist)** ◆ Study type: retrospective review ◆ Confounding: probably (high risk) ◆ Rate of participation/Exclusions reported (selection bias into the study): reasons for exclusion reported ◆ Exposure/Intervention · Assessment reliable: yes · Assessed more than once: no · Possibly affected by knowledge of outcome status: no (low risk due to retrospective data collection and no possible influence) ◆ Drop-out rate & reasons reported: not reported ◆ Outcome · Outcome measure is well-defined, valid and reliable: yes · Blind outcome assessment to exposure: (→If not, Knowledge of exposure status likely to

Reference/ Study type	Population	Interventions	Main results	Methodological evaluation
	◆ Stadium · RT: NR · No RT: NR ◆ Previous Chemotherapy (% yes): 29 (39.7%) ◆ Reconstruction type (flap type) (%) · RT: DIEP (64.4%), TRAM (35.6%), SIEA (0.0%) · No RT: DIEP (63.0%), TRAM (35.6%), SIEA (1.4%)			influence the outcome: no (low risk due to retrospective data collection and no possible influence) ◆ Main cofounders taken into account: no ◆ Confidence intervals reported: no ◆ Selective reporting (comparison with protocol): no protocol found **Other limitations or comments**: retrospective design

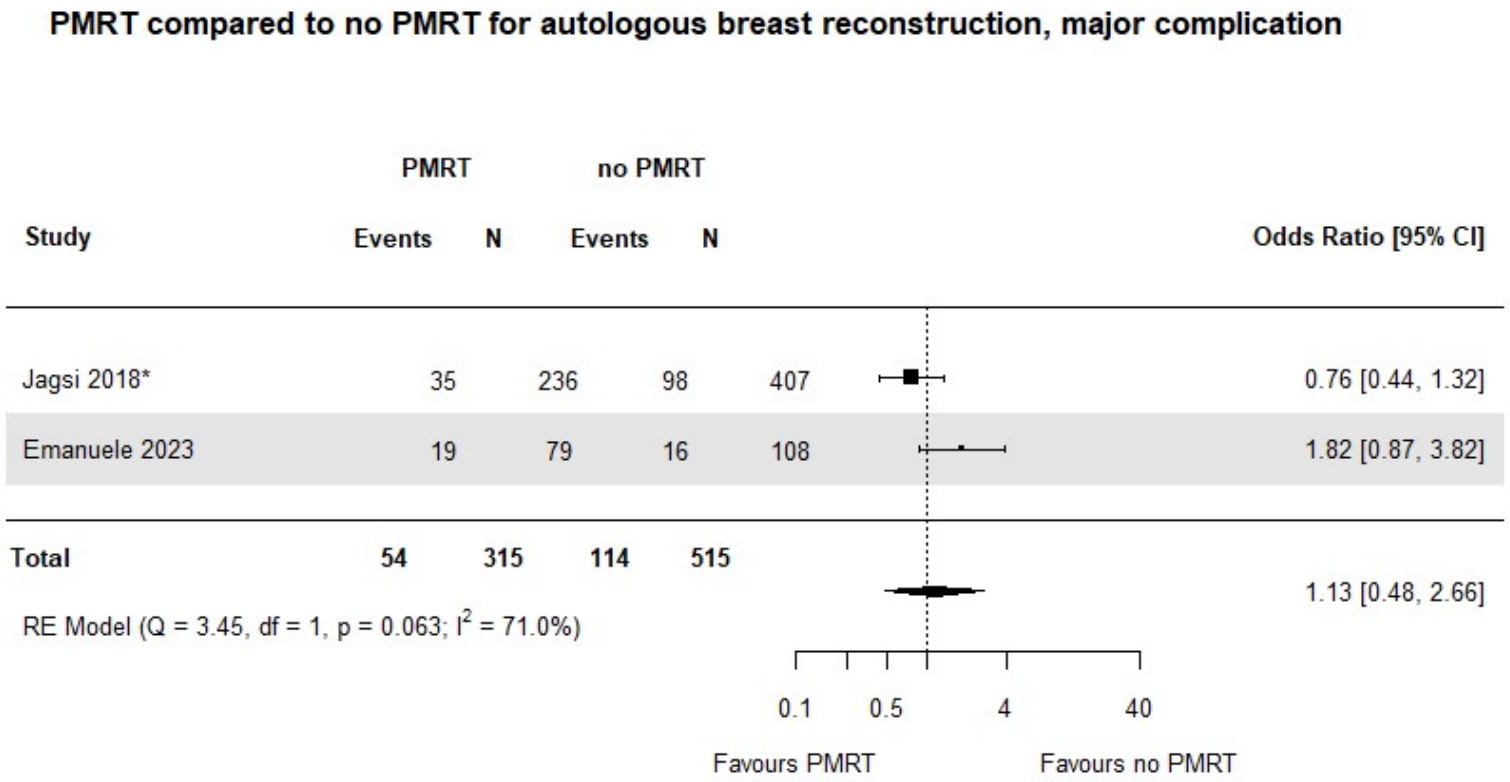
6.3.3 Meta-Analysen

Erklärungen: Mit * markierte Studien haben einen adjustierten Effektschätzer für den Endpunkt berichtet, der hier verwendet wurde.

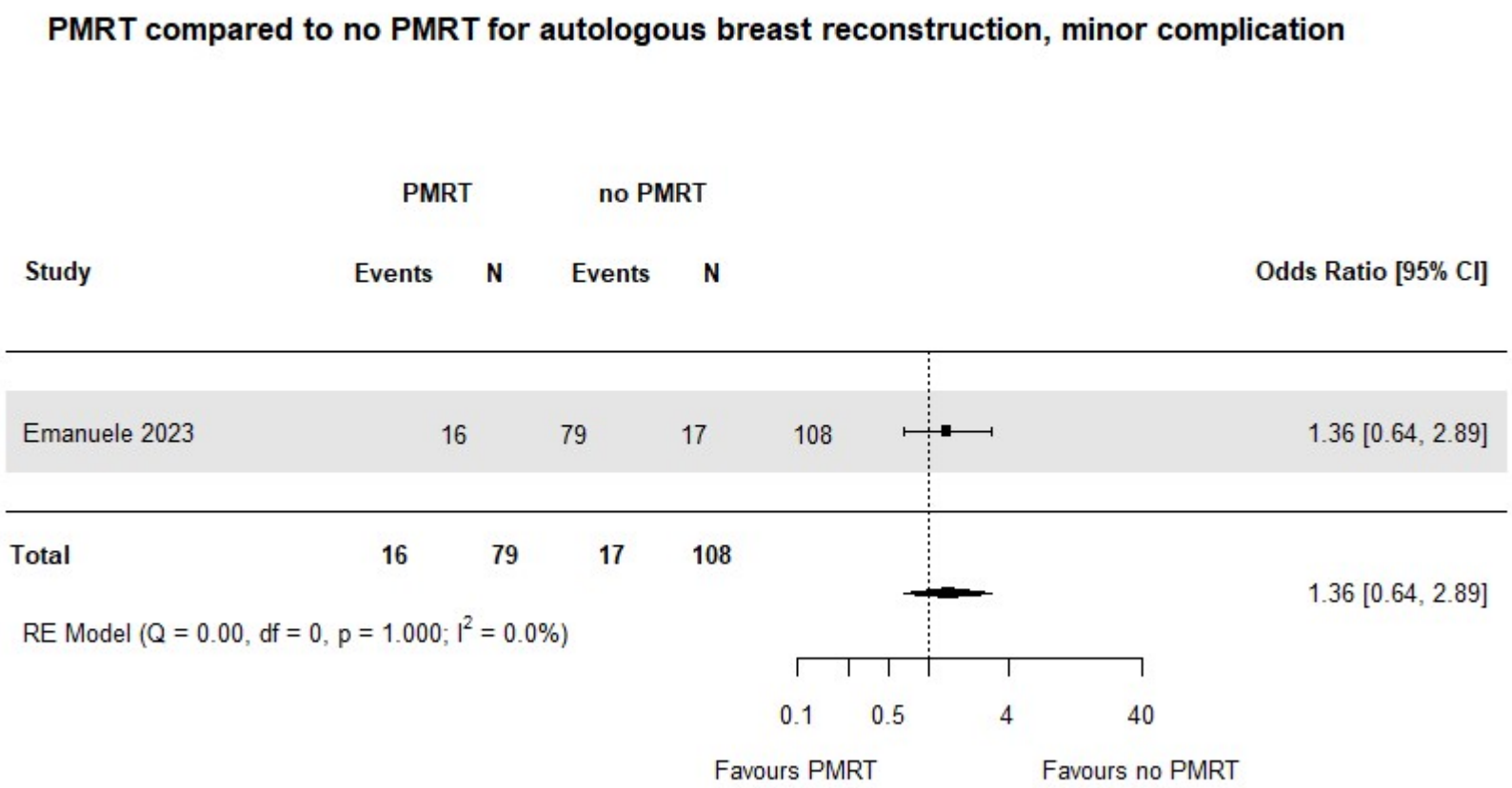
6.3.3.1 Any complication



6.3.3.2 Major complication

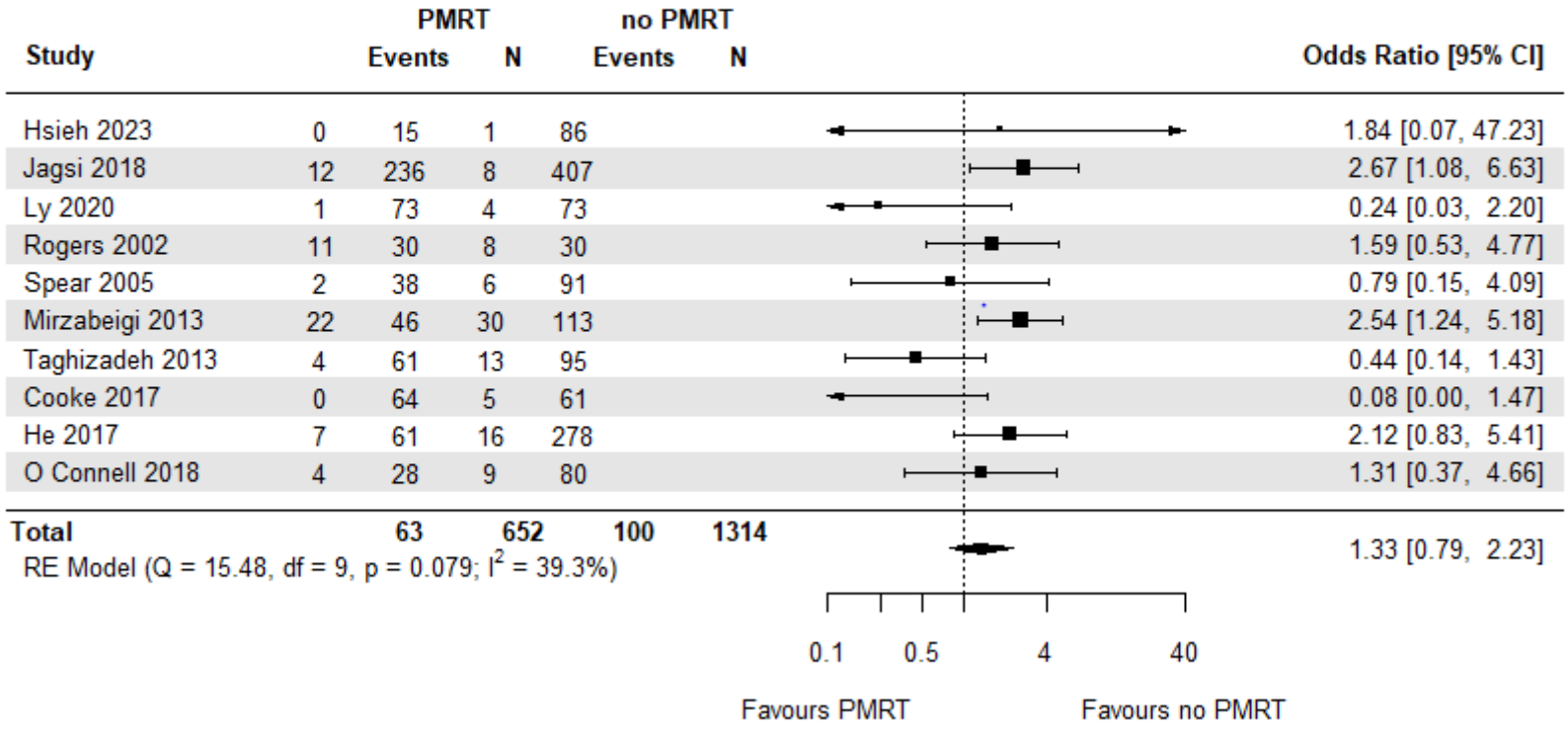


6.3.3.3 Minor complication



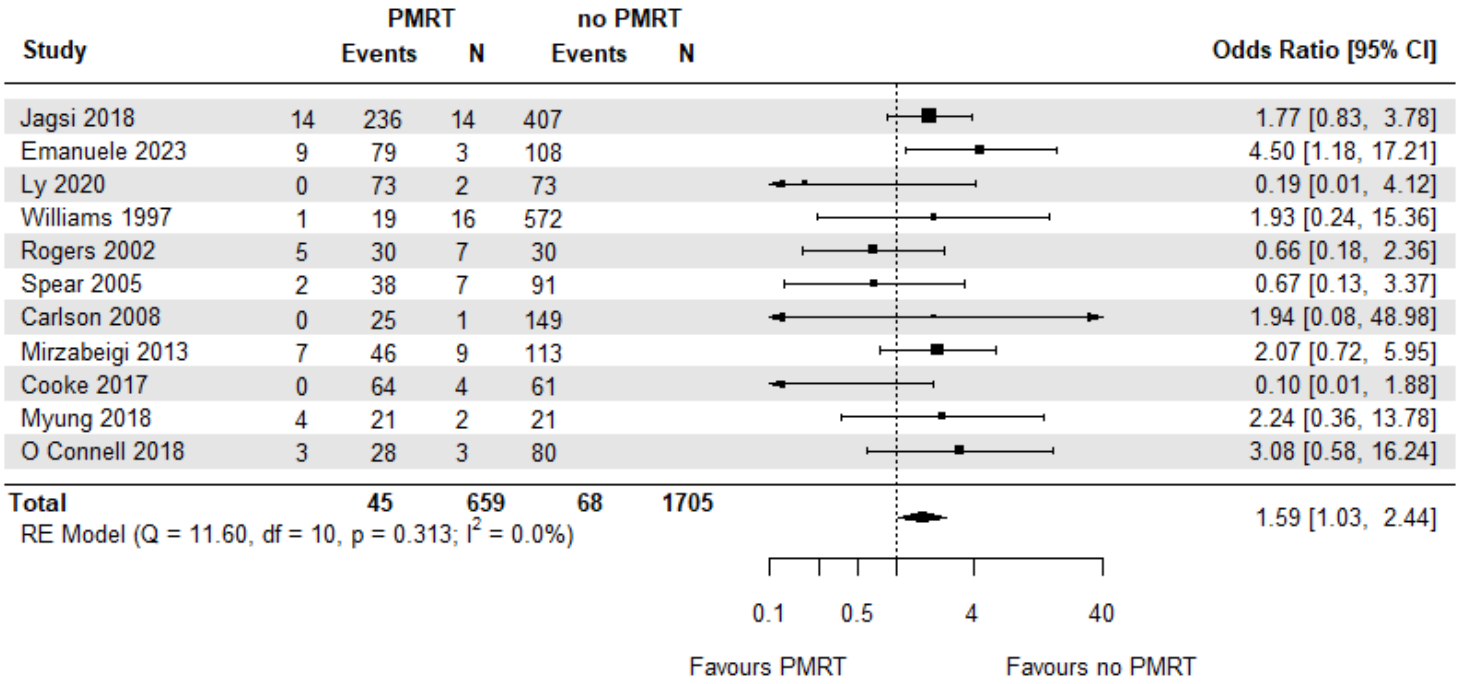
6.3.3.4 Wound complications

PMRT compared to no PMRT for autologous breast reconstruction, wound complications

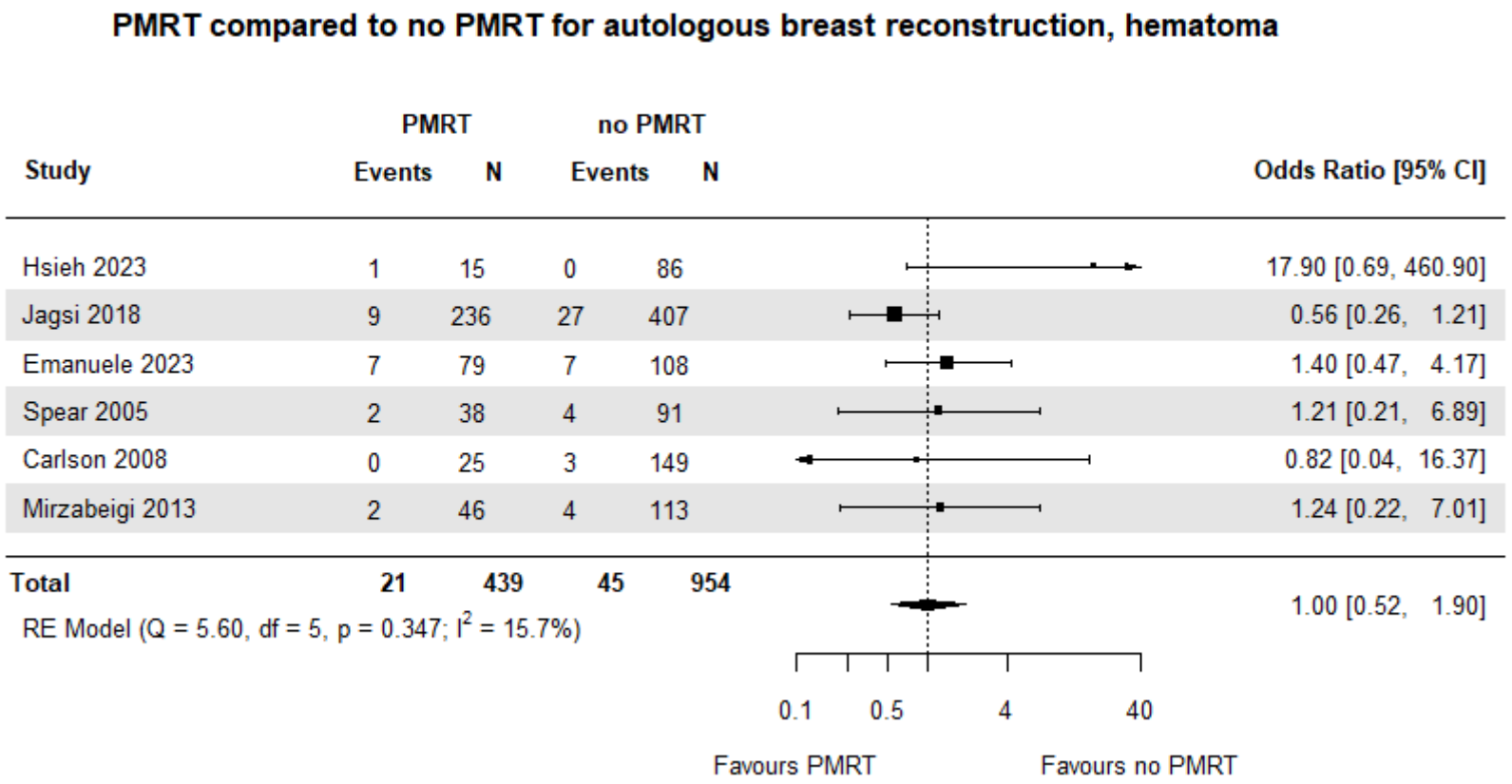


6.3.3.5 Infections

PMRT compared to no PMRT for autologous breast reconstruction, infections

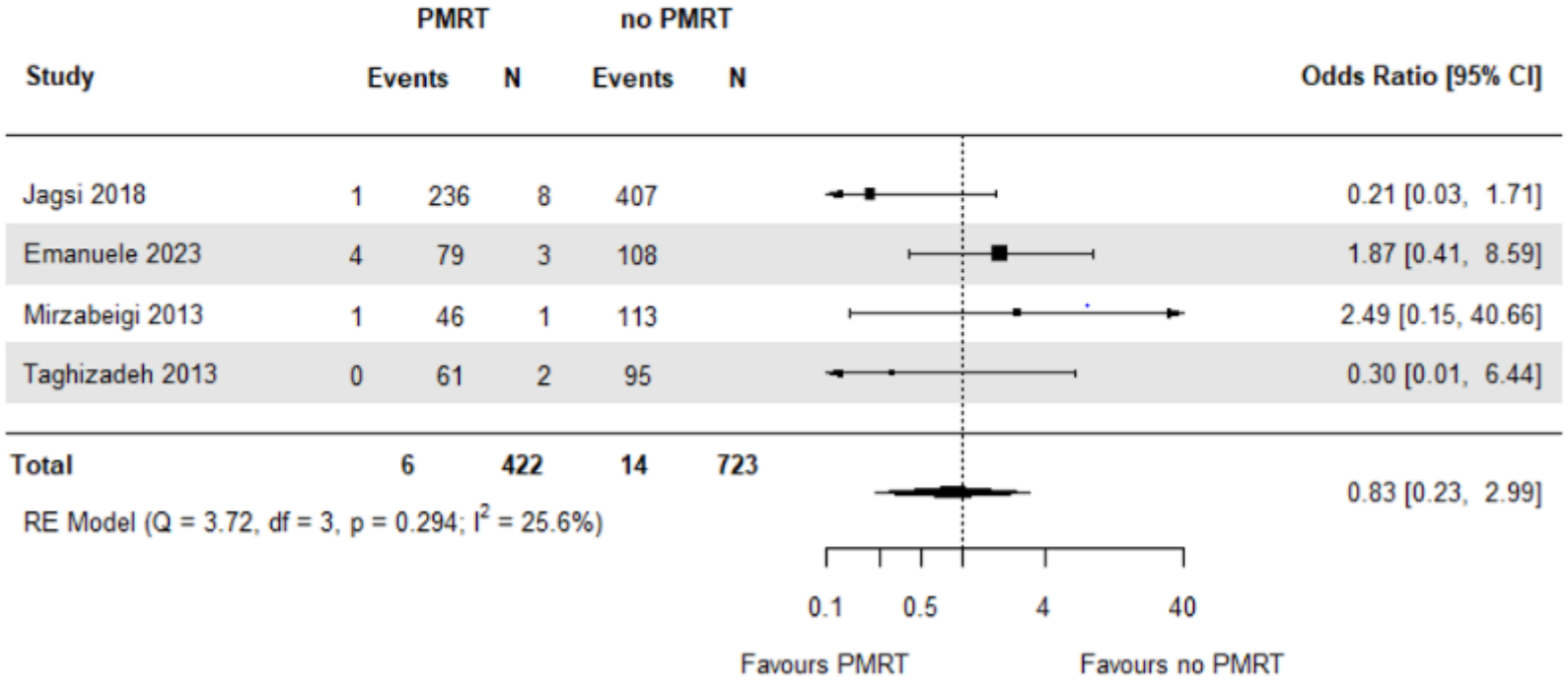


6.3.3.6 Hematoma



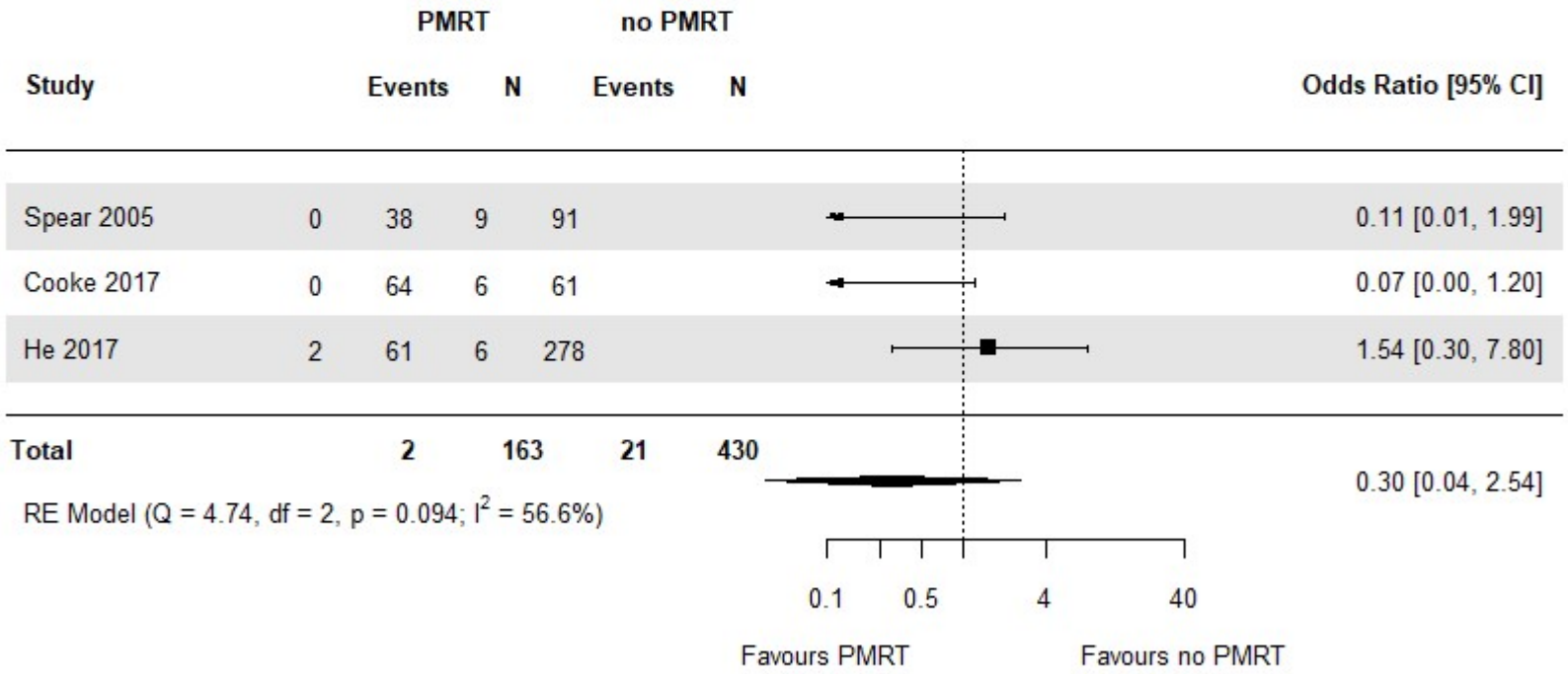
6.3.3.7 Total flap loss

PMRT compared to no PMRT for autologous breast reconstruction, total flap loss

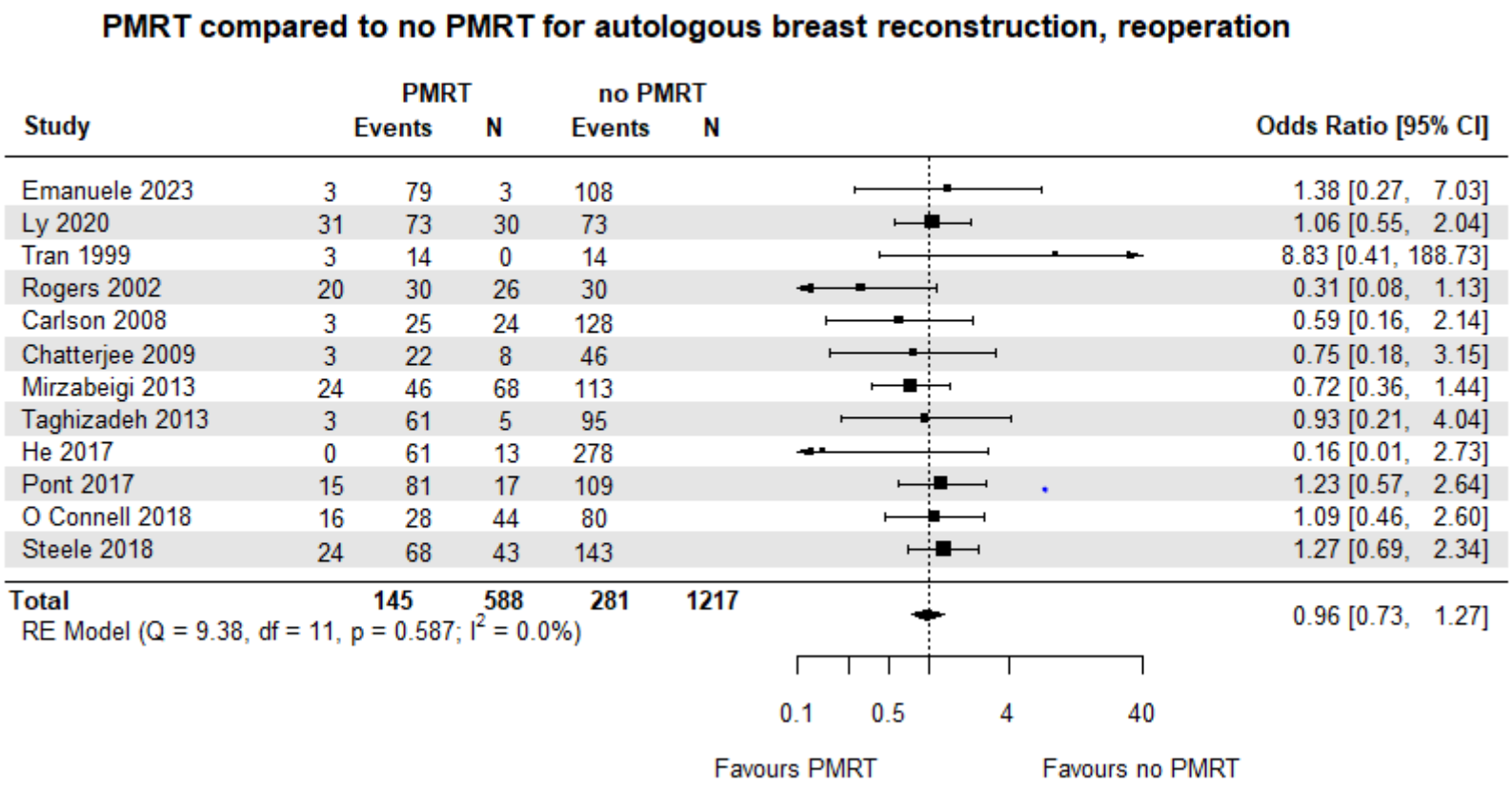


6.3.3.8 Partial flap loss

PMRT compared to no PMRT for autologous breast reconstruction, partial flap loss

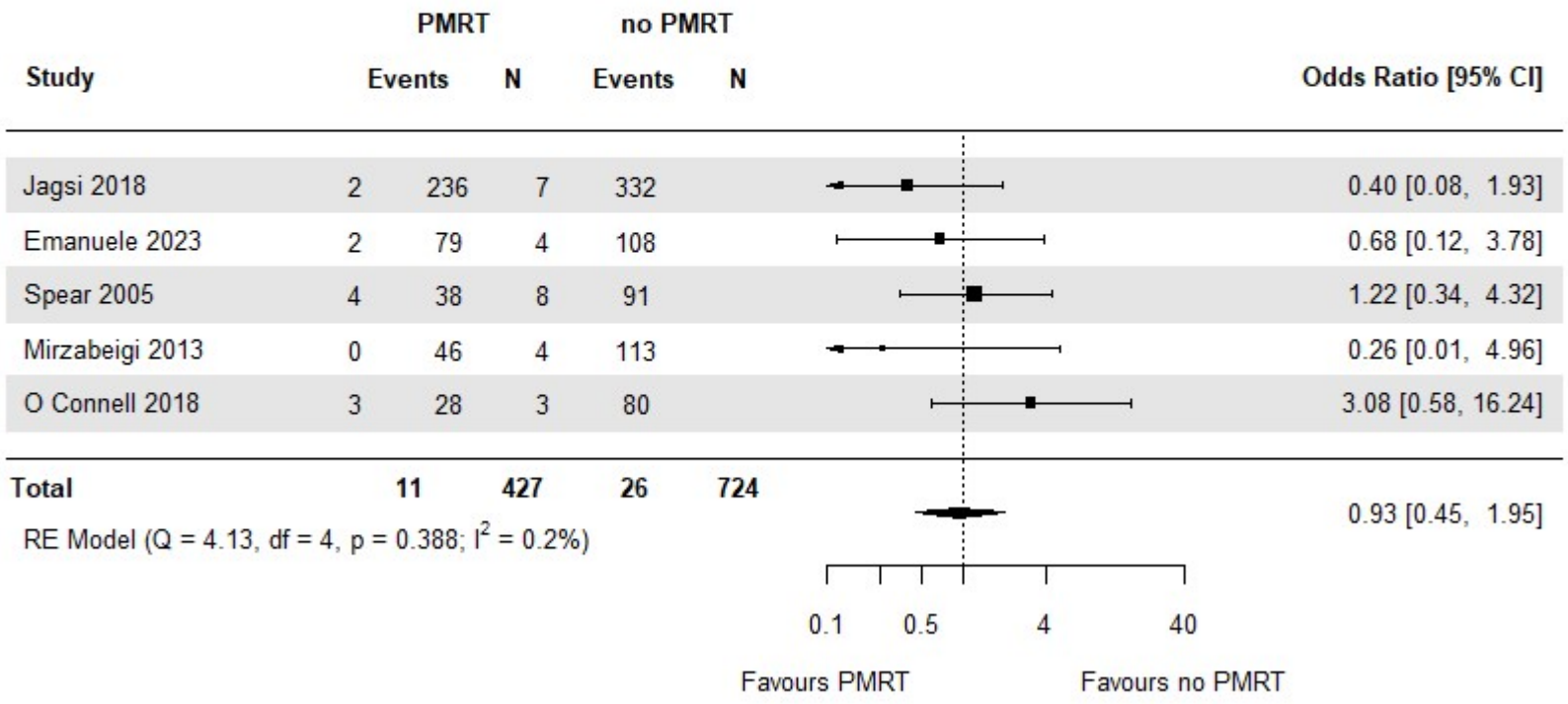


6.3.3.9 Reoperation



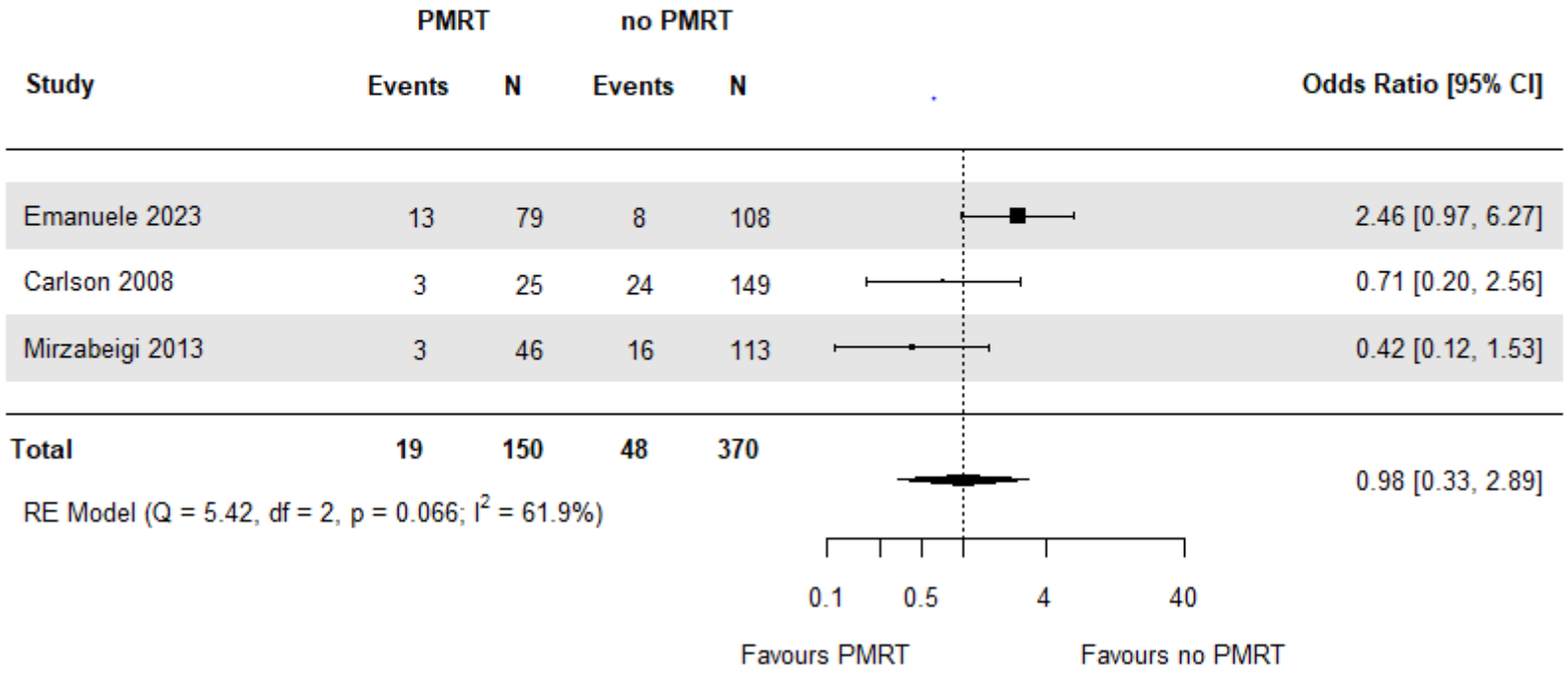
6.3.3.10 Seroma

PMRT compared to no PMRT for autologous breast reconstruction, seroma

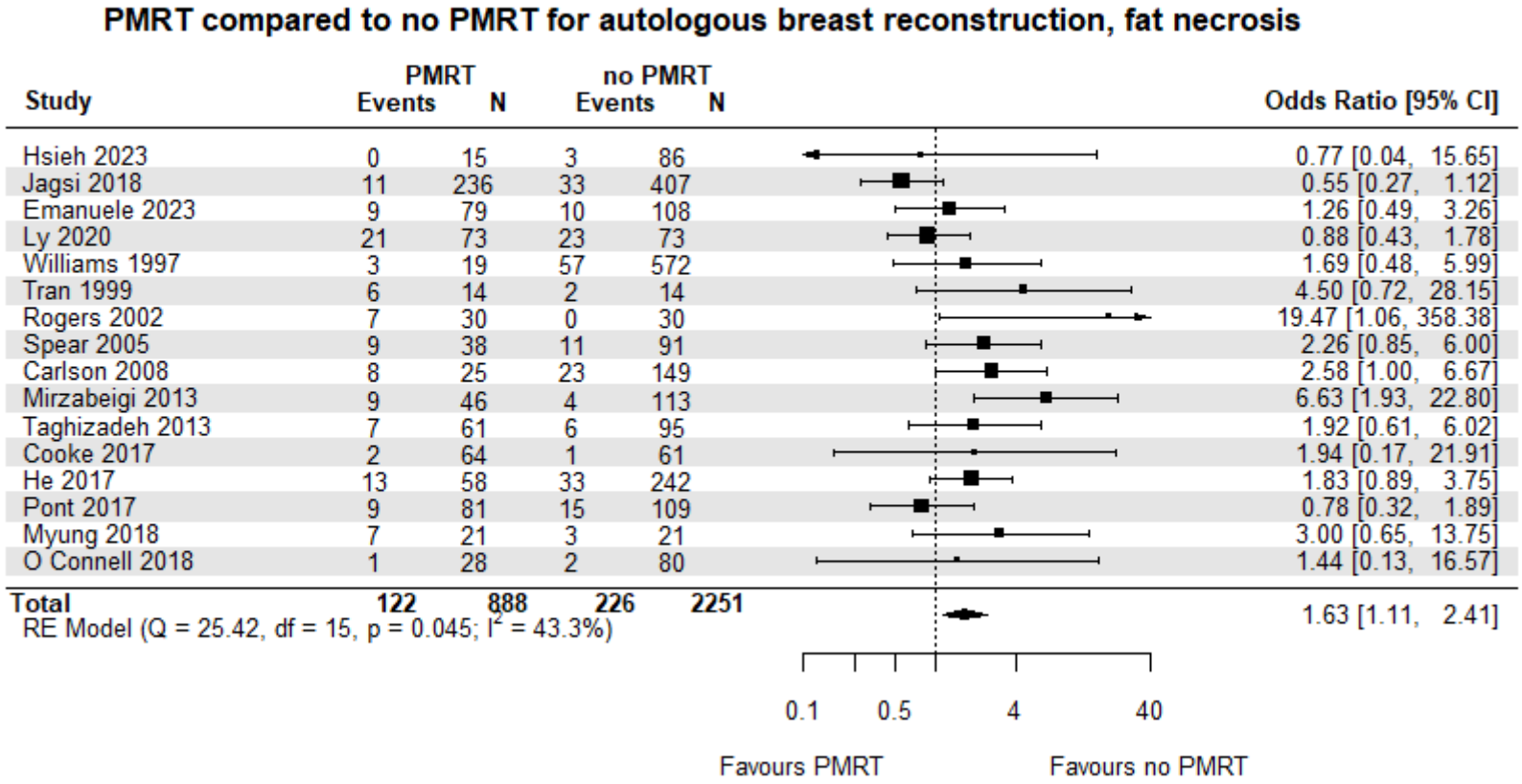


6.3.3.11 Flap necrosis

PMRT compared to no PMRT for autologous breast reconstruction, flap necrosis

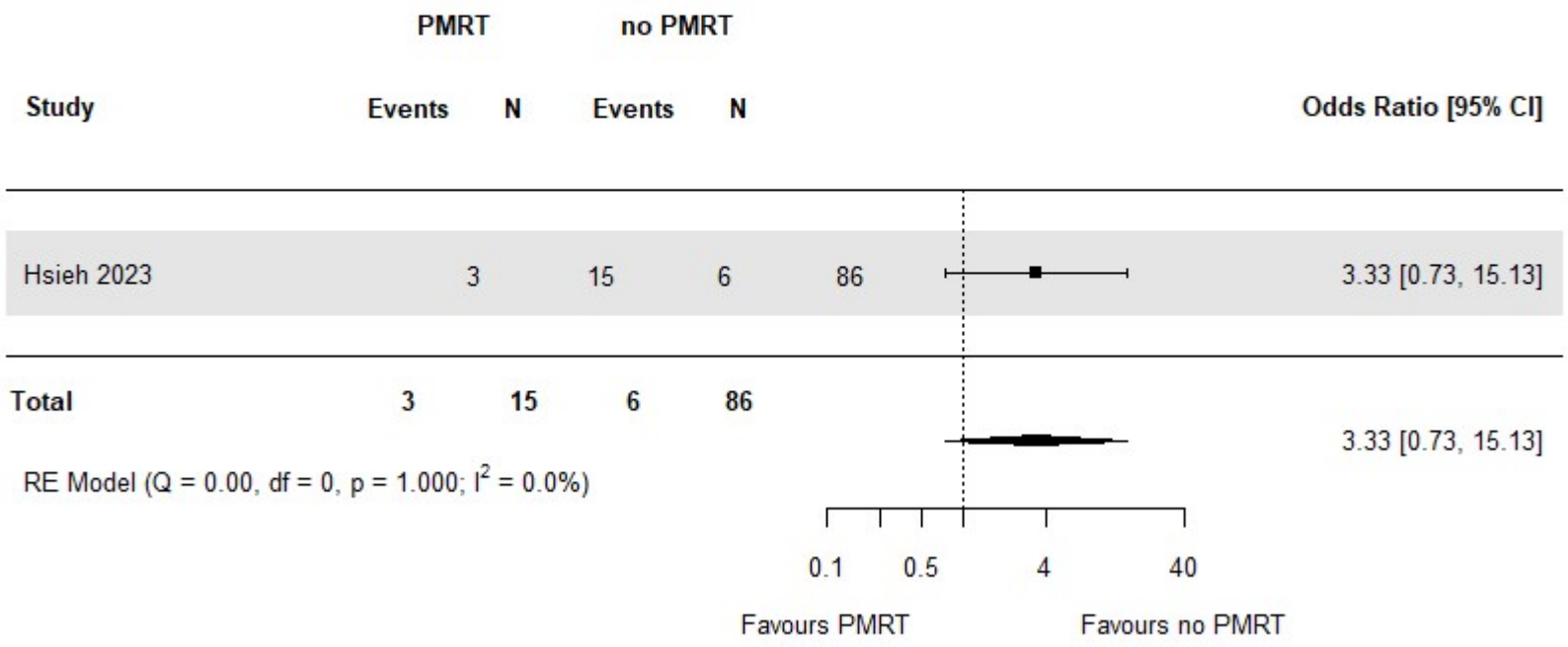


6.3.3.12 Fat necrosis



6.3.3.13 Distant metastases

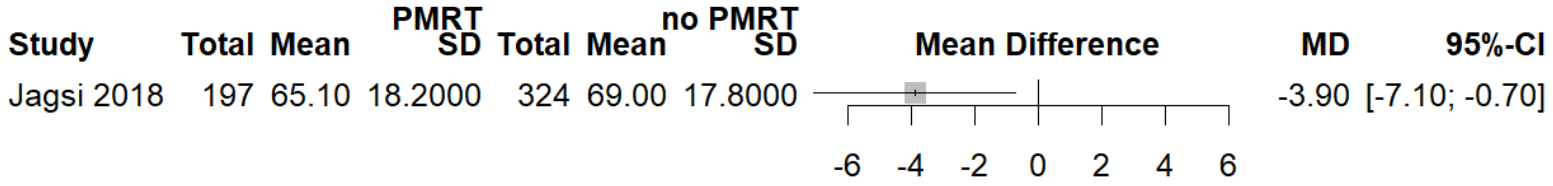
PMRT compared to no PMRT for autologous breast reconstruction, distant metastases



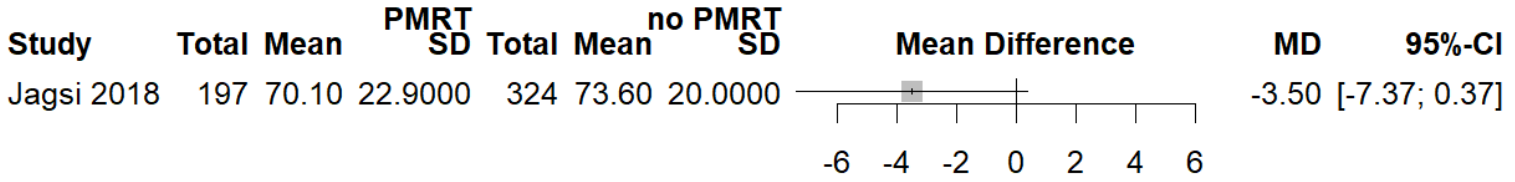
6.3.3.14 BREAST-Q dimensions only measurements between 1-2 years after reconstruction (according to median follow-up or time point of QoL measurement)

Note: For this outcome, we identified only one study (Jagsi 2018) reporting a follow-up time between 1-2 years. No identified study reported a longer follow-up.

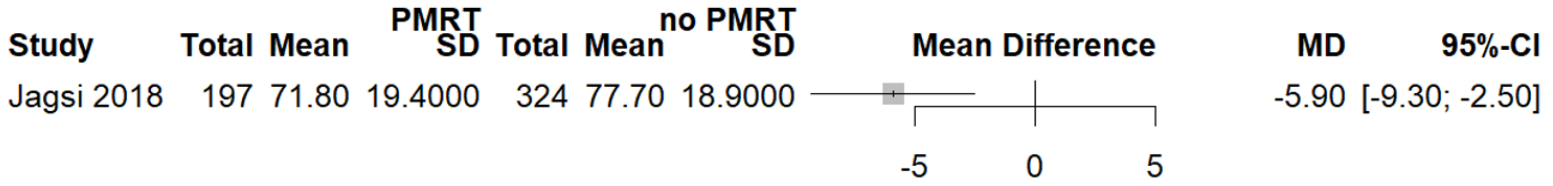
6.3.3.14.1 Satisfaction with breast



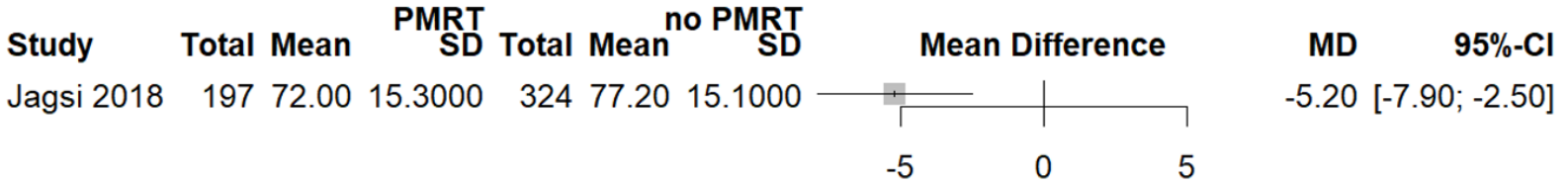
6.3.3.14.2 Satisfaction with overall outcome



6.3.3.14.3 Psychosocial well-being



6.3.3.14.4 Physical well-being



6.3.4 Vertrauen in die Evidenz (nach GRADE, https://www.gradepro.org/)

Summary of findings:

Radiotherapy compared to no radiotherapy for autologous breast reconstruction after reconstruction

Patient or population: autologous breast reconstruction after reconstruction

Intervention: Radiotherapy after autologous breast reconstruction

Comparison: No radiotherapy after autologous breast reconstruction

Outcomes	**Anticipated absolute effects*** (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with no radiotherapy	**Risk with Radiotherapy**				
Any complication	306 per 1.000	**340 per 1.000** (295 to 391)	**OR 1.17** (0.95 to 1.46)	2331 (8 non-randomised studies)	⊕◯◯◯ Very low[a,b]	It is uncertain whether radiotherapy after autologous breast reconstruction increases or decreases the incidence of any complications.
Major complication	221 per 1.000	**243 per 1.000** (120 to 431)	**OR 1.13** (0.48 to 2.66)	830 (2 non-randomised studies)	⊕◯◯◯ Very low[a,b]	It is uncertain whether radiotherapy after autologous breast reconstruction increases or decreases the incidence of major complications.
Minor complication	157 per 1.000	**203 per 1.000** (107 to 351)	**OR 1.36** (0.64 to 2.89)	187 (1 non-randomised study)	⊕◯◯◯ Very low[a,b]	It is uncertain whether radiotherapy after autologous breast reconstruction increases or decreases the incidence of minor complications.
Wound complications (Dehiscence)	76 per 1.000	**99 per 1.000** (61 to 155)	**OR 1.33** (0.79 to 2.23)	1966 (10 non-randomised studies)	⊕◯◯◯ Very low[a,b]	It is uncertain whether radiotherapy after autologous breast reconstruction increases or decreases the incidence of wound complications (dehiscence).

Summary of findings:						
Infections	40 per 1.000	**62 per 1.000** (41 to 92)	**OR 1.59** (1.03 to 2.44)	2364 (11 non-randomised studies)	⊕⊕◯◯ Low[a]	Radiotherapy after autologous breast reconstruction may increase the incidence of infections.
Hematoma	47 per 1.000	**47 per 1.000** (25 to 86)	**OR 1.00** (0.52 to 1.90)	1393 (6 non-randomised studies)	⊕◯◯◯ Very low[a,b]	It is uncertain whether radiotherapy after autologous breast reconstruction increases or decreases the incidence of hematoma.
Total flap loss	19 per 1.000	**16 per 1.000** (5 to 56)	**OR 0.83** (0.23 to 2.99)	1145 (4 non-randomised studies)	⊕◯◯◯ Very low[a,b]	It is uncertain whether radiotherapy after autologous breast reconstruction increases or decreases the incidence of total flap loss.
Partial flap loss	49 per 1.000	**15 per 1.000** (2 to 115)	**OR 0.30** (0.04 to 2.54)	593 (3 non-randomised studies)	⊕◯◯◯ Very low[a,b]	It is uncertain whether radiotherapy after autologous breast reconstruction increases or decreases the incidence of partial flap loss.
Reoperation	231 per 1.000	**224 per 1.000** (180 to 276)	**OR 0.96** (0.73 to 1.27)	1805 (12 non-randomised studies)	⊕◯◯◯ Very low[a,b]	It is uncertain whether radiotherapy after autologous breast reconstruction increases or decreases the incidence of reoperations.
Seroma	36 per 1.000	**33 per 1.000** (16 to 68)	**OR 0.93** (0.45 to 1.95)	1151 (5 non-randomised studies)	⊕◯◯◯ Very low[a,b]	It is uncertain whether radiotherapy after autologous breast reconstruction increases or decreases the incidence of seroma.
Flap necrosis	132 per 1.000	**130 per 1.000** (48 to 306)	**OR 0.98** (0.33 to 2.89)	520 (3 non-randomised studies)	⊕◯◯◯ Very low[a,b]	It is uncertain whether radiotherapy after autologous breast reconstruction increases or decreases the incidence of flap necrosis.
Fat necrosis	100 per 1.000	**154 per 1.000** (110 to 212)	**OR 1.63** (1.11 to 2.41)	3139 (16 non-randomised studies)	⊕◯◯◯ Very low[a,b]	It is uncertain whether radiotherapy after autologous breast reconstruction increases or decreases the incidence of fat necrosis.

Summary of findings:						
Distant metastases	70 per 1.000	**200 per 1.000** (52 to 532)	**OR 3.33** (0.73 to 15.13)	101 (1 non-randomised study)	⊕◯◯◯ Very low[a,b]	It is uncertain whether radiotherapy after autologous breast reconstruction increases or decreases the incidence of distant metastases.
Satisfaction with breast assessed with: BREAST-Q 1-2 years follow-up	The mean satisfaction with breast was **69**	MD **3.9 lower** (7.1 lower to 0.7 lower)	-	521 (1 non-randomised study)	⊕⊕◯◯ Low[a]	Radiotherapy after autologous breast reconstruction may result in a reduction in satisfaction with breast, measured with the BREAST-Q questionnaire.
Satisfaction with overall outcome assessed with: BREAST-Q 1-2 years follow-up	The mean satisfaction with overall outcome was **74**	MD **3.5 lower** (7.37 lower to 0.37 higher)	-	521 (1 non-randomised study)	⊕◯◯◯ Very low[a,b]	It is uncertain whether radiotherapy after autologous breast reconstruction results in a reduction in satisfaction with overall outcome, measured with the BREAST-Q questionnaire.
Psychosocial well-being assessed with: BREAST-Q 1-2 years follow-up	The mean psychosocial well-being was **78**	MD **5.9 lower** (9.3 lower to 2.5 lower)	-	521 (1 non-randomised study)	⊕⊕◯◯ Low[a]	Radiotherapy after autologous breast reconstruction may result in a reduction in psychosocial well-being, measured with the BREAST-Q questionnaire.
Physical well-being assessed with: BREAST-Q 1-2 years follow-up	The mean physical well-being was **77**	MD **5.2 lower** (7.9 lower to 2.5 lower)	-	521 (1 non-randomised study)	⊕⊕◯◯ Low[a]	Radiotherapy after autologous breast reconstruction may result in a reduction in physical well-being, measured with the BREAST-Q questionnaire.

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: confidence interval; **OR:** odds ratio

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.

Summary of findings:
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect. **Very low certainty:** we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

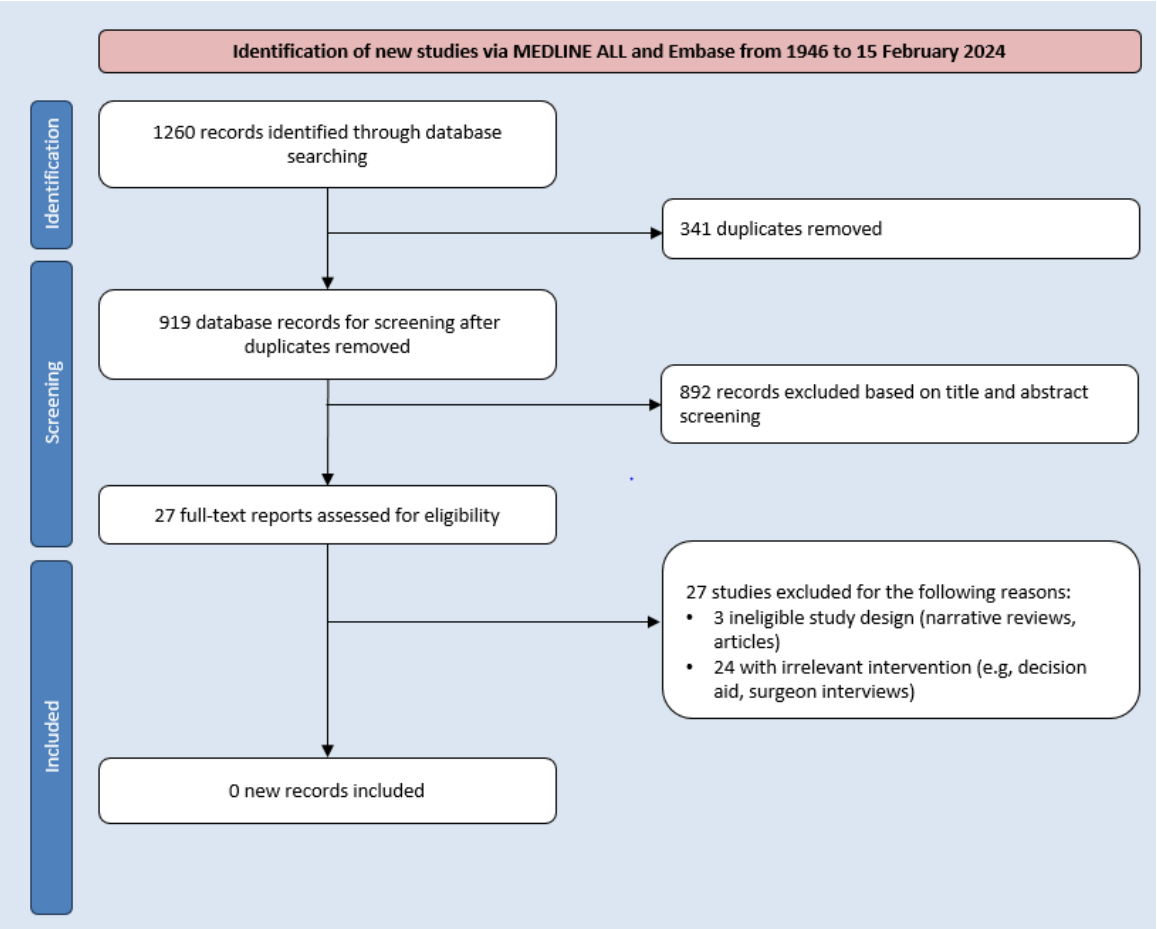
Explanations

a. Downgraded by two levels due to very serious risk of bias: Included studies were observational only, and the majority did not adjust at all for relevant baseline characteristics. Results are thus prone to confounding / bias by indication - those receiving radiotherapy were probably at higher stage or higher likelihood of disease progression.

b. Downgraded by one level due to serious imprecision; the 95% confidence interval includes both favorable and unfavorable effect of radiotherapy after reconstruction.

6.4 PICO 13

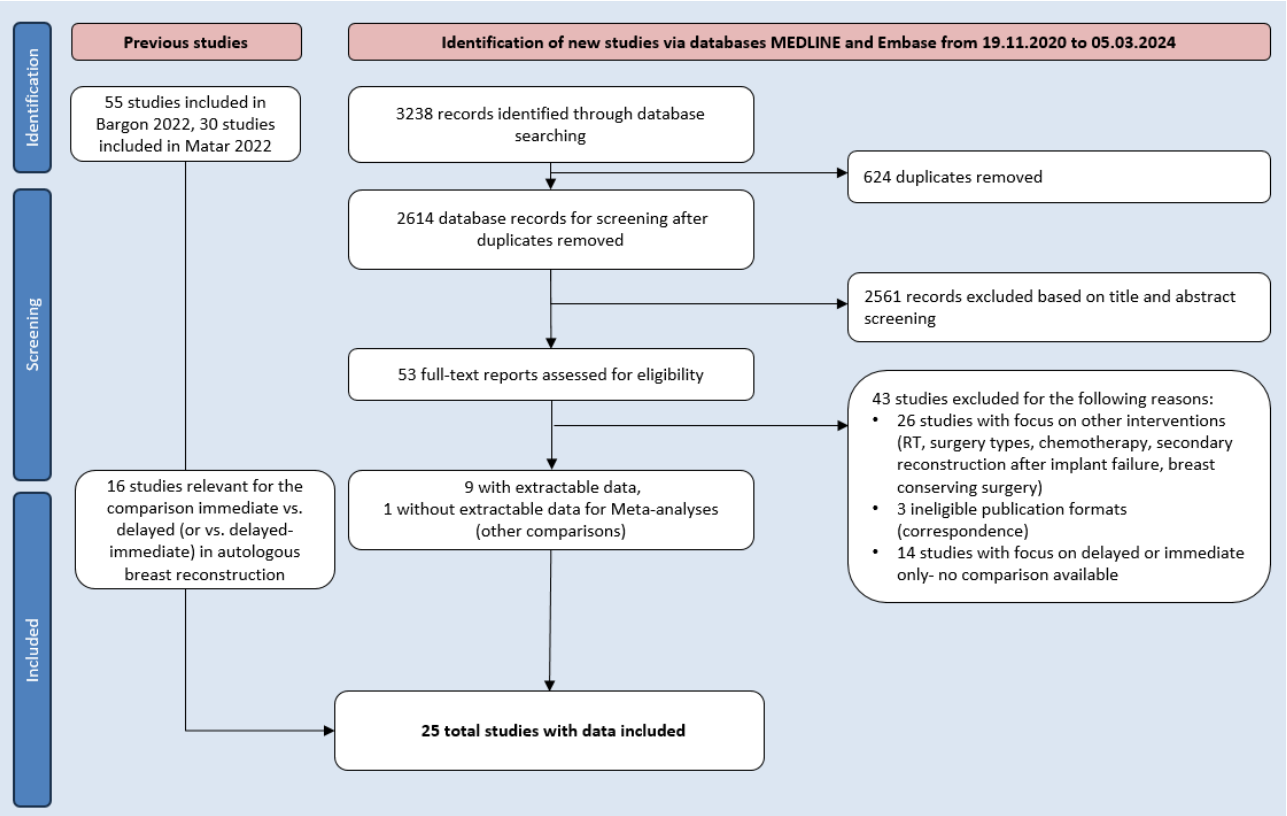
6.4.1 PRISMA Flowdiagramm



Hinweis: Da zu dieser PICO-Fragestellung keine geeignete Literatur identifiziert werden konnte, konnten weitere methodische Schritte nicht durchgeführt werden. Daher ist geplant, eine oder mehrere Empfehlungen auf Basis von Expertenkonsens zu formulieren.

6.5 PICO 16A

6.5.1 PRISMA Flowdiagramm



*Correction: 14 studies (from Reviews Matar 2022 and Bargon 2022 with data included); 23 total studies with data included

6.5.2 Evidenztabellen

6.5.2.1 Systematisches Review

6.5.2.1.1 Evidenztabellen systematische Reviews Bargon 2022 & Matar 2022

Bargon CA, Young-Afat DA, Ikinci M, Braakenburg A, Rakhorst HA, Mureau MAM, Verkooijen HM, Doeksen A. Breast cancer recurrence after immediate and delayed postmastectomy breast reconstruction-A systematic review and meta-analysis. Cancer. 2022 Oct 1;128(19):3449-3469. doi: 10.1002/cncr.34393. Epub 2022 Jul 27. PMID: 35894936; PMCID: PMC9546326.

Reference/ Study type	Review description	Interventions	Study Population	Ergebnisse der untersuchten Endpunkte	Methodological comments	Included publications
Bargon 2022 Systematisches Review mit Meta-Analyse	**Study design** ◆ Retrospective and prospective studies **Search dates** ◆ Searched from inception until 19.11.2020 **Databases** ◆ MEDLINE ◆ Embase ◆ Cochrane Library **Inclusion criteria** ◆ Original articles including patients >18 years old and reporting oncological outcomes (i.e., “local,” “regional,” “locoregional” or	**Question/ Aim** “Therefore, with this SR/MA, we aim to investigate whether delayed PMBR leads to different (loco) regional recurrence, distant metastasis, and overall recurrence rates than immediate PMBR in patients with primary breast cancer. Because of differences in nature and indications of implant-based and autologous breast reconstructive techniques,5 this question was evaluated separately for autologous and	55 studies published between February 2003 and October 2020, including 14,452 pts that received post-mastectomy breast reconstruction *Overall population (autologous and implnt-based):* ◆ Immediate: 12480 ◆ Delayed: 1852 ◆ Unclear setting: 337,65 **Descriptive statistics (available only for combined for studies with autologous and implant-based reconstruction)**	**Local recurrence** ◆ 31 studies ◆ Immediate: 163/6249; Weighted average proportion: 0.03 (95% CI, 0.02–0.03) ◆ Delayed: 22/1037; Weighted average proportion: 0.02 (95% CI, 0.01–0.04) **Regional recurrence** ◆ 14 studies ◆ Immediate: 83/3454; Weighted average proportion: 0.02 (95% CI, 0.01–0.03) ◆ Delayed: 14/674; Weighted average proportion: 0.02 (95% CI, 0.01–0.03)	**Risk of bias assessment of studies**: assessed using The Methological Index For Non-Randomized Studies (Minors) tool) *„The quality of included studies ranged from 6 to 12 points for noncomparative studies, and from 10 to 20 points for comparative studies “* **Overall confidence in results of SR (AMSTAR-2):** ◆ PICO elements: yes ◆ A priori design: yes	***Included and checked for additional outcomes:*** Maalouf 2017 **Excluded for this PICO (only immediate or only delayed-no comparison available):** Adam 2014 Adam 2018 Bjöhle 2019 Caruso 2006 Chen 2018 Cont 2017 Dillekas 2016

Bargon CA, Young-Afat DA, Ikinci M, Braakenburg A, Rakhorst HA, Mureau MAM, Verkooijen HM, Doeksen A. Breast cancer recurrence after immediate and delayed postmastectomy breast reconstruction-A systematic review and meta-analysis. Cancer. 2022 Oct 1;128(19):3449-3469. doi: 10.1002/cncr.34393. Epub 2022 Jul 27. PMID: 35894936; PMCID: PMC9546326.

"total breast cancer recurrences," and "distant metastasis") after PMBR in patients with breast cancer
- prospective and retrospective observational studies
- Comparative studies with only one study arm meeting in- and exclusion criteria

Exclusion criteria

- other publication types
- non-English or non-Dutch language articles
- studies published before 2000
- studies including cohorts with <50 patients
- studies with mean follow-up <24 months or unknown follow-up
- studies including patients with PMBR after initial breast-conserving surgery or implant-based breast reconstruction."

Interventions

A: Immediate autologous PMBR

B: delayed autologous PMBR

C: Immediate implant-based PMBR

D: Immediate implant-based PMBR

- Age (mean/median): 33-53

Locoregional recurrence

- 16 studies
- Immediate: Average weighted proportion: 0.04 (95% CI, 0.03–0.06
- Delayed: Average weighted proportion: 0.01 (95% CI, <0.01–0.03)

Distant metastasis

- Immediate: 368/5476
- Delayed: 125/1380

- Justification for design: no
- Literature search >= 2 databases, search strategy + other sources: yes
- Selection in duplicate: yes
- Data extraction in duplicate: yes
- List of excluded studies: no
- sufficient detail on studies: yes
- RoB assessed: no
- Funding of incl. studies: no
- MA appropriate: no
- RoB considered in MA: no
- RoB in interpretation: no
- Heterogeneity explained: yes
- Publication bias investigated: yes
- Sources of CoI: no

Sources of funding

- NR

Du 2017

Early 2020

Eriksen 2011

Fujimoto 2016

Geers 2018

Greenway 2005

Ha 2020

Hölmich 2008

Huang 2006

Kim 2010

Kim 2012

Lee 2016

Lee 2020

Lee 2018

Lee 2019

Lee 2012

Liang 2013

Lindford 2013

Lim 2010

Mc Carthy 2008

Metere 2020

Bargon CA, Young-Afat DA, Ikinci M, Braakenburg A, Rakhorst HA, Mureau MAM, Verkooijen HM, Doeksen A. Breast cancer recurrence after immediate and delayed postmastectomy breast reconstruction-A systematic review and meta-analysis. Cancer. 2022 Oct 1;128(19):3449-3469. doi: 10.1002/cncr.34393. Epub 2022 Jul 27. PMID: 35894936; PMCID: PMC9546326.

prophylactic mastectomy, • studies including patients with distant metastasis at time of diagnosis or PMBR, and breast cancer recurrence before PMBR • Nonavailable full-text articles	Min 2010 Munhoz 2013 Murphy 2017 Mustonen 2005 Narui 2015 Nava 2012 Ota 2014 Ozmen 2020 Park 2016 Parvez 2020 Patterson 2012 Reddy 2011 Romics 2012 Sakamoto 2016 Scholz 2008 Serra 2013 Snoj 2007 Spiegel 2003 Tanos 2016 Ueda 2008 Valente 2019

Bargon CA, Young-Afat DA, Ikinci M, Braakenburg A, Rakhorst HA, Mureau MAM, Verkooijen HM, Doeksen A. Breast cancer recurrence after immediate and delayed postmastectomy breast reconstruction-A systematic review and meta-analysis. Cancer. 2022 Oct 1;128(19):3449-3469. doi: 10.1002/cncr.34393. Epub 2022 Jul 27. PMID: 35894936; PMCID: PMC9546326.

Vaughan 2007

Wu 2020

Wu 2020

Yamada 2020

Characteristics of the systematic review chosen for this PICO 16A.

Matar DY, Wu M, Haug V, Orgill DP, Panayi AC. Surgical complications in immediate and delayed breast reconstruction: A systematic review and meta-analysis. J Plast Reconstr Aesthet Surg. 2022 Nov;75(11):4085-4095. doi: 10.1016/j.bjps.2022.08.029. Epub 2022 Aug 22. PMID: 36202732.

Reference/ Study type	Review description	Interventions	Study Population	Ergebnisse der untersuchten Endpunkte	Methodological comments	Included publications
Matar 2022 Systematisches Review mit Meta-Analyse	**Study/design** ◆ prospective studies, case series **Search dates** Searched from inception until 01.05.2021 **Databases** ◆ PubMed ◆ EMBASE ◆ Cochrane **Inclusion criteria**	**Question/ Aim** This review seeks to analyze and summarize the litera-ture to provide a better understanding of the surgical risks and complication rates associated with breast reconstruction in immediate versus delayed	30 studies on 14,034 pts undergoing breast reconstruction ◆ Immediate (unclear number of pts) ◆ Delayed (unclear number of pts) **Descriptive statistics** ◆ NR	**Surgical complications** ◆ 29 studies ◆ Immediate: 7275 pts ◆ Delayed: 6477 pts ◆ OR 1.30, 95% CI 1.03, 1.65 ◆ p = 0.03 **Infection** ◆ 14 studies ◆ Immediate: 5558 ◆ Delayed: 4984 ◆ OR: 1.21 [0.82, 1.79] ◆ p = 0.34 **Fat necrosis** ◆ 13 studies	**Risk of bias assessment of study:** assessment not available; reported level of evidence (LoE) of 4 as defined by the Oxford Centre for Evidence-Based Medicine **Overall confidence in results of SR (AMSTAR-2):** ◆ PICO elements: partial yes ◆ A priori design: partial yes	***Included and checked for additional outcomes:*** Beugels 2018 Carlson 2008 Chang 2015 Cheng 2006 Cook 2007

Matar DY, Wu M, Haug V, Orgill DP, Panayi AC. Surgical complications in immediate and delayed breast reconstruction: A systematic review and meta-analysis. J Plast Reconstr Aesthet Surg. 2022 Nov;75(11):4085-4095. doi: 10.1016/j.bjps.2022.08.029. Epub 2022 Aug 22. PMID: 36202732.

- cohort studies, case series, randomized controlled trials, and case-control studies re- porting original data on breast reconstruction outcomes in immediate versus delayed reconstruction who underwent mastectomy for the treatment or prophylaxis of any type of breast cancer
- The following surgical interventions were considered: prosthetic implants, including tissue ex- pander, and autologous reconstruction, including abdominal advance flaps, LDM flaps, pedicled, free and muscle- sparing TRAM flaps, SIEA flaps, GAP flaps, and DIEP flaps
- Only English language studies

reconstructions following mastectomy.

- Immediate: 3211
- Delayed: 1982
- OR: 1.31 [0.79, 2.17]
- p = 0.29

Skin necrosis

- 13 studies
- Immediate: 2549
- Delayed: 1758
- OR: 1.61 [0.81, 3.22]
- p = 0.18

Hematoma or seroma

- 12 studies
- Immediate: 2647
- Delayed: 1734
- OR: 2.01 [1.27, 3.17]
- p = 0.003

Wound dehiscence

- 7 studies
- Immediate: 2403
- Delayed: 1444
- OR: 0.81 [0.44, 1.50]
- p = 0.51

Reoperation rate

- 17 studies
- Immediate: 6387
- Delayed: 5091
- OR 3.13, 95% CI -3.43, 9.68
- p = 0.35

- Justification for design: no
- Literature search >= 2 databases, search strategy + other sources: partial yes
- Selection in duplicate: yes
- Data extraction in duplicate: no
- List of excluded studies: no
- sufficient detail on studies: partial yes
- RoB assessed: no
- Funding of incl. studies: no
- MA appropriate: no
- RoB considered in MA: no
- RoB in interpretation: no
- Heterogeneity explained: no
- Publication bias investigated: no
- Sources of CoI: yes

Sources of funding

This work was funded by The Gillian Reny Stepping Strong Center for Trauma Innovation./The authors report no proprietary or

DeBono 2002

Dewael 2019

Maalouf 2017

Manyam 2019

Prantl 2020

Steele 2017

Sternberg 2006

Tran 2001

Yoon 2018

Excluded for this PICO (no comparison or another irrelevant comparison available):

Alderman 2002

Alstrup 2018

Billig 2017

Browne 2017

Matar DY, Wu M, Haug V, Orgill DP, Panayi AC. Surgical complications in immediate and delayed breast reconstruction: A systematic review and meta-analysis. J Plast Reconstr Aesthet Surg. 2022 Nov;75(11):4085-4095. doi: 10.1016/j.bjps.2022.08.029. Epub 2022 Aug 22. PMID: 36202732.

Exclusion criteria • NR		commercial interest in any product mentioned or concept discussed in this article.	Drazan 2008 Kronowitz 2006 Gschwantler-Kaulich 2018 Hirsch 2012 Hughes 2012 Meshulam-Derazon 2018 Miller 1991 Sharabi 2020 Sue, L. 2017 Sue, S. 2017 Sulivan 2008 Trabulsy 1994 Yoon 2018

Characteristics of the systematic review chosen for this PICO 16A.

6.5.2.1.2 Characteristics of studies included in Bargon 2022 (Table 2 in the study)

First Author, Year	Country	Journal	Study design	N Patients	N breasts	Age (mean, range)	Follow- up (range), months	Reconstruction method
Maalouf 2017	Canada	Ann Chir Plast Est	Retrospective	62	62	Immediate: 50 (SD. 9.5) Delayed: 47 (SD. 8)	Immediate: 32 (11-67) Delayed: 92 (26-240)	Immediate and delayed autologous

Characteristics of studies included in Bargon 2022 that were eligible for inclusion for PICO 16A.

6.5.2.1.3 Characteristics of studies included in Matar 2022 (Table 2 in the study)

First Author, Year	Country	Type of study	Procedure type	N patients	Outcomes
Beugels 2018	Netherlands	Retrospective	DIEP	737	Surgical, Reop, LoS
Carlson 2008	USA	Retrospective	TRAM	199	Surgical, Reop
Chang 2015	USA	Retrospective	DIEP, SIEA, TRAM	376	Surgical, Reop
Cheng 2006	Taiwan	Retrospective	DIEP, SIEA	42	Surgical, Reop, LoS
Cook 2017	USA	Retrospective	TRAM	126	Surgical
DeBono2002	UK	Retrospective	LO	97	Surgical, Reop
Dewael 2019	Belgium	Retrospective	DIEP, SIEA	60	Surgical, Reop

First Author, Year	Country	Type of study	Procedure type	N patients	Outcomes
Drazan 2008	Czech Rep.	Retrospective	DIEP	110	Surgical
Maalouf 2017	Canada	Retrospective	DIEP	62	Surgical, Reop
Manyam 2019	USA	Retrospective	DIEP, E/ 1, LO, TRAM	204	Surgical, Reop
Prantl 2020	Germany	Retrospective	DIEP	3,913	Surgical, Reop, LoS
Steele 2017	UK	Retrospective	LO	488	Surgical, Reop, LoS
Sternberg 2006	USA	Retrospective	LO	100	Surgical, Reop
Tran 2001	USA	Retrospective	TRAM	102	Surgical, Reop

Abbreviations: ABO, abdominal advance; DIEP, deep inferior epigastric artery perforator; FLAP, autologous flap with no specification; GAP, gluteal artery perforator; LO, latissimus dorsi; MS, muscle-sparing; SIEA, superficial inferior epigastric artery; TRAM, transverse rectus abdominis myocutaneous; R, retrospective; P, prospective; Reop, reoperation; LoS, length of stay.

Characteristics of studies included in Matar 2022 that were eligible for inclusion for PICO 16A.

6.5.2.1.4 Risk of Bias assessment of (relevant to our PICO) Studies included in Bargon 2022 (with Risk Of Bias Appraisal Following The Methological Index For Non-Randomized Studies (Minors) Criteria)

Authors Years	A stated aim of the study	Inclusion of consecutive patient	Prospective collection of data	Endpoint appropriate to the study aim	Unbiased evaluation of endpoint	Follow-up period appropriate to the major endpoint	loss to follow-up <5%	prospective sample size claculation	gold standard for control group	contemporary groups	baseline equivalence	statistical analysis for study design	Total score
Maalouf 2017	high	high	low	moderate	high	high	low	low	high	high	low	high	17

Authors Years	A stated aim of the study	Inclusion of consecutive patient	Prospective collection of data	Endpoint appropriate to the study aim	Unbiased evaluation of endpoint	Follow-up period appropriate to the major endpoint	loss to follow-up <5%	prospective sample size claculation	gold standard for control group	contemporary groups	baseline equivalence	statistical analysis for study design	Total score

Abbreviation: MINORS, methodological index for non-randomized studies.

Note: Each item was scored 0–2 points: 0 indicates that this item was not reported in the article, 1 indicates that it was reported, but inadequately, and 2 indicates that it was reported adequately. A higher total score corresponds with less risk of bias. Green, 2 points; yellow, 1 point; red, 0 points.

Risk of bias assessment of studies included in Bargon 2022 that were eligible for inclusion for PICO 16A.

6.5.2.1.5 Risk of Bias assessment of (relevant to our PICO) Studies included in Matar 2022 (RoB assessment adapted from SIGN for cohort studies)

Authors Years	Study Design	Bias due to confounding	Selection bias	Assessment reliable: • Assessed more than once: • Possibly affected by knowledge of outcome status?	Attrition Bias	Outcome • well-defined, valid and reliable: • Blind outcome assessment to exposure	CI reported?	Reporting Bias
Beugels 2018	retrospective study	Moderate risk: Adjusted for unilateral vs. bilateral reconstruction, body mass index (kg/m2), smoking status (yes vs. no), radiation therapy (yes vs. no), chemotherapy (yes vs. no), endocrine therapy (yes vs. no),	Low risk	yes/no/no (retrospective cohort study)	High risk: not reported	Reliable outcome measure; no blind outcome assessment	partly (for adjusted OR)	no protocol accessible.

Authors Years	Study Design	Bias due to confounding	Selection bias	Assessment reliable: • Assessed more than once: • Possibly affected by knowledge of outcome status?	Attrition Bias	Outcome • well-defined, valid and reliable: • Blind outcome assessment to exposure	CI reported?	Reporting Bias
		and university vs. community hospital. - Still moderate, as other confounders possible						
Carlson 2008	retrospective study	High risk: no adjustment	Unclear, no information provided	yes/no/no (retrospective cohort study)	High risk: not reported	Reliable outcome measure; no blind outcome assessment	no	no protocol accessible.
Chang 2015	retrospective study	High risk: no adjustment	Unclear, no information provided	yes/no/no (retrospective cohort study)	High risk: not reported	Reliable outcome measure; no blind outcome assessment	no	no protocol accessible.
Cheng 2006	retrospective study	High risk: no adjustment	Unclear, no information provided	yes/no/no (retrospective cohort study)	High risk: not reported	Reliable outcome measure; no blind outcome assessment	no	no protocol accessible.
Cook 2017	retrospective study	High risk: no adjustment	High risk: "Inclusion criteria were any patient who underwent MSLD flap reconstruction	yes/no/no (retrospective cohort study)	High risk: not reported	Reliable outcome measure; no blind outcome assessment	no	no protocol accessible.

Authors Years	Study Design	Bias due to confounding	Selection bias	Assessment reliable: • Assessed more than once: • Possibly affected by knowledge of outcome status?	Attrition Bias	Outcome • well-defined, valid and reliable: • Blind outcome assessment to exposure	CI reported?	Reporting Bias
			by our senior author during the defined study period and had a minimum of 3 months of follow-up."					
DeBono 2002	retrospective study	High risk: no adjustment	Low risk	yes/no/no (retrospective cohort study)	High risk: not reported	Reliable outcome measure; no blind outcome assessment	no	no protocol accessible.
Dewael 2019	retrospective study	High risk: no adjustment	Low risk	yes/no/no (retrospective cohort study)	High risk: not reported	Reliable outcome measure; no blind outcome assessment	no	no protocol accessible.
Maalouf 2017	retrospective study	High risk: no adjustment	Low risk	yes/no/no (retrospective cohort study)	High risk: not reported	Reliable outcome measure; no blind outcome assessment	no	no protocol accessible.
Prantl 2020	retrospective study	High risk: no adjustment	Low risk	yes/no/no (retrospective cohort study)	High risk: not reported	Reliable outcome measure; no blind outcome assessment	no	no protocol accessible.

Authors Years	Study Design	Bias due to confounding	Selection bias	Assessment reliable: • Assessed more than once: • Possibly affected by knowledge of outcome status?	Attrition Bias	Outcome • well-defined, valid and reliable: • Blind outcome assessment to exposure	CI reported?	Reporting Bias
Steele 2017	retrospective study	High risk: no adjustment	Low risk	yes/no/no (retrospective cohort study)	High risk: not reported	Reliable outcome measure; no blind outcome assessment	no	no protocol accessible.
Sternberg 2006	retrospective study	High risk: no adjustment	Unclear, no information provided	yes/no/no (retrospective cohort study)	High risk: not reported	Reliable outcome measure; no blind outcome assessment	no	no protocol accessible.
Tran 2001	retrospective study	High risk: no adjustment	Unclear, no information provided	yes/no/no (retrospective cohort study)	High risk: not reported	Reliable outcome measure; no blind outcome assessment	no	no protocol accessible.
Drazan 2008	retrospective study	High risk: no adjustment	Unclear, no information provided	yes/no/no (retrospective cohort study)	High risk: not reported	Reliable outcome measure; no blind outcome assessment	no	no protocol accessible.
Manyam 2019	retrospective study	High risk: no adjustment	Low risk	yes/no/no (retrospective cohort study)	High risk: not reported	Reliable outcome measure; no blind outcome assessment	no	no protocol accessible.

Risk of bias assessment of studies included in Matar 2022 that were eligible for inclusion for PICO 16A.

6.5.2.2 Primärstudien – neu identifiziert

Reference/ Study type	Population	Interventions	Main results	Methodological evaluation
Barnes 2023 Retrospective study	**Inclusion criteria (for analysis):** ◆ NR **Exclusion criteria (for analysis):** ◆ no reconstruction at the time of NSM ◆ completed implant-based breast reconstruction at the time of autologous reconstruction ◆ patients who were noted to be planning for 2-stage implant-based breast reconstruction at the time of their NSM with tissue expander placement **Enrolment period** ◆ January 2004 – September 2021 **Follow-up** ◆ NR **Descriptive statistics** ◆ Age (mean (SD)) · Immediate: 47.71 (8.48) · Delayed: 47.23 (9.69) ◆ BMI (mean (SD)) · Immediate: 27.24 (4.24) · Delayed: 28.26 (5.24) ◆ Stadium · Immediate: NR · Delayed: NR	**Interventions** A: Immediate autologous breast reconstruction · N = 59 (89 breasts) B: Delayed-immediate autologous breast reconstruction · N = 42 (62 breasts) **Analysis** ◆ frequencies ◆ No matching ◆ No adjustment	**Hematoma** · Immediate: 4/89 · Delayed: 2/62 **Any infection** · Immediate: 4/89 · Delayed: 13/62 **Infection requiring PO antibiotics** · Immediate: 4/89 · Delayed: 13/62 **Infection requiring IV antibiotics** · Immediate: 0/89 · Delayed: 7/62 **Fat necrosis** · Immediate: 8/89 · Delayed: 1/62 **Delayed wound healing** · Immediate: 16/89 · Delayed: 7/62 **Wound requiring reoperation** · Immediate: 8/89 · Delayed: 4/62 **Mastectomy skin flap necrosis** · Immediate: 18/89 · Delayed: 0/62	**General information** ◆ Follow-up: NR ◆ Funding: Conflicts of interest and sources of funding: none declared. ◆ CoI: Conflicts of interest and sources of funding: none declared. **Risk of bias considerations (adapted from SIGN cohort study checklist)** ◆ Study type: retrospective chart review ◆ Confounding: high ◆ Rate of participation/Exclusions reported (selection bias into the study): no (retrospective) ◆ Exposure/Intervention · Assessment reliable: unclear · Assessed more than once: no · Possibly affected by knowledge of outcome status? no ◆ Drop-out rate & reasons reported: not reported ◆ Outcome · Outcome measure is well-defined, valid and reliable: unclear · Blind outcome assessment to exposure: Unclear, probably no (→If not, Knowledge of exposure

Reference/ Study type	Population	Interventions	Main results	Methodological evaluation
	◆ Chemotherapy (% yes) · Immediate: NR · Delayed: NR ◆ Reconstruction type (flap type) (%) · Abdomen-based free flap breast reconstruction		**Total flap loss** · Immediate: 1/89 · Delayed: 1/62 **Partial flap loss** · Immediate: 1/89 · Delayed: 0/62 **Reoperation** · Immediate: 18/89 · Delayed: 10/62	status likely to influence the outcome) no ◆ Main cofounders taken into account: no ◆ Confidence intervals reported: no ◆ Selective reporting (comparison with protocol): no protocol found **Other limitations or comments:** ◆ retrospective design
Christopher 2022 Retrospective study	**Inclusion criteria (for analysis):** ◆ ABR with superficial inferior epigastric artery (SIEA), deep inferior epigastric perforator (DIEP), or muscle-sparing transverse rectus abdominis myocutaneous (TRAM) flaps, where one or both of the lateral and medial segments of the rectus muscle are preserved. ◆ Flaps that were reconstructed in a delayed-immediate fashion only if they had DI-ABR with radiation therapy between mastectomy/TE placement and autologous reconstruction (DI-ABR cohort). **Exclusion criteria (for analysis):**	**Interventions** A: Immediate autologous reconstruction · N = 66 B: Delayed-immediate autologous reconstruction · N = 66 **Analysis** ◆ frequencies; median (SD); univariate analyses; Wilcoxon rank-sum test	**Hematoma** · Immediate: 4/66 · Delayed-immediate: 4/66 **Surgical site infection** · Immediate: 3/66 · Delayed-immediate: 1/66 **Delayed healing** · Immediate: 12/66 · Delayed-immediate: 4/66 **Fat necrosis** · Immediate: 16/66 · Delayed-immediate: 6/66 **Skin necrosis** · Immediate: 12/66	**General information** ◆ **Follow-up**: 3.1 (2.2-8.5) vs. 2.0 (1.3-6.0) ◆ Funding: NR ◆ **CoI**: Non declared. **Risk of bias considerations (adapted from SIGN cohort study checklist)** ◆ Study type: retrospective review ◆ Confounding: high ◆ Rate of participation/Exclusions reported (selection bias into the study): not reported ◆ Exposure/Intervention · Assessment reliable: yes · Assessed more than once: no

Reference/ Study type	Population	Interventions	Main results	Methodological evaluation
	◆ Patients undergoing non-abdominally based flap procedures **Enrolment period** ◆ 2005 – 2018 **Follow-up (median (IQR))** ◆ Immediate: 3.1 (2.2 - 8.5) ◆ Delayed-immediate: 2.0 (1.3 - 6.0) **Descriptive statistics** ◆ Age (mean, SD) · Immediate: 48.7 (43–56) · Delayed-immediate: 49.4 (40–53) ◆ BMI (mean, SD) · Immediate: 29.1 (26–33) · Delayed-immediate: 28.2 (25–32) ◆ Stadium · Immediate: NR · Delayed-immediate: NR ◆ Chemotherapy (% yes) · Immediate: 51.1% (34/66) · Delayed-immediate: 87.9% (58/66) ◆ Reconstruction type (flap type) (%) · Immediate: TRAM: 71.2% (47/66); DIEP: 24.2% (16/66); SIEA: 4.55% (3/66) · Delayed-immediate: TRAM: 71.2% (47/66); DIEP: 24.2% (16/66); SIEA: 4.55% (3/66)	◆ No matching ◆ No adjustment	· Delayed-immediate: 0/66 **Flap loss due to vascular compromise** · Immediate: 1/66 · Delayed-immediate: 0/66 **Readmission with reoperation** · Immediate: 2/66 · Delayed-immediate: 1/66	· Possibly affected by knowledge of outcome status? no ◆ Drop-out rate & reasons reported: not reported ◆ Outcome · Outcome measure is well-defined, valid and reliable: yes · Blind outcome assessment to exposure: (→If not, Knowledge of exposure status likely to influence the outcome) no (retrospective) ◆ Main cofounders taken into account: no ◆ Confidence intervals reported: no ◆ Selective reporting (comparison with protocol): no protocol found **Other limitations or comments:** ◆ retrospective design

Reference/ Study type	Population	Interventions	Main results	Methodological evaluation
Marquez 2023 Prospective cohort study	**Inclusion criteria (for analysis):** ◆ NR **Exclusion criteria (for analysis):** ◆ NR **Enrolment period** ◆ 2010 – 2020 **Follow-up** ◆ 30 days **Descriptive statistics** ◆ Age (median, IQR) · Immediate: 51.0 (44.2, 58.0) · Delayed-immediate: 49.0 (43.0, 56.0) · Delayed: 51.0 (44.0, 58.0) ◆ BMI (median, IQR) · Immediate: 29.0 (25.5, 32.9) · Delayed-immediate: 29.4 (26.3, 33.1) · Delayed: 29.2 (25.8, 33.0) ◆ Stadium · Immediate: NR · Delayed-immediate: NR · Delayed: NR ◆ Chemotherapy (% yes) · Immediate: NR · Delayed-immediate: NR · Delayed: NR ◆ Reconstruction type (flap type) (%)	**Interventions** A: immediate autologous reconstruction · N = 7,907 B: delayed-immediate autologous reconstruction · N = 976 C: delayed autologous breast reconstruction · N = 6713 **Analysis** ◆ univariate analysis; single-step multinomial logistic regression ◆ No matching ◆ Adjustment: Yes (adjusted for age, race, body mass index (BMI), diabetes, hypertension, ASA classification, and	**Surgical site infection** · Immediate: 494/7907 · Delayed-immediate: 54/976 · Delayed: 408/6713 **Wound dehiscence** · Immediate: 147/7907 · Delayed-immediate: 17/976 · Delayed: 120/6713 **Return to operating room** · Immediate: 1045/7907 · Delayed-immediate: 88/976 · Delayed: 734/6713	**General information** ◆ Follow-up: 30 days ◆ Funding: None. ◆ CoI: None declared. **Risk of bias considerations (adapted from SIGN cohort study checklist)** ◆ Study type: ◆ Confounding: adjusted for but still possible (moderate risk) ◆ Rate of participation/Exclusions reported (selection bias into the study): no ◆ Exposure/Intervention · Assessment reliable: yes · Assessed more than once: no · Possibly affected by knowledge of outcome status? no ◆ Drop-out rate & reasons reported: not reported ◆ Outcome · Outcome measure is well-defined, valid and reliable: yes · Blind outcome assessment to exposure: (→If not, Knowledge of exposure status likely to influence the outcome?:) no ◆ Main cofounders taken into account: yes ◆ Confidence intervals reported: no

Reference/ Study type	Population	Interventions	Main results	Methodological evaluation
	· Free flap breast reconstruction only	laterality of reconstruction)		◆ Selective reporting (comparison with protocol): no protocol found **Other limitations or comments:** ◆ NA
Ochoa 2022 Prospective study	**Inclusion criteria (for analysis):** ◆ NR **Exclusion criteria (for analysis):** ◆ Patients that did not complete all three required questionnaires were excluded from patient-reported outcomes analysis (non-responders) **Enrolment period** ◆ July 2012 – August 2016 **Follow-up** ◆ Unclear (1 month following completion of planned breast revision, nipple reconstruction, and contralateral symmetry procedure, if applicable) **Descriptive statistics** ◆ Age (median, range) · Immediate: 52 (22-73) · Delayed: 47.5 (41-51) ◆ BMI (median, range) · Immediate: 28 (20-40) · Delayed: 28 (20-38) ◆ Stadium	**Interventions** A: Immediate autologous reconstruction · N = 57 B: Delayed autologous reconstruction · N = 16 **Analysis** ◆ Mean (SD); linear mixed models for BREAST-Q ◆ No matching ◆ No adjustment	**Hematoma** · Immediate: 4/103 · Delayed: 0/27 **Mild infection** · Immediate: 11/103 · Delayed: 1/27 **Mild delayed wound healing** · Immediate: 11/103 · Delayed: 5/27 **Moderate delayed wound healing** · Immediate: 2/103 · Delayed: 0/27 **Severe delayed wound healing** · Immediate: 1/103 · Delayed: 1/27 **Total delayed wound healing** · Immediate: 14/103 · Delayed: 6/27 **Fat necrosis** · Immediate: 8/103 · Delayed: 3/27	**General information** ◆ Follow-up: unclear ◆ Funding: The authors have no financial interest to declare in relation to the content of this article. ◆ CoI: NR **Risk of bias considerations (adapted from SIGN cohort study checklist)** ◆ Study type: prospective study ◆ Confounding: high ◆ Rate of participation/Exclusions reported (selection bias into the study): yes ◆ Exposure/Intervention · Assessment reliable: yes · Assessed more than once: no · Possibly affected by knowledge of outcome status? possible ◆ Drop-out rate & reasons reported: yes · Similar across groups: unclear · If high: comparison of those lost with available: unclear

Reference/ Study type	Population	Interventions	Main results	Methodological evaluation
	· Immediate: NR · Delayed: NR ◆ Chemotherapy (% yes) · Immediate: 26.3% (15/57) · Delayed: 81.3% (13/16) ◆ Reconstruction type (flap type) (%) · Immediate: DIEP flap (only) · Delayed:DIEP flap (only)		**Flap loss** · Immediate: 0/103 · Delayed: 1/27 **QoL-outcomes: Breast -Q (mean, SD):** ◆ Satisfaction with breast: · Immediate: 54.7 (19.2) · Delayed: 35.4 (24.5) ◆ Sexual well-being: · Immediate: 52.7 (18.8) · Delayed: 36.5 (20.8) ◆ Physical well-being (chest): · Immediate: 79.7 (12.4) · Delayed: 66.4 (13)	◆ Outcome · Outcome measure is well-defined, valid and reliable: unclear · Blind outcome assessment to exposure: (→If not, Knowledge of exposure status likely to influence the outcome) no ◆ Main cofounders taken into account: no ◆ Confidence intervals reported: no ◆ Selective reporting (comparison with protocol): protocol not available **Other limitations or comments:** ◆ NA
Pittelkow 2022 Retrospective study	**Inclusion criteria (for analysis):** ◆ Patients were included if their preference was for DIEP flap **Exclusion criteria (for analysis):** ◆ no immediate reconstruction (DIEP or tissue expander) at the time of ◆ latissimus flap or thigh-based free flap ◆ final implant reconstruction and initially chose implant reconstruction during the preoperative evaluation. ◆ initial tissue expander reconstruction, but the preoperative documentation was unclear about patients preference for implant or DIEP	**Interventions** A: Immediate autologous reconstruction · N = 36 B: Delayed-immediate autologous reconstruction · N = 11 **Analysis** ◆ Mean (SD) ◆ No matching	**Hematoma** · Immediate: 0/36 · Delayed-immediate: 1/11 **Surgical site infection** · Immediate: 2/36 · Delayed-immediate: 0/11 **Breast skin flap necrosis** · Immediate: 3/36 · Delayed-immediate: 0/11 **Fat necrosis** · Immediate: 1/36 · Delayed-immediate: 1/11	**General information** ◆ Follow-up: NR ◆ Funding: NR ◆ CoI: None declared. **Risk of bias considerations (adapted from SIGN cohort study checklist)** ◆ Study type: retrospective study ◆ Confounding: high ◆ Rate of participation/Exclusions reported (selection bias into the study): not reported ◆ Exposure/Intervention · Assessment reliable: yes

Reference/ Study type	Population	Interventions	Main results	Methodological evaluation
	Enrolment period ◆ 2017 – 2019 **Follow-up** ◆ NR **Descriptive statistics** ◆ Age (median, range) · Immediate: 48.8 · Delayed-immediate: 50.7 ◆ BMI (median, range) · Immediate: 30.1 · Delayed-immediate: 31.3 ◆ Stadium · Immediate: NR · Delayed-immediate: NR ◆ Chemotherapy (% yes) · Immediate: NR · Delayed-immediate: NR ◆ Reconstruction type (flap type) (%) · DIEP for both groups	◆ No adjustment	**Flap loss** · Immediate: 0/36 · Delayed-immediate: 0/11	· Assessed more than once: no · Possibly affected by knowledge of outcome status? no ◆ Drop-out rate & reasons reported: not reported ◆ Outcome · Outcome measure is well-defined, valid and reliable: yes · Blind outcome assessment to exposure: (→If not, Knowledge of exposure status likely to influence the outcome) no (retrospective) ◆ Main cofounders taken into account: no ◆ Confidence intervals reported: no ◆ Selective reporting (comparison with protocol): no protocol found **Other limitations or comments:** ◆ retrospective design
Wu Young 2022 Retrospective study	**Inclusion criteria (for analysis):** ◆ NR **Exclusion criteria (for analysis):** ◆ NR **Enrolment period**	**Interventions** A: Immediate autologous reconstruction · N = 36	**Surgical site infection** · Immediate: 5/36 · Delayed: 11/89 **Partial flap necrosis** · Immediate: 0/36 · Delayed: 4/89	**General information** ◆ Follow-up: NR ◆ Funding: NR ◆ CoI: The authors declare no conflict of interest.

Reference/ Study type	Population	Interventions	Main results	Methodological evaluation
	◆ January 2015 – December 2019 **Follow-up** ◆ NR **Descriptive statistics** ◆ Age (median, range) · Immediate: 51.6 · Delayed: 51.5 ◆ BMI (median, range) · Immediate: 29.6 · Delayed: 29.8 ◆ Stadium · Immediate: 0: 0% (0/36); IA: 5.56% (2/36); IB: 0% (0/36); IIA: 22.2% (8/36; IIB: 44.4% (16/36); IIIA: 16.7% (6/36); IIIB: 5.6% (2/36); IIIC: 5.6% (2/36) · Delayed: 0: 2.2% (2/89); IA: 1.1% (1/89); IB: 0% (0/89); IIA: 13.5% (12/89); IIB: 18.0% (16/89); IIIA: 229.2% (26/89); IIIB: 5.6% (5/89); IIIC: 5.6% (5/89) ◆ Chemotherapy (% yes) · Immediate: 50.0% (18/36) · Delayed: 35.9% (28/89) ◆ Reconstruction type (flap type) (%) · Immediate: NR · Delayed: NR	B: Delayed autologous reconstruction · N = 89 **Analysis** ◆ frequencies ◆ No matching ◆ No adjustment	**Mastectomy flap necrosis** · Immediate: 5/36 · Delayed: 3/89 **Wound dehiscence** · Immediate: 11/36 · Delayed: 24/89 **Fat necrosis** · Immediate: 13/36 · Delayed: 28/89 **Patients requiring revision** · Immediate: 17/36 · Delayed: 62/89	**Risk of bias considerations (adapted from SIGN cohort study checklist)** ◆ Study type: retrospective chart review ◆ Confounding: high ◆ Rate of participation/Exclusions reported (selection bias into the study): not reported ◆ Exposure/Intervention · Assessment reliable: yes · Assessed more than once: no · Possibly affected by knowledge of outcome status? no ◆ Drop-out rate & reasons reported: not reported ◆ Outcome · Outcome measure is well-defined, valid and reliable: yes · Blind outcome assessment to exposure: (→If not, Knowledge of exposure status likely to influence the outcome) no (retrospective) ◆ Main cofounders taken into account: no ◆ Confidence intervals reported: no ◆ Selective reporting (comparison with protocol): no protocol found **Other limitations or comments:**

Reference/ Study type	Population	Interventions	Main results	Methodological evaluation
				◆ retrospective design
Joosen 2021 Multicenter retrospective cohort study	**Inclusion criteria (for analysis):** ◆ Female ◆ older than 18 years ◆ diagnosis of breast cancer in the breast to be reconstructed **Exclusion criteria (for analysis):** ◆ Reconstructions after prophylactic mastectomy ◆ women who had a metastasis at the time of mastectomy ◆ Women who had a delayed reconstruction and experienced a recurrence after mastectomy, but before reconstructive surgery, were excluded as well. **Enrolment period** ◆ January 2010 – December 2018 **Follow-up** · Immediate: 46 months (45) · Delayed: 56 months (56) **Descriptive statistics** ◆ Age (median, range) · Immediate: 52.79 ± 8.28 · Delayed: 50.92 ± 8.48 ◆ BMI (mean, SD) · Immediate: 52.79 ± 8.28	**Interventions** A: Immediate autologous reconstruction · N = 326 B: Delayed autologous reconstruction · N = 536 **Analysis** ◆ Cox proportional hazards regression analysis, multivariable Cox regression ◆ No matching ◆ Adjustment for: Adjusted for immortal time bias, age at operation, histological tumor type, TN stage, y stage, Bloom Richardson grade, axillary treatment,	**Local recurrence** · Immediate: 5/326 · Delayed: 9/536 · HR: 0.804 (95%-CI: 0.483–1.337); p = 0.001 **Regional recurrence** · Immediate: 12/326 · Delayed: 13/536 · HR: 0.306 (95%-CI: 0.214–0.436); p = 0.631 **Distant recurrence** · Immediate: 7/251 · Delayed: 32/466 · HR: 1.351 (95%-CI: 0.960–1.903); p < 0.001	**General information** ◆ Follow-up: 46 months vs. 56 months ◆ Funding: NR ◆ CoI: The authors declare that they have no conflict of interest to disclose. **Risk of bias considerations (adapted from SIGN cohort study checklist)** ◆ Study type: multicenter retrospective cohort study ◆ Confounding: moderate ◆ Rate of participation/Exclusions reported (selection bias into the study): yes ◆ Exposure/Intervention · Assessment reliable: yes · Assessed more than once: no · Possibly affected by knowledge of outcome status? no ◆ Drop-out rate & reasons reported: no ◆ Outcome · Outcome measure is well-defined, valid and reliable: yes · Blind outcome assessment to exposure: (→If not, Knowledge of

Reference/ Study type	Population	Interventions	Main results	Methodological evaluation
	· Delayed: 50.92 ± 8.48 ◆ Stadium · Immediate: 0: 73.9% (241/326); Tis: 24.5% (80/326); 1: 40.5% (132/326); 2: 23.6% (77/326); 3: 2.1% (7/326); 4: 0.3% (7/326); missing: 5.2% (17/326) · Delayed: 0: 5.2% (28/536); Tis: 9.3% (50/536); 1: 31.2% (167/536); 2: 34.1% (183/536); 3: 8.8% (47/536); 4: 2.1% (11/536); missing:9.3% (50/536) ◆ Chemotherapy (% yes) · Immediate: 49.1% (160/326) · Delayed: 68.8% (369/536) ◆ Reconstruction type (flap type) (%) · DIEP flap breast reconstruction only	chemotherapy, radiation therapy, endocrine therapy and immunotherapy		exposure status likely to influence the outcome) no ◆ Main cofounders taken into account: yes (for local, regional & distant recurrence) ◆ Confidence intervals reported: no ◆ Selective reporting (comparison with protocol): no protocol found **Other limitations or comments:** ◆ retrospective design
Shammas 2023 Retrospective study	**Inclusion criteria (for analysis):** ◆ women ≥18 years ◆ diagnosed with breast cancer ◆ underwent a mastectomy with eventual free-flap breast reconstruction ◆ continuous enrollment 12 months pre-mastectomy to 90 days post free-flap breast reconstruction **Exclusion criteria (for analysis):** ◆ displayed codes for a free-flap prior to their mastectomy ◆ no breast cancer diagnosis on the date of or in the year prior to mastectomy ◆ distant metastasis	**Interventions** A: Immediate autologous reconstruction · N = 2310 B: Delayed autologous reconstruction · N = 388 C: Delayed-immediate	**Wound dehiscence** · Immediate: 266/2310 · Delayed: 52/388 · Delayed-immediate: 113/612 **Wound infection** · Immediate: 93/2310 · Delayed: 13/388 · Delayed-immediate: 64/612 **Hematoma** · Immediate: 132/2310 · Delayed: 36/388 · Delayed-immediate: 33/612	**General information** ◆ Follow-up: 90 days ◆ Funding: CTSA Grant (UL1TR002553) from the National Center for Advancing Translational Sciences (NCATS) of the NIH and the NIH Roadmap for Medical Research ◆ CoI: No conflicts of interest pertaining to this manuscript are present or need to be disclosed **Risk of bias considerations (adapted from SIGN cohort study checklist)** ◆ Study type: retrospective study ◆ Confounding: high

Reference/ Study type	Population	Interventions	Main results	Methodological evaluation
	◆ breast implant procedure within 1 year of mastectomy to 90 days after the free-flap ◆ tissue expander placed prior to mastectomy and not on the index surgery ◆ free-flap performed within 2 weeks of the index mastectomy but not within the index admission ◆ tissue expander placed after the index admission but before freeflap reconstruction ◆ pedicled flap performed prior to their free-flap procedure **Enrolment period** ◆ 1 January 2014 - 31 December 2018 **Follow-up** ◆ 90 days **Descriptive statistics** ◆ Age (median, range) · Immediate: mean (SD): 51.3 (8.3); median: 52.0 ; Q1, Q3: 45.0, 58.0; range: 21.0 - 75.0 · Delayed: mean (SD): 49.6 (8.8); median: 50.0 ; Q1, Q3: 43.0, 57.0; range: 19.0 - 68.0 · Delayed-immediate: mean (SD): 49.4 (8.1); median: 49.0 ; Q1, Q3: 44.0, 56.0; range: 22.0 - 68.0 ◆ BMI (median, range)	autologous reconstruction · N = 612 **Analysis** ◆ Means and standard deviation, frequencies, modified Poisson regression ◆ No matching ◆ Adjustment for: age, NCI comorbidity index, urban/rural ZIP code, geographic region, employment status, laterality of mastectomy, lymph node surgery at the time of mastectomy, chemotherapy before or after mastectomy, radiation before or after mastectomy, and presence of	**Fat necrosis** · Immediate: 126/2310 · Delayed: 31/388 · Delayed-immediate: 53/612 **Hematoma requiring reoperation** · Immediate: 128/2310 · Delayed: 41/388 · Delayed-immediate: 45/612 **Wound infection requiring reoperation** · Immediate: 148/2310 · Delayed: 24/388 · Delayed-immediate: 57/612 **Wound complication requiring reoperation** · Immediate: 46/2310 · Delayed: 10/388 · Delayed-immediate: 32/612 **Any reoperations** · Immediate: 276/2310 · Delayed: 67/388 · Delayed-immediate:188/612	◆ Rate of participation/Exclusions reported (selection bias into the study): not reported ◆ Exposure/Intervention · Assessment reliable: yes · Assessed more than once: no · Possibly affected by knowledge of outcome status? no ◆ Drop-out rate & reasons reported: no ◆ Outcome · Outcome measure is well-defined, valid and reliable: unclear · Blind outcome assessment to exposure: (→If not, Knowledge of exposure status likely to influence the outcome) no (retrospective) ◆ Main cofounders taken into account: no ◆ Confidence intervals reported: no ◆ Selective reporting (comparison with protocol): no protocol found **Other limitations or comments:** ◆ retrospective design

Reference/ Study type	Population	Interventions	Main results	Methodological evaluation
	· Immediate: NR · Delayed: NR · Delayed-immediate: NR ◆ Stadium · Immediate: NR · Delayed: NR · Delayed-immediate: NR ◆ Chemotherapy (% yes) · Immediate: 184 (8.0%) · Delayed: 58 (14.9%) · Delayed-immediate: 84 (13.7%) ◆ Reconstruction type (flap type) (%) · Immediate: 37 (1.6%) · Delayed: 2 (0.5%) · Delayed-immediate: 2 (0.3%)	other cancer diagnoses		
Shammas 2021 Retrospective study	**Inclusion criteria (for analysis):** ◆ Patients had undergone postmastectomy radiation therapy ◆ Patients had significant medical comorbidities ◆ Patients were uncertain about their reconstruction and/or had tenuous skin flaps at the time of mastectomy **Exclusion criteria (for analysis):** ◆ patients who did not undergo free-flap breast reconstruction ◆ incomplete medical records	**Interventions** A: Delayed autologous reconstruction · N = 140 B: Delayed-immediate autologous reconstruction · N = 54 **Analysis** ◆ frequencies	**Surgical site infection** · Delayed: 9/140 · Delayed-immediate: 7/54 **Wound healing complications** · Delayed: 17/140 · Delayed-immediate: 4/54 **Hematoma** · Delayed: 1/140 · Delayed-immediate: 2/54 **Return to operation room** · Delayed: 6/140	**General information** ◆ Follow-up: NR ◆ Funding: None of the authors has a financial disclosure to report ◆ CoI: None of the authors has a financial disclosure to report. **Risk of bias considerations (adapted from SIGN cohort study checklist)** ◆ Study type: retrospective study ◆ Confounding: high ◆ Rate of participation/Exclusions reported (selection bias into the study): yes

Reference/ Study type	Population	Interventions	Main results	Methodological evaluation
	◆ those who did not carry a cancer diagnosis ◆ Patients who did not have staged or delayed autologous breast reconstruction or who had both autologous and implant-based reconstruction **Enrolment period** ◆ 2010 – 2018 **Follow-up** ◆ Delayed: 4.9 ± 2.58 ◆ Delayed-immediate: 2.9 ± 1.91 **Descriptive statistics** ◆ Age (median, range) · Delayed: mean: 48.6 ± 8.51; range: 30.5–69.1 · Delayed-immediate: mean: 47.8 ± 8.46; range: 28.1–70.3 ◆ BMI (median, range) · Delayed: <25: 16.5% (22/140); 25-30: 46.1% (48/140); < 30: 47.4% (63/140); missing: 7/140 · Delayed-immediate: <25: 24.1% (13/54); 25-30: 38.9% (21/54); < 30: 37.0% (20/54); missing: 0/54 ◆ Stadium · Delayed: 0: 10.1% (14/140); I: 23.2% (32/140); IIA:13.8% (19/140); IIB:22.5% (31/140); IIIA:19.6%	◆ atching ◆ Adjustment: No	· Delayed-immediate: 4/54	◆ Exposure/Intervention · Assessment reliable: yes · Assessed more than once: no · Possibly affected by knowledge of outcome status? no ◆ Drop-out rate & reasons reported: no ◆ Outcome · Outcome measure is well-defined, valid and reliable: unclear · Blind outcome assessment to exposure: (→If not, Knowledge of exposure status likely to influence the outcome) no (retrospective) ◆ Main cofounders taken into account: no ◆ Confidence intervals reported: no ◆ Selective reporting (comparison with protocol): no protocol found **Other limitations or comments:** ◆ retrospective design

Reference/ Study type	Population	Interventions	Main results	Methodological evaluation
	(27/140); IIIB: 1.4% (2/140); IIIC:7.2% (310140); IV: 2.2% (3/140); missing: 2 · Delayed-immediate: 0: 20.8% (11/54); I: 18.9% (10/54); IIA:24.5% (13/54); IIB:17.0% (9/54) ; IIIA:11.3% (6/54); IIIB:3.8% (2/54); IIIC:1.9% (1/54); IV:1.9% (1/54); missing: 1 ◆ Chemotherapy (% yes) · Delayed: 49.6% (69/140) · Delayed-immediate: 31.5% (17/54) ◆ Reconstruction type (flap type) (%) · autologous free flap breast reconstruction in both groups			

Extra Comparison: *delayed vs. mixed timing*

Reference/ Study type	Population	Interventions	Main results	Methodological evaluation
Kerebijn 2021 Retrospective cohort study	**Inclusion criteria (for analysis):** ◆ All patients who had successful re-construction and completed baseline and 12-month post- operative BREAST Q questionnaires **Exclusion criteria (for analysis):** ◆ bilateral breast cancer ◆ known genetic mutations or other clinical indications for CPM ◆ total or partial flap loss **Enrolment period** ◆ June 2013 – June 2017 **Follow-up** ◆ NR **Descriptive statistics** ◆ Age (mean, SD) · unilateral delayed: 52.3 (8.1) · bilateral mixed timing: 48.7 (8.0) ◆ BMI (mean, SD) · unilateral delayed: 28.0 (4.7) · bilateral mixed timing: 29.1 (4.4) ◆ Stadium · unilateral delayed: NR · bilateral mixed timing: NR ◆ Chemotherapy (% yes)	**Interventions** A: **unilateral delayed** autologous reconstruction · N = 85 B: **bilateral mixed timing** autologous reconstruction · N = 56 **Analysis** ◆ Wilcoxon's Rank-Sum test, linear regression ◆ Matching: No ◆ Adjustment: yes ◆ If yes, for which confounders? age and baseline BREAST Q scores	**QoL-outcomes: Breast -Q (mean, SD):** ◆ Breast satisfaction: · unilateral delayed: 37.8 (15.6) · bilateral mixed timing: 36.6 (15.5) · Adjusted (95% CI): -12.2 (-18.8—5.6) · p = 0.0013 ◆ Psychosocial wellbeing (mean, SD): · unilateral delayed: 54.5 (15.9) · bilateral mixed timing: 50.6 (15.5) · Adjusted (95% CI): -6.4 (-13.3–0.6) · p < 0.0001 ◆ Physical chest (mean, SD): · unilateral delayed: 74.2 (14.5) · bilateral mixed timing: 72.5 (13.9) ◆ Physical abdomen (mean, SD): · unilateral delayed: 89.7 (13.0) · bilateral mixed timing: 86.0 (16.0) ◆ Sexual (mean, SD): · unilateral delayed: 37.2 (17.6) · bilateral mixed timing: 35.4 (20.9)	**General information** ◆ Follow-up: 12- and 18-months ◆ Funding: NR ◆ CoI: The authors have no conflict of interest. **Risk of bias considerations (adapted from SIGN cohort study checklist)** ◆ Study type: retrospective cohort study ◆ Populations comparable: unclear (moderate) ◆ Rate of participation/Exclusions reported (selection bias into the study): no (high) ◆ Exposure/Intervention · Assessment reliable: yes (low) · Assessed more than once: yes · Possibly affected by knowledge of outcome status? no ◆ Drop-out rate & reasons reported: no (high) · Similar across groups: · If high: comparison of those lost with available: unclear (moderate) ◆ Outcome

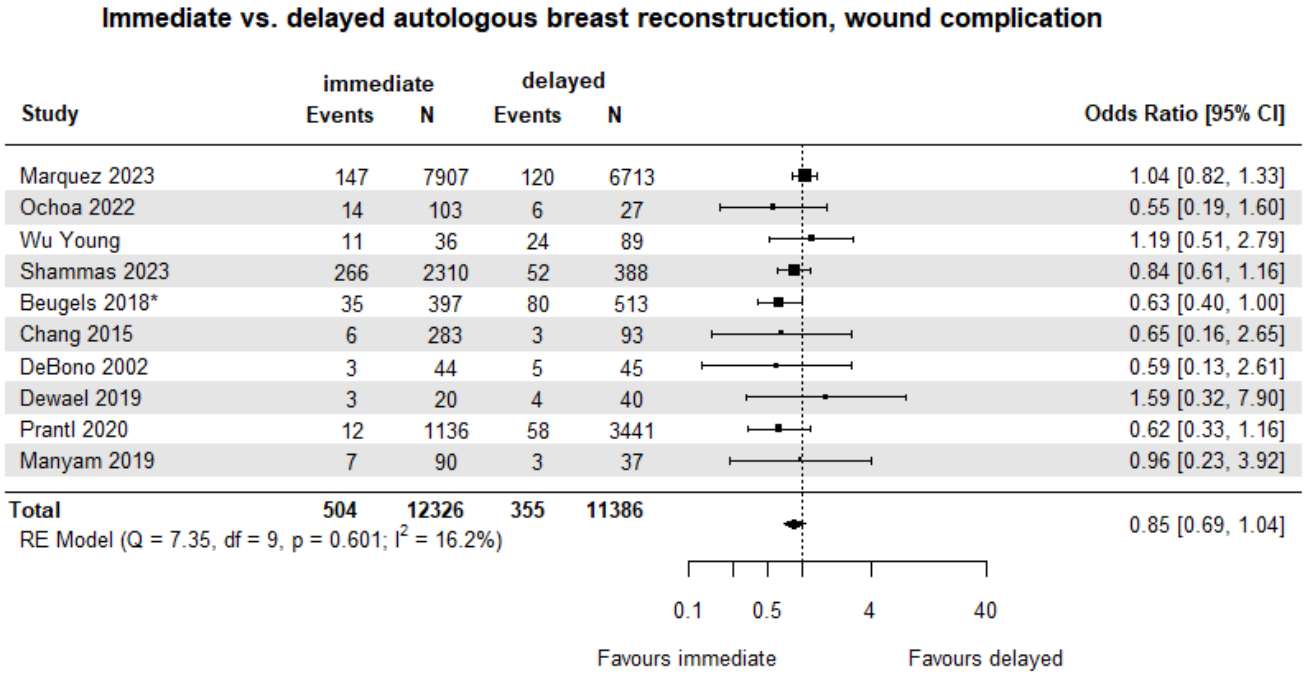
Reference/ Study type	Population	Interventions	Main results	Methodological evaluation
	· unilateral delayed: 68/85 (81.0%) · bilateral mixed timing: 41/56 (82.0%) ◆ Reconstruction type (flap type) (%) · unilateral delayed: NR · bilateral mixed timing: NR			· Outcome measure is well-defined, valid and reliable: unclear (moderate) · Blind outcome assessment to exposure: unclear (moderate) (→If not, Knowledge of exposure status likely to influence the outcome) no ◆ Main cofounders taken into account: yes ◆ Confidence intervals reported: no (high) ◆ Selective reporting (comparison with protocol): yes (high) **Other limitations or comments:** ◆ NR

6.5.3 Meta-Analysen

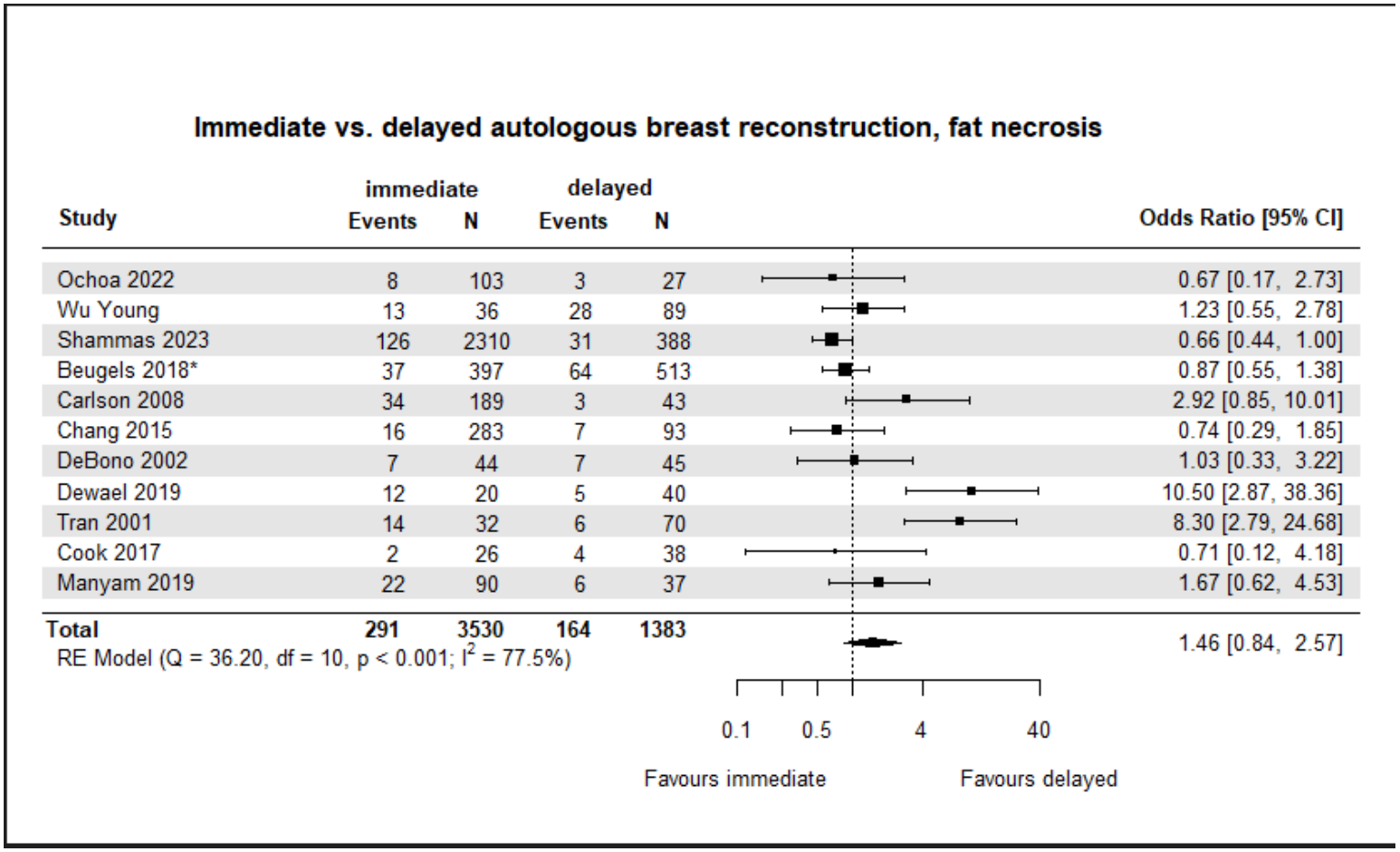
Erklärungen: Mit * markierte Studien haben einen adjustierten Effektschätzer für den Endpunkt berichtet, der hier verwendet wurde.

6.5.3.1 Immediate vs. Delayed autologous breast reconstruction

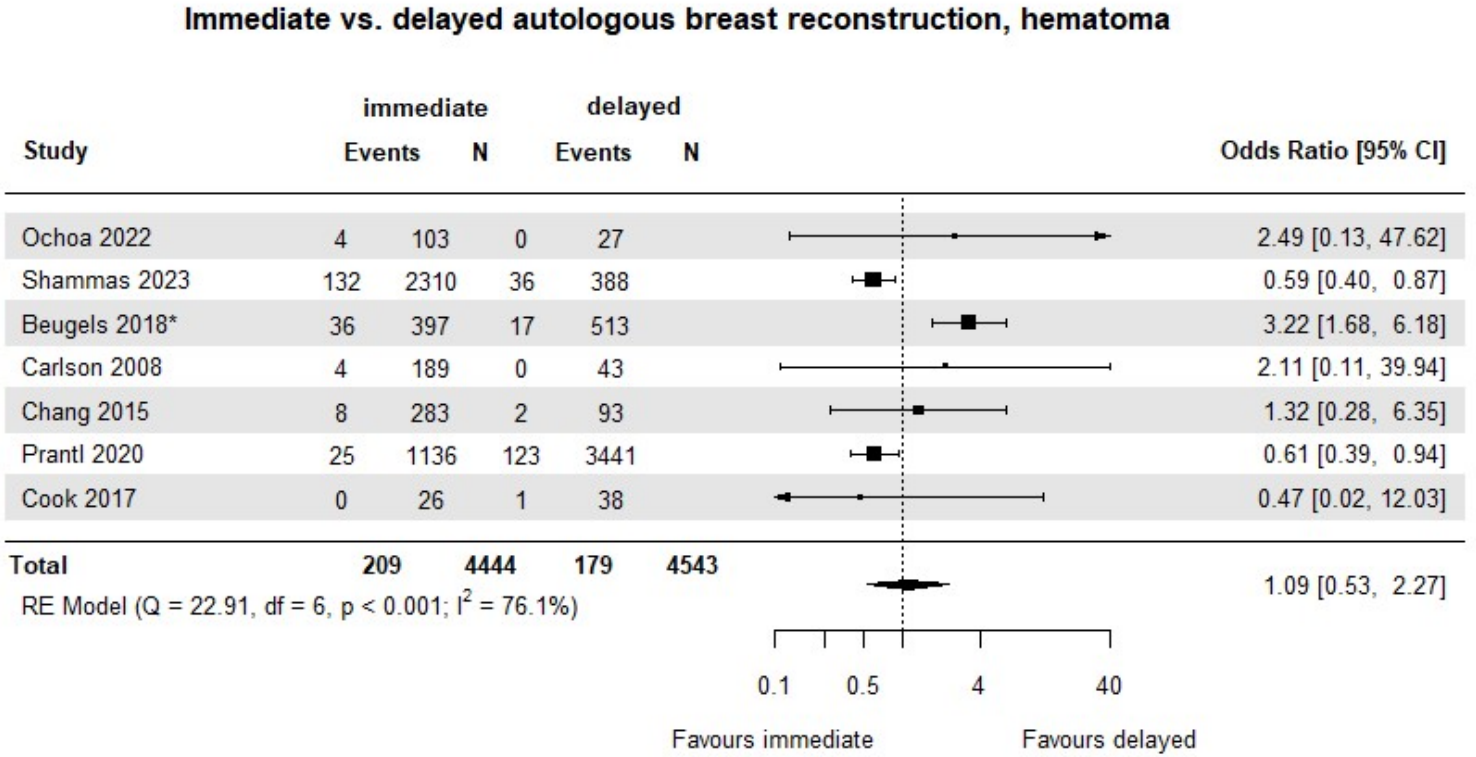
6.5.3.1.1 Wound complication



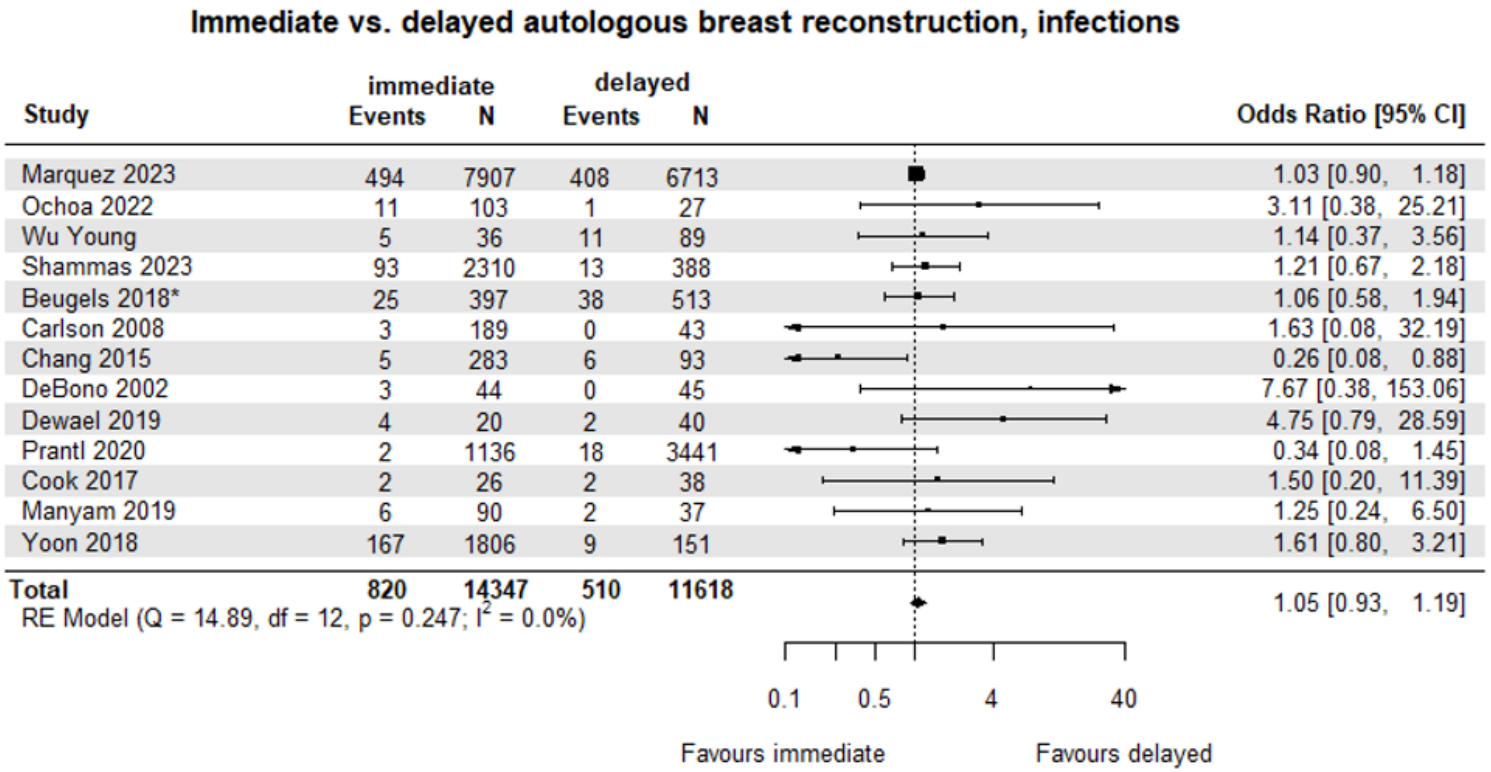
6.5.3.1.2 Fat necrosis



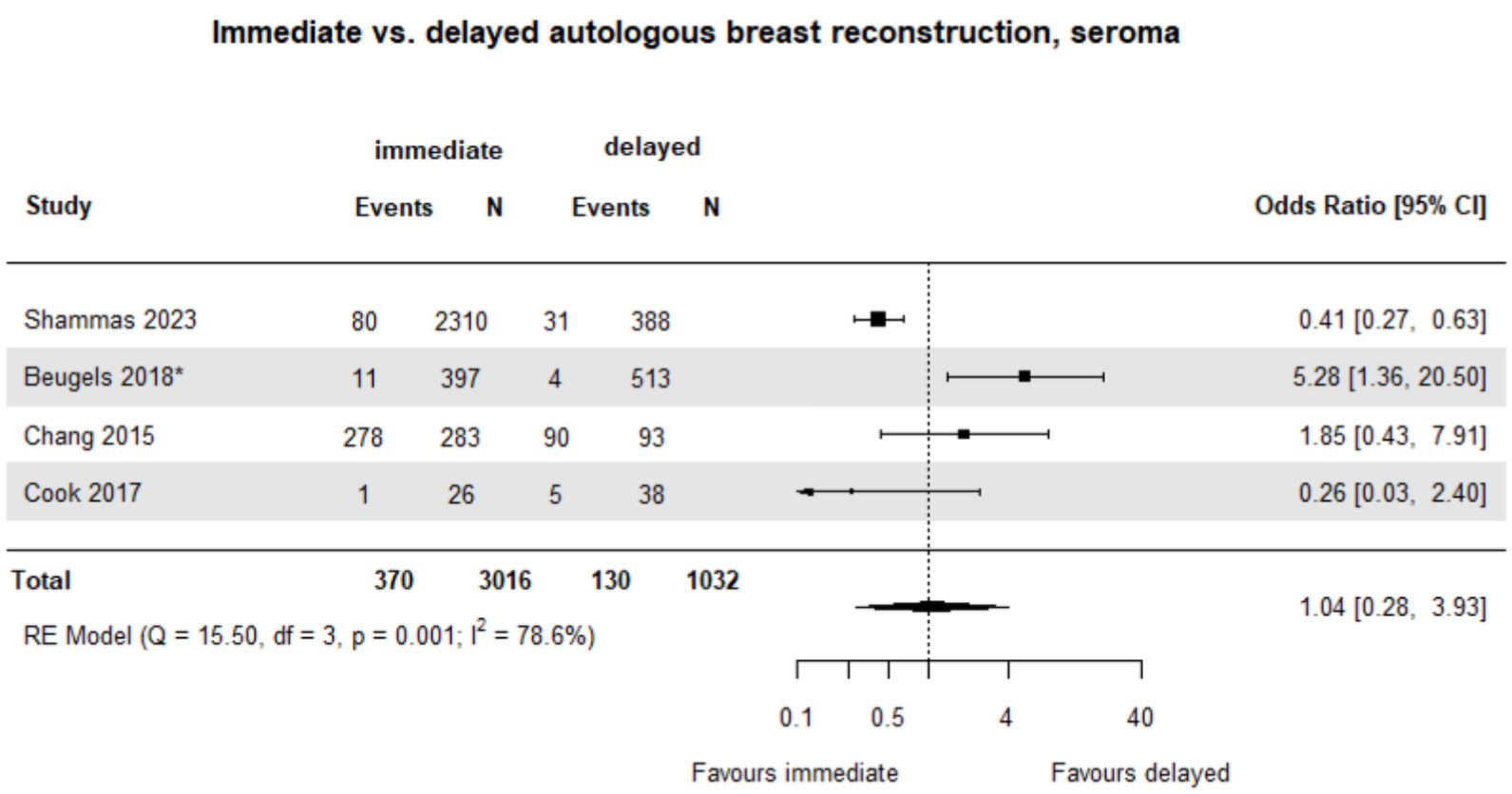
6.5.3.1.3 5.1.4. Hematoma



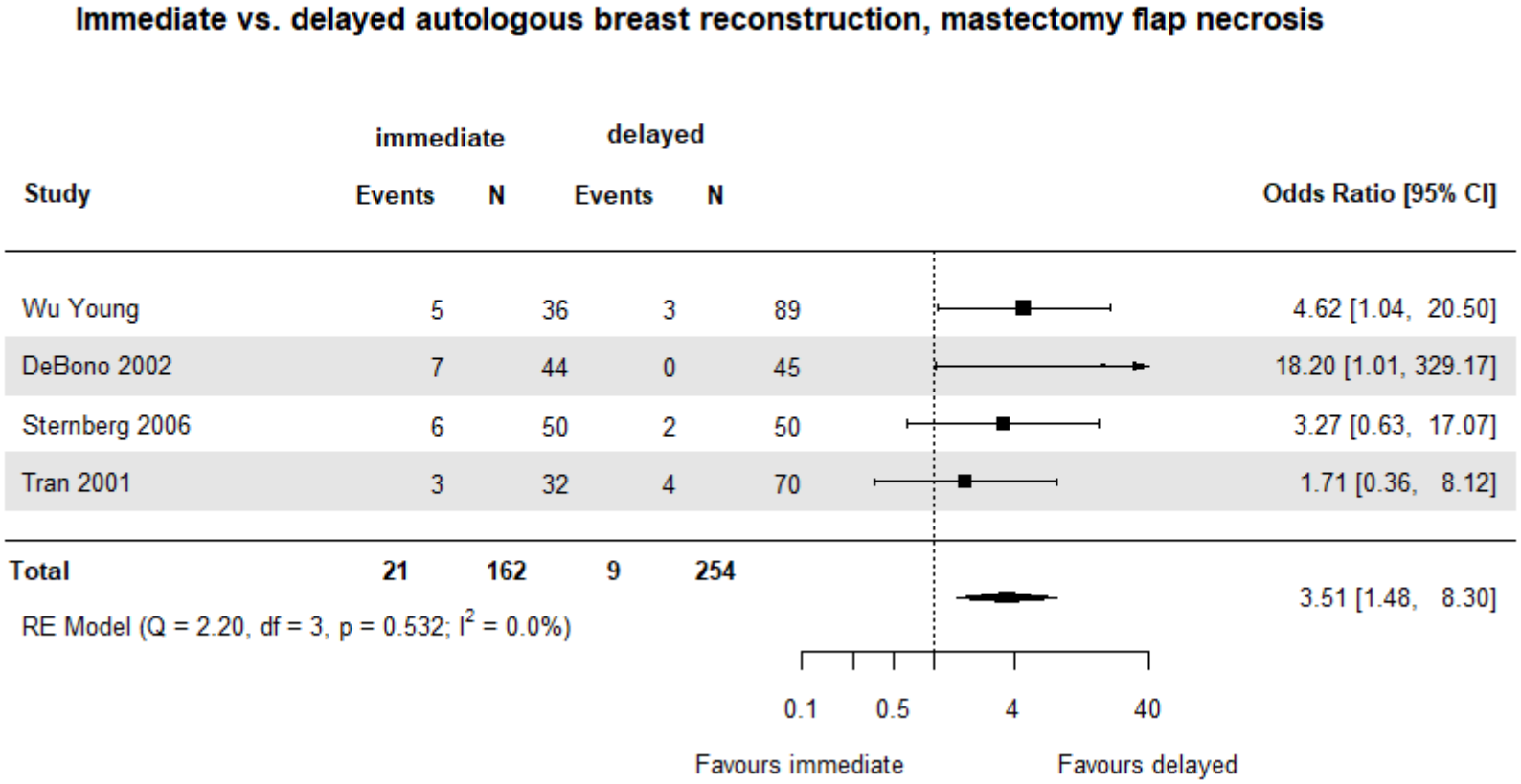
6.5.3.1.4 Infections



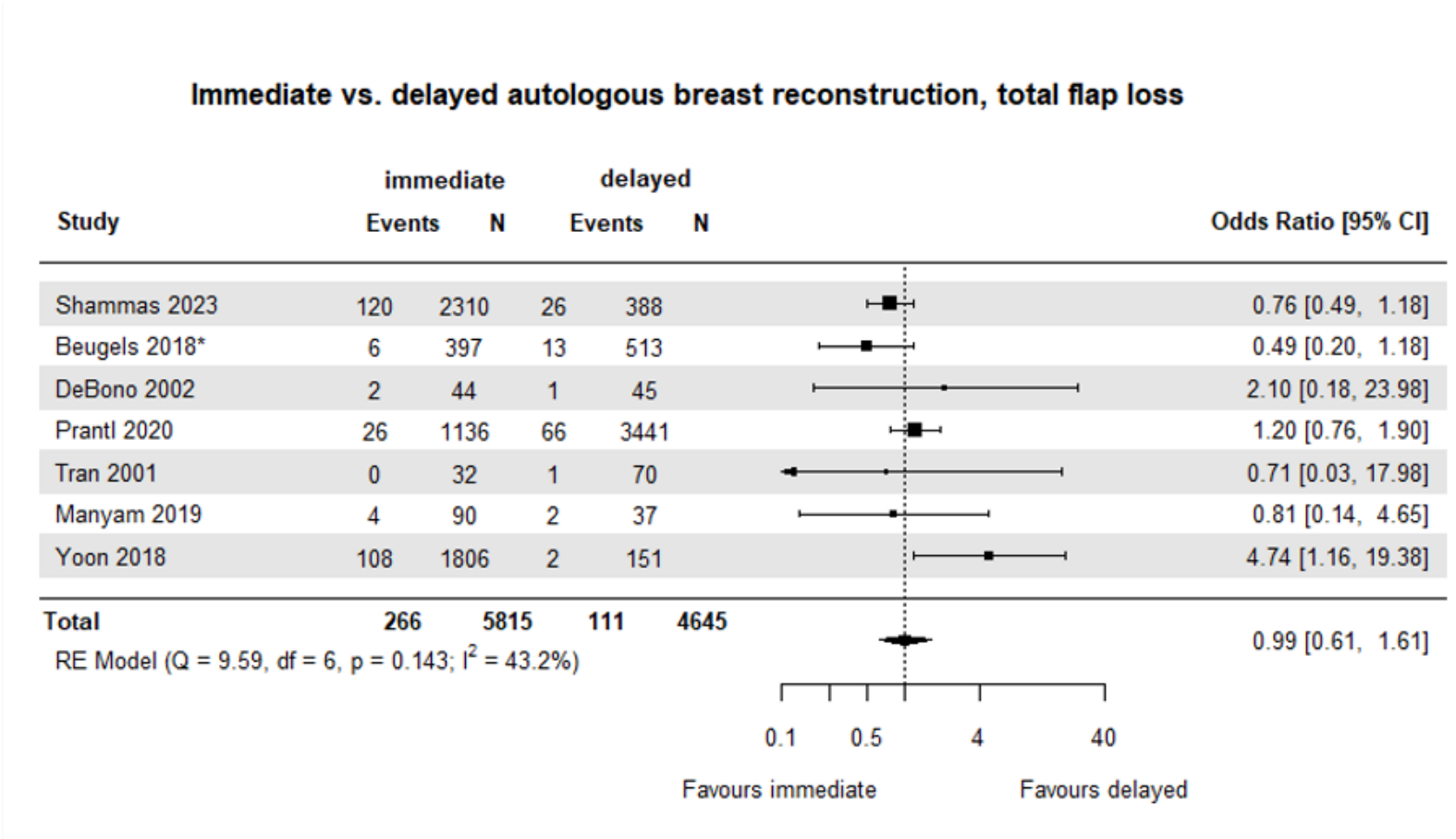
6.5.3.1.5 Seroma



6.5.3.1.6 Mastectomy flap necrosis



6.5.3.1.7 Total flap loss

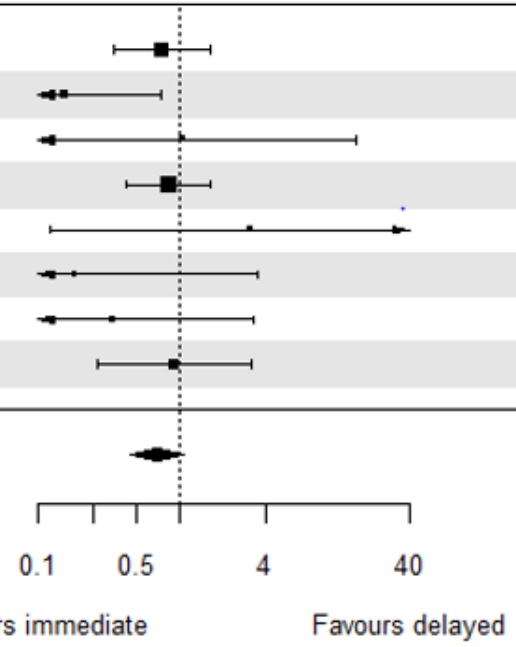


6.5.3.1.8 Partial flap loss

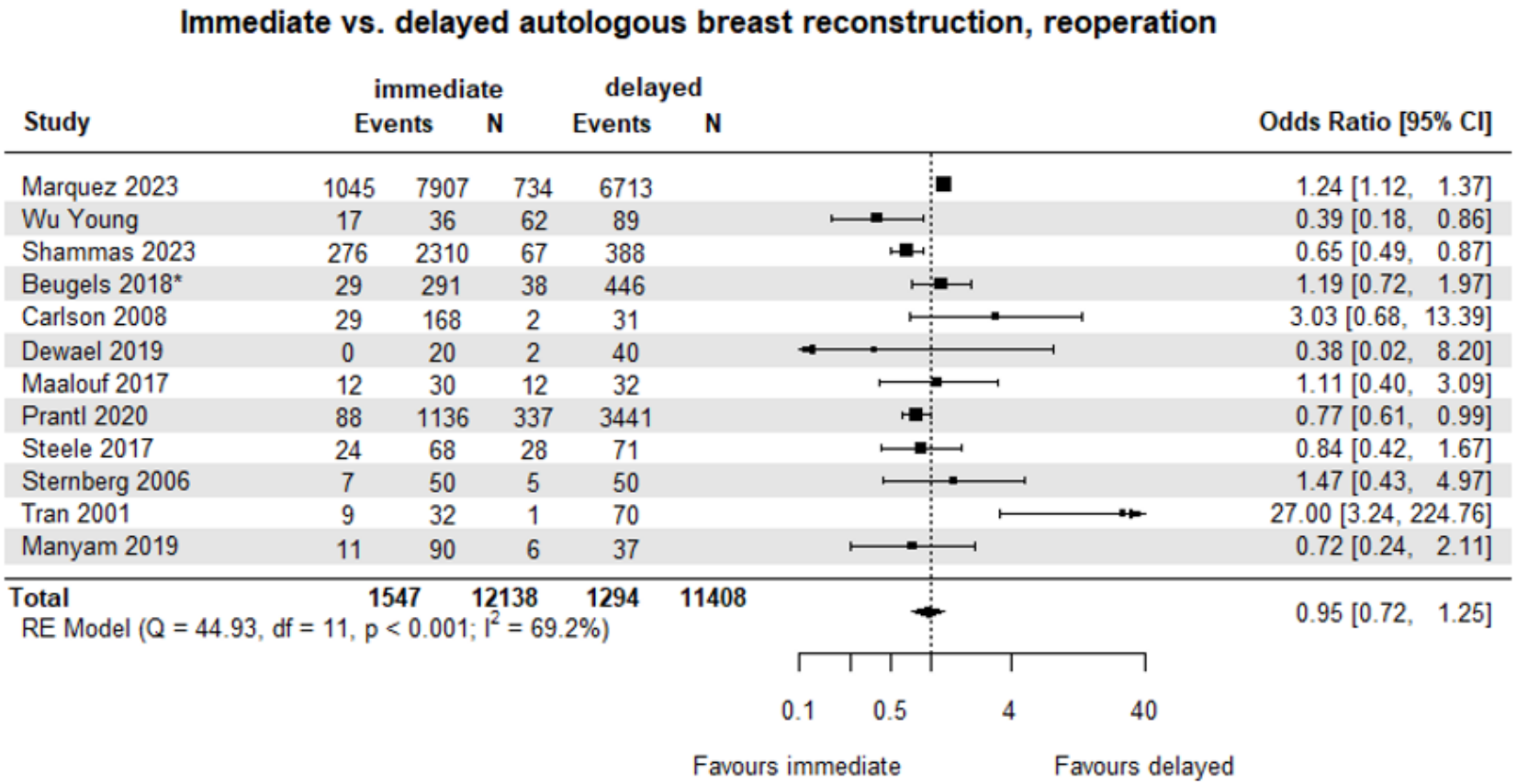
Immediate vs. delayed autologous breast reconstruction, partial flap loss

Study	immediate Events	immediate N	delayed Events	delayed N	Odds Ratio [95% CI]
Beugels 2018*	14	397	25	513	0.74 [0.34, 1.62]
Carlson 2008	3	189	4	43	0.16 [0.03, 0.73]
DeBono 2002	1	44	1	45	1.02 [0.06, 16.89]
Prantl 2020	11	1136	40	3441	0.83 [0.43, 1.63]
Sternberg 2006	1	50	0	50	3.06 [0.12, 76.95]
Tran 2001	0	32	5	70	0.18 [0.01, 3.42]
Cook 2017	1	26	4	38	0.34 [0.04, 3.23]
Manyam 2019	9	90	4	37	0.92 [0.26, 3.18]
Total	**40**	**1964**	**83**	**4237**	0.69 [0.45, 1.06]

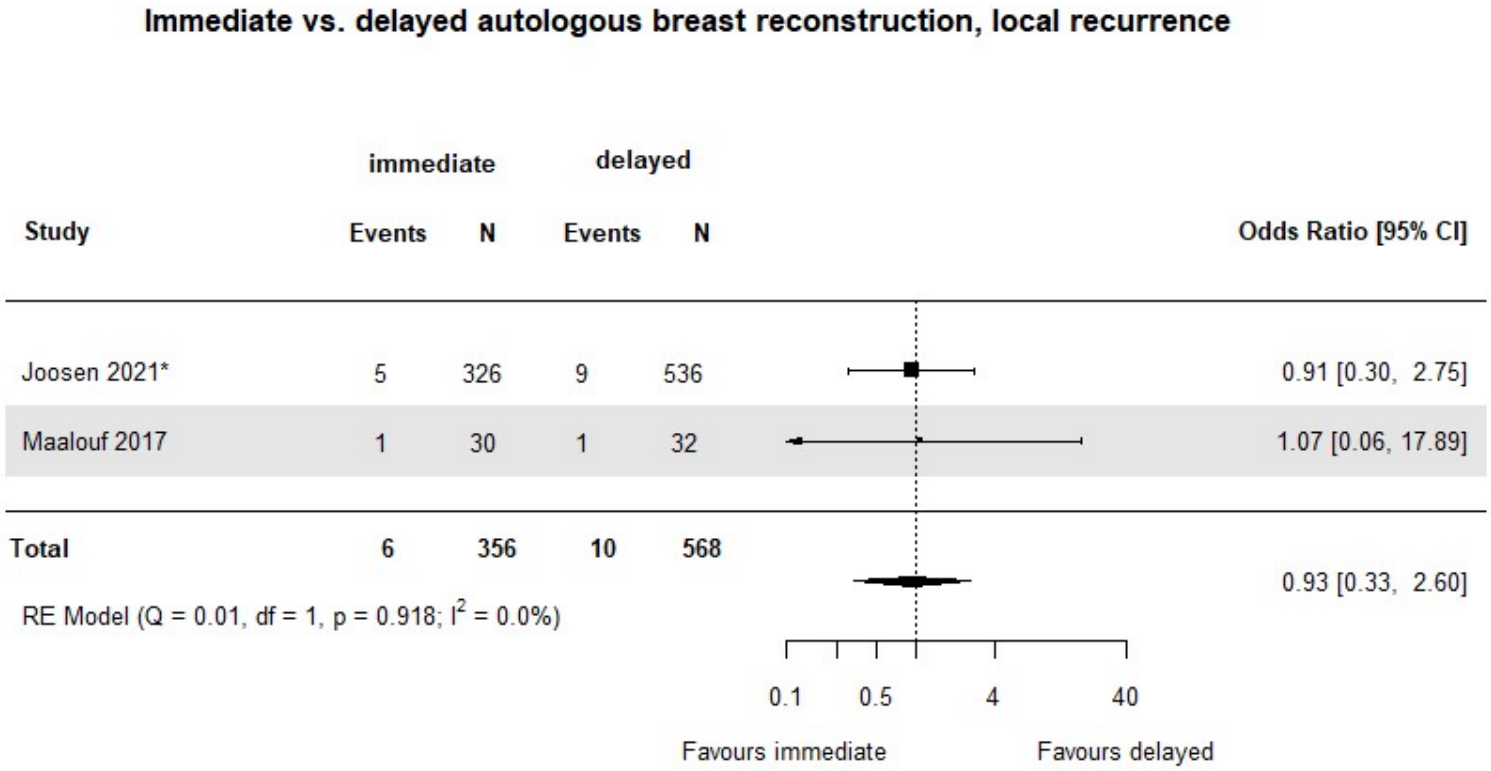
RE Model (Q = 6.15, df = 7, p = 0.522; I^2 = 0.0%)



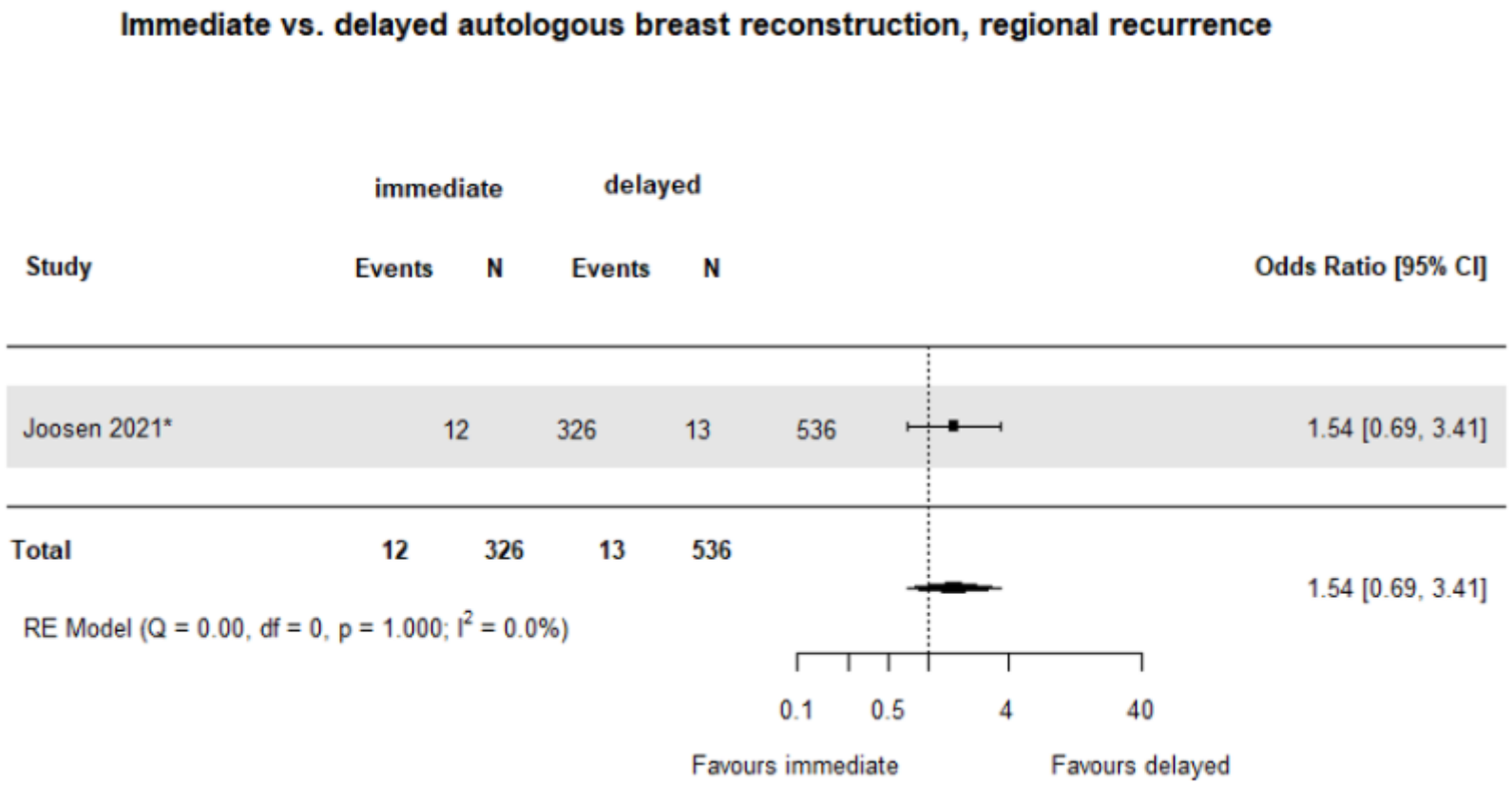
6.5.3.1.9 Reoperation



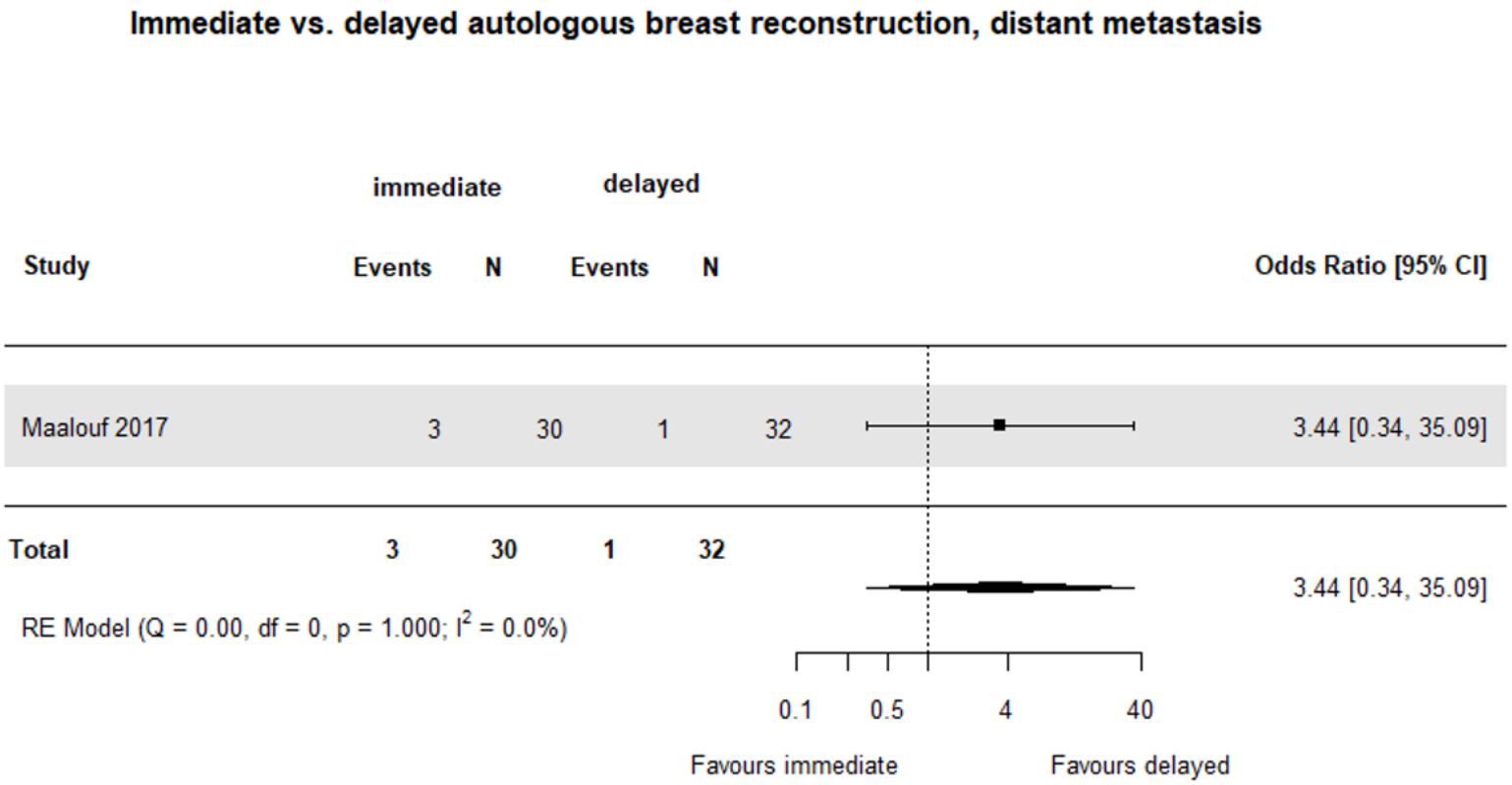
6.5.3.1.10 Local recurrence



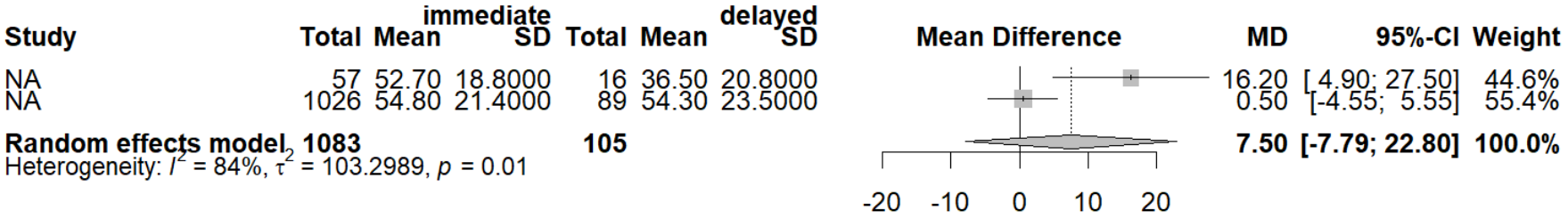
6.5.3.1.11 Regional recurrence



6.5.3.1.12 Distant metastasis

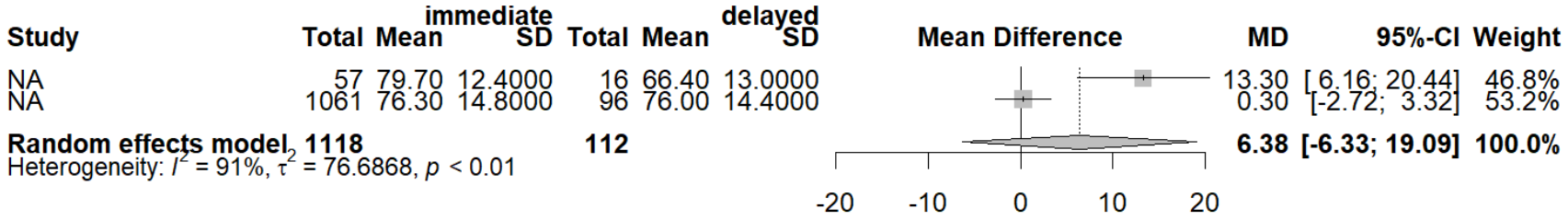


6.5.3.1.13 Sexual well-being (BREAST-Q)



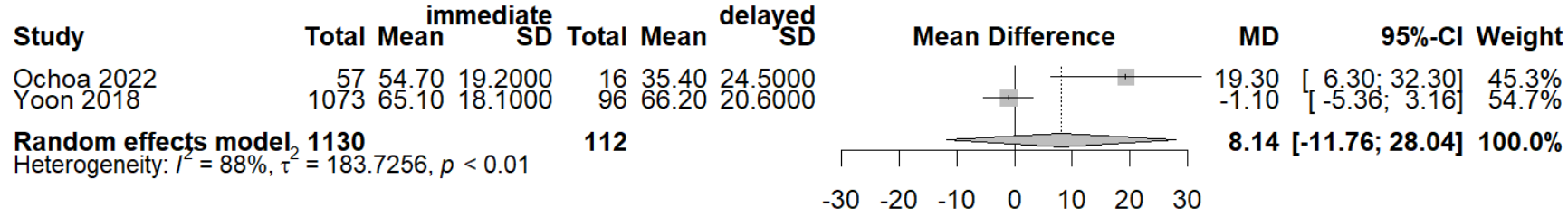
Notes forest plot: first NA= Ochoa 2022 study; second NA= Yoon 2018

6.5.3.1.14 Physical well-being



Notes forest plot: first NA= Ochoa 2022 study; second NA= Yoon 2018

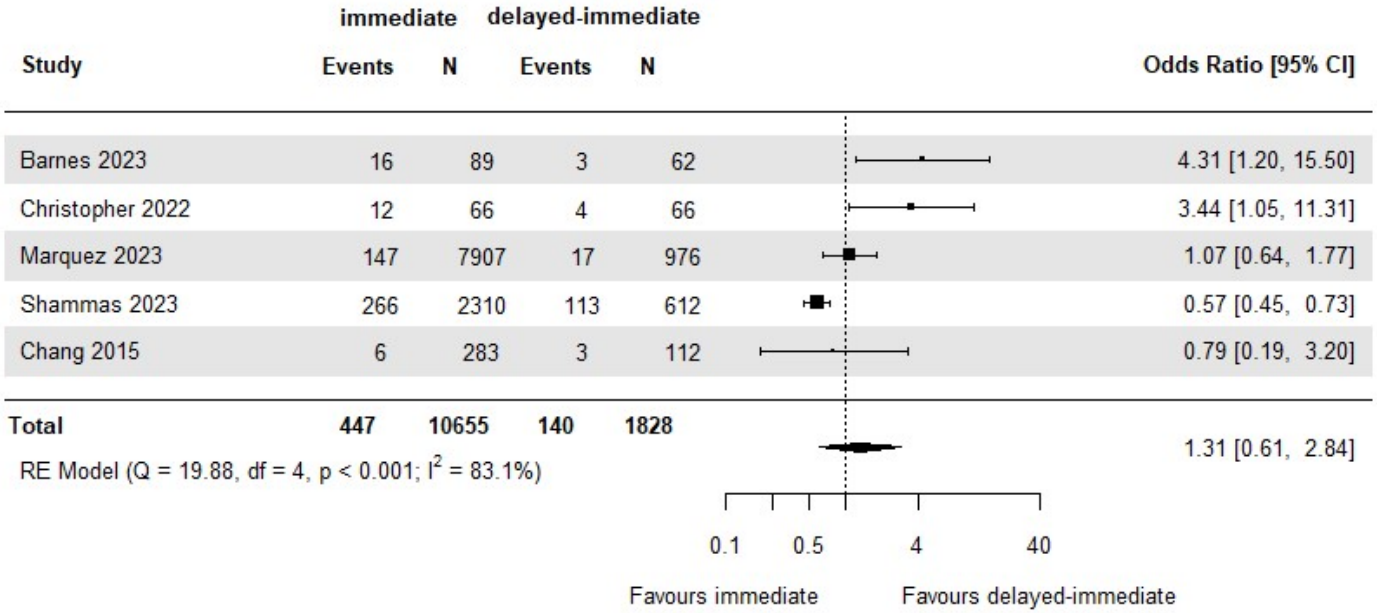
6.5.3.1.15 Satisfaction with breasts



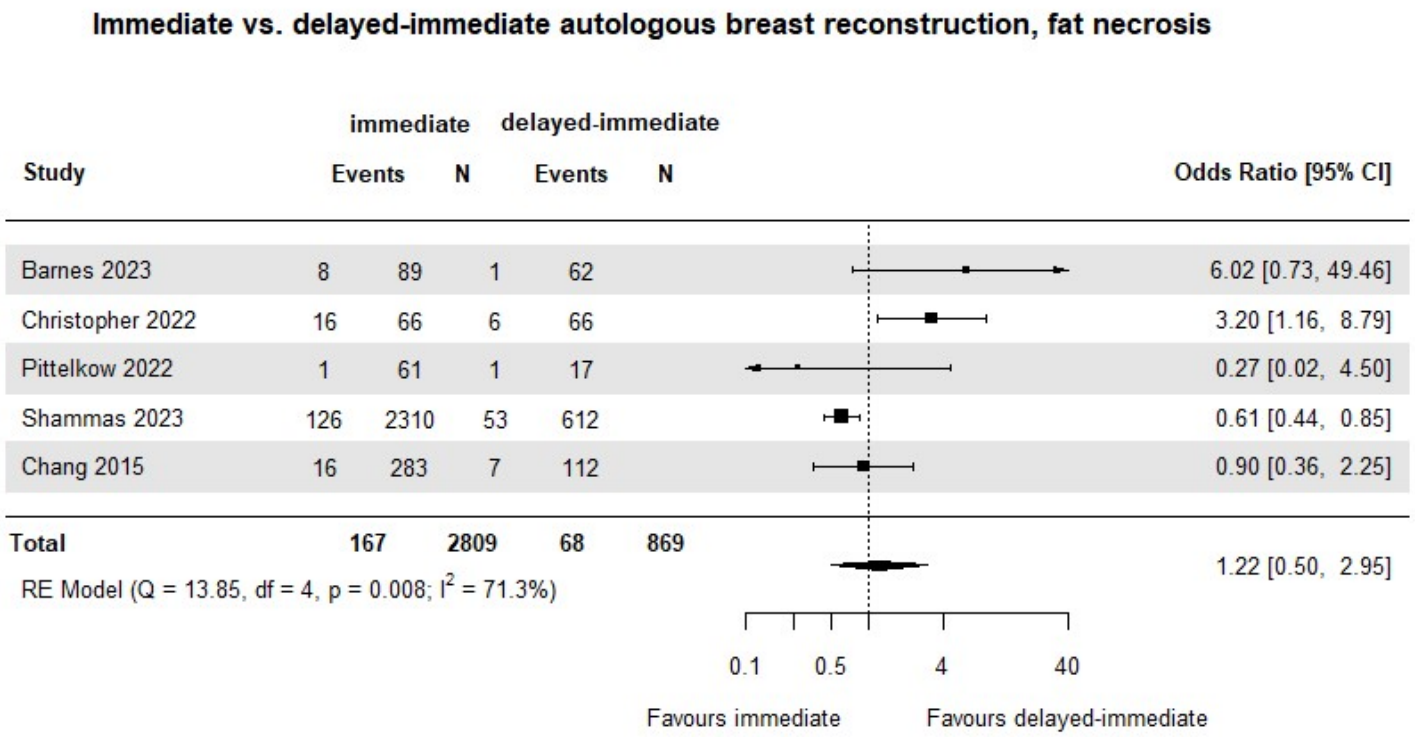
6.5.3.2 Immediate vs. Delayed-Immediate autologous breast reconstruction

6.5.3.2.1 Wound complication

Immediate vs. delayed-immediate autologous breast reconstruction, wound complication

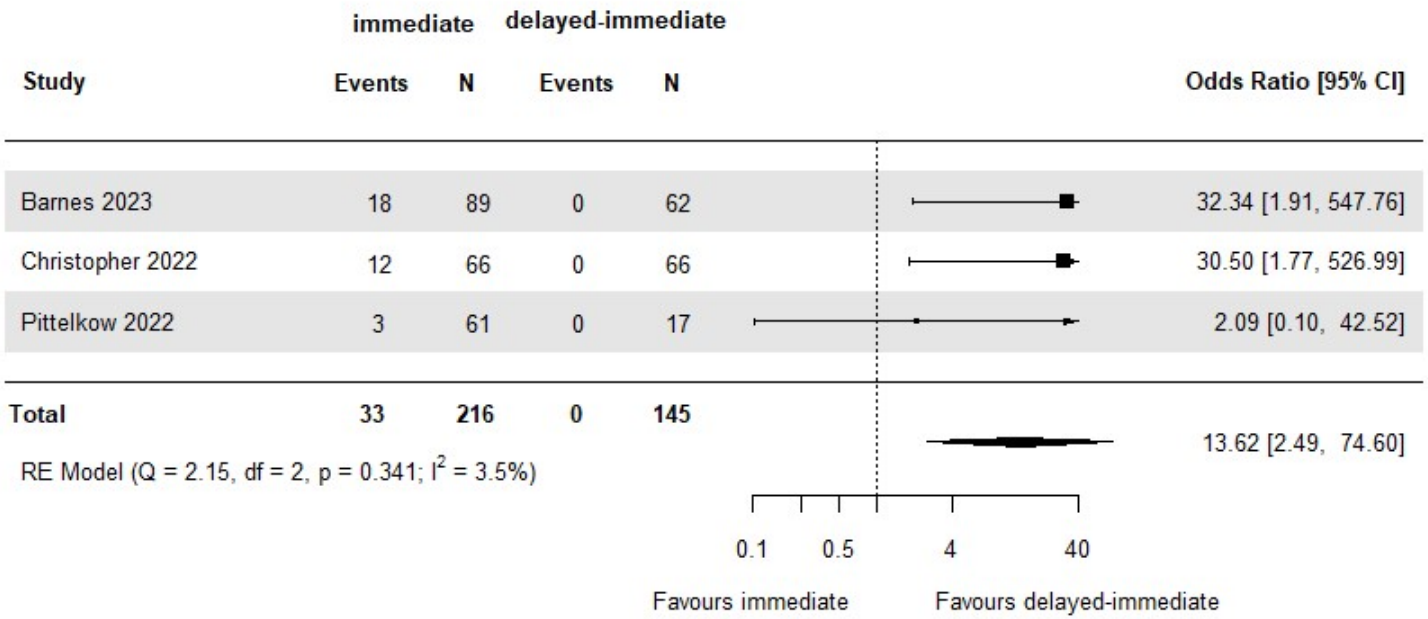


6.5.3.2.2 Fat necrosis

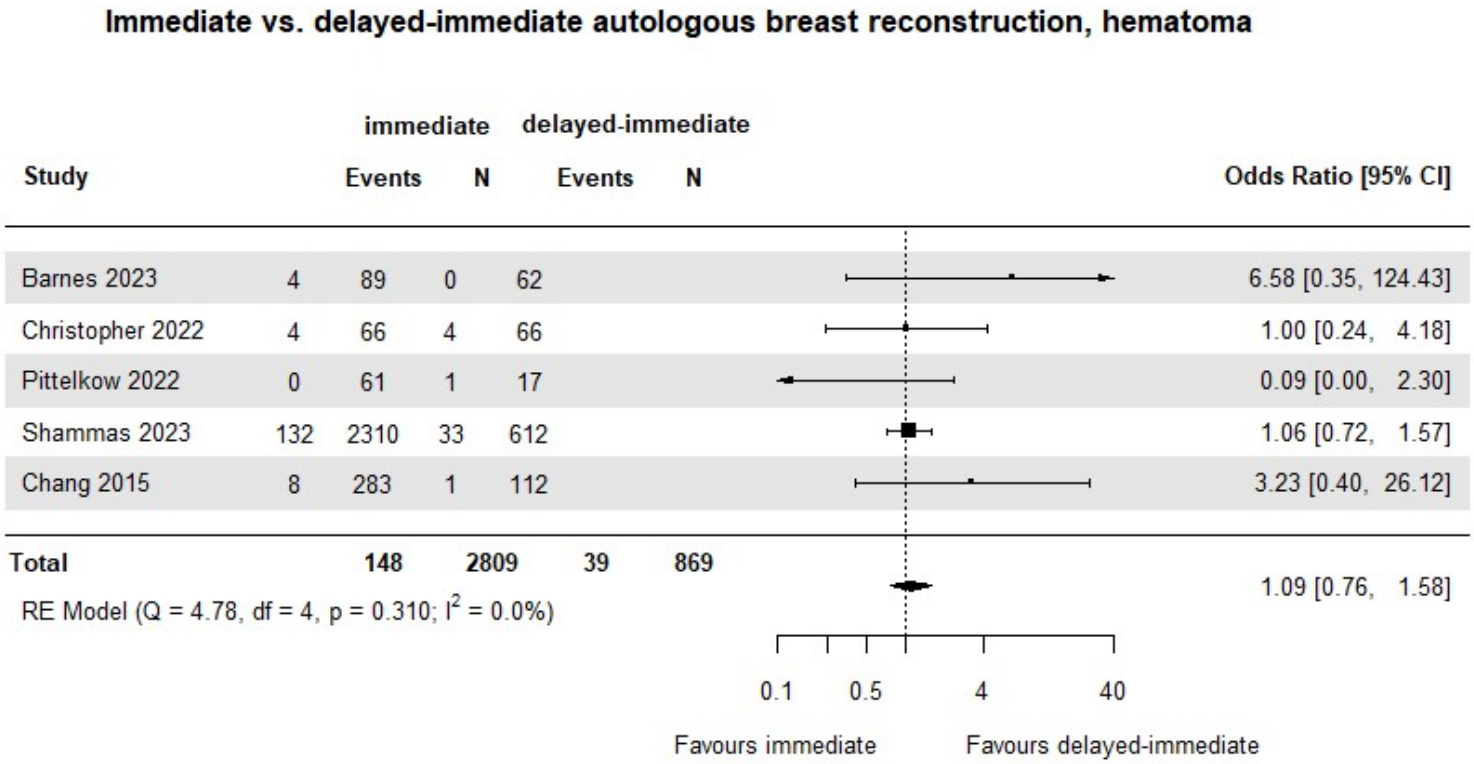


6.5.3.2.3 Mastectomy flap necrosis

Immediate vs. delayed-immediate autologous breast reconstruction, flap necrosis

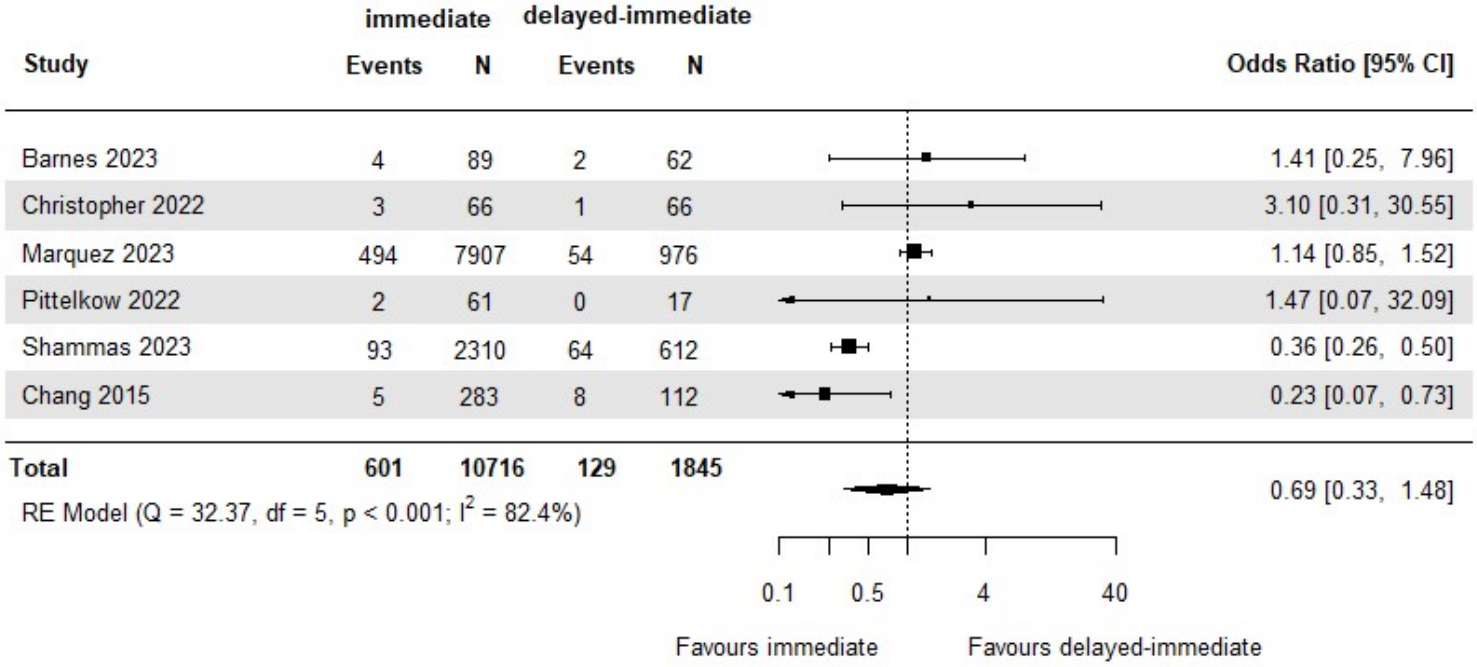


6.5.3.2.4 Hematoma

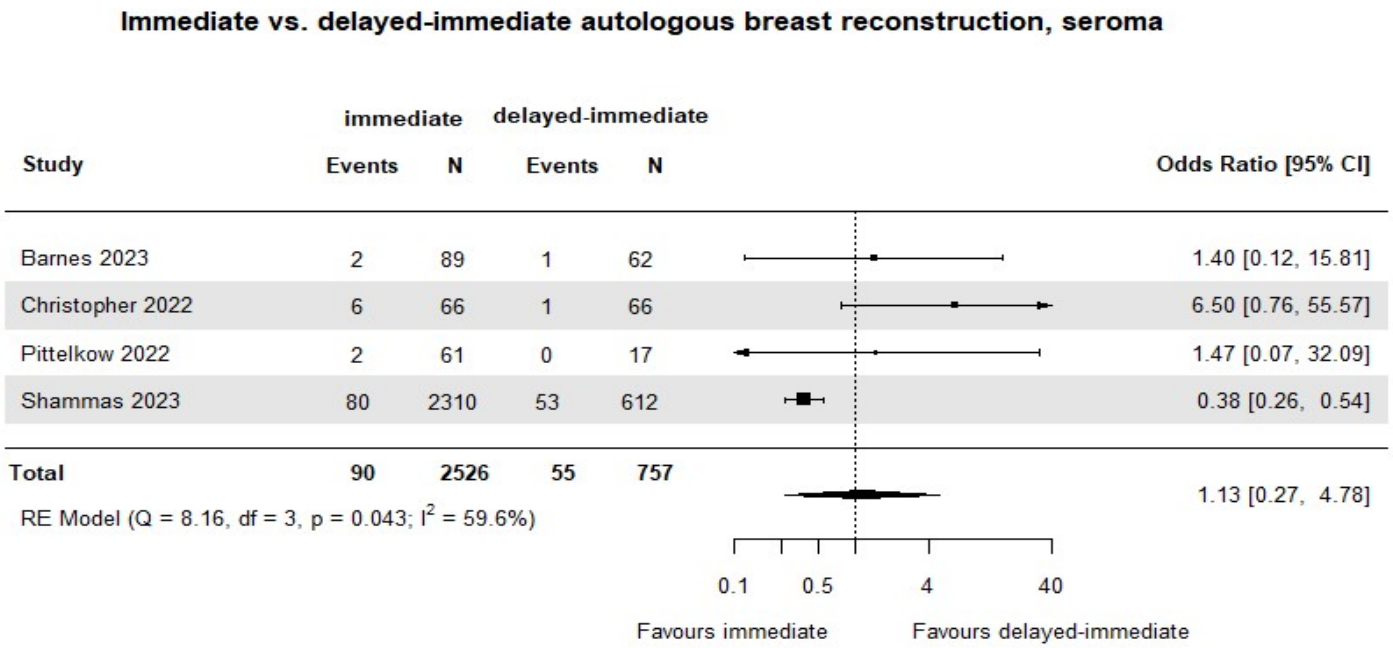


6.5.3.2.5 Infections

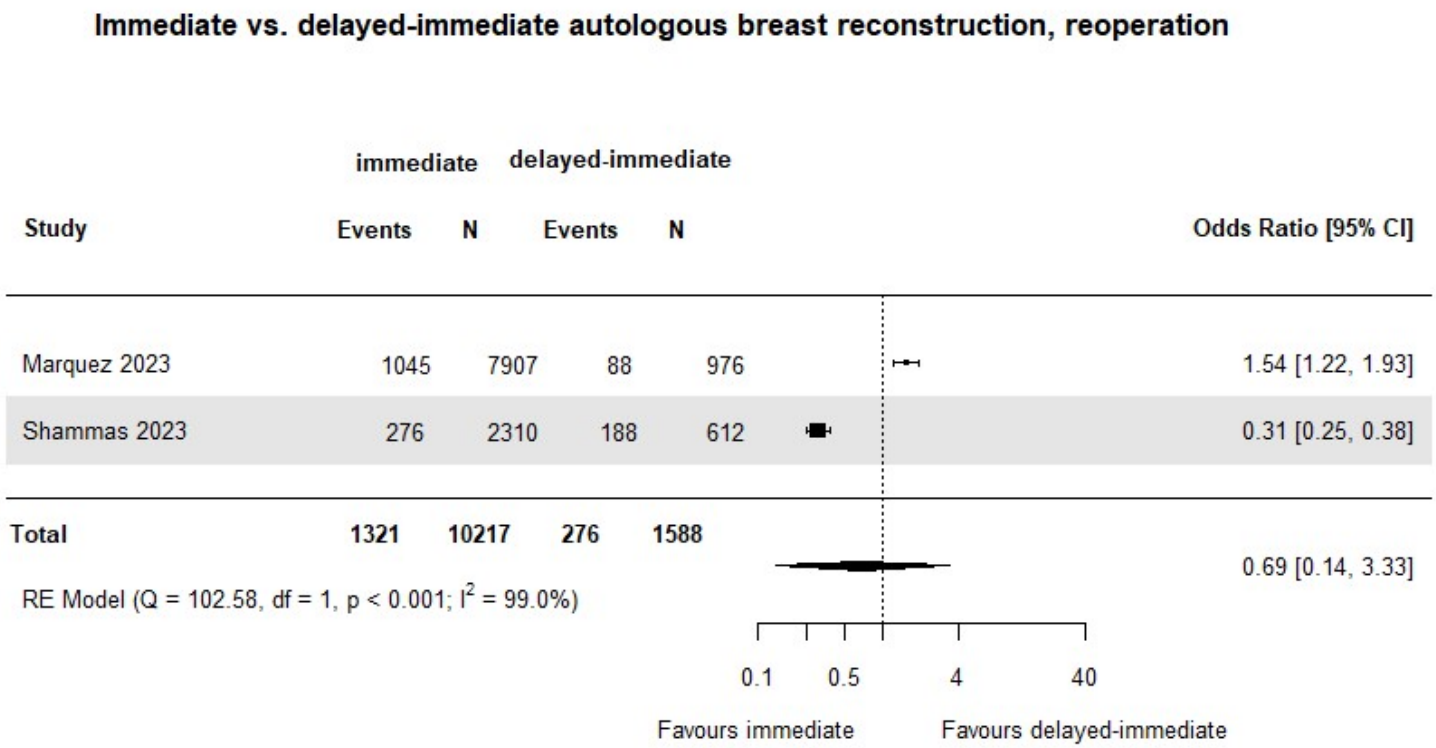
Immediate vs. delayed-immediate autologous breast reconstruction, infections



6.5.3.2.6 Seroma



6.5.3.2.7 Reoperation

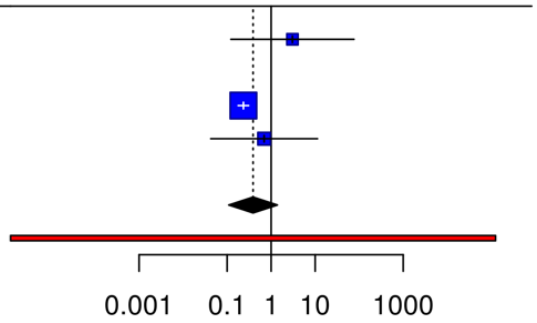


6.5.3.2.8 Total flap loss

Study	immediate Events	immediate Total	delayed-immediate Events	delayed-immediate Total	Weight	Odds Ratio MH, Random, 95% CI
Christopher 2022	1	66	0	66	12.9%	3.05 [0.12; 76.13]
Pittelkow 2022	0	61	0	17	0.0%	
Shammas 2023	120	2310	116	612	70.9%	0.23 [0.18; 0.31]
Barnes 2023	1	89	1	62	16.2%	0.69 [0.04; 11.30]
Total (95% CI)		**2526**		**757**	**100.0%**	**0.39 [0.11; 1.39]**
Prediction interval						**[0.00; 125361.95]**

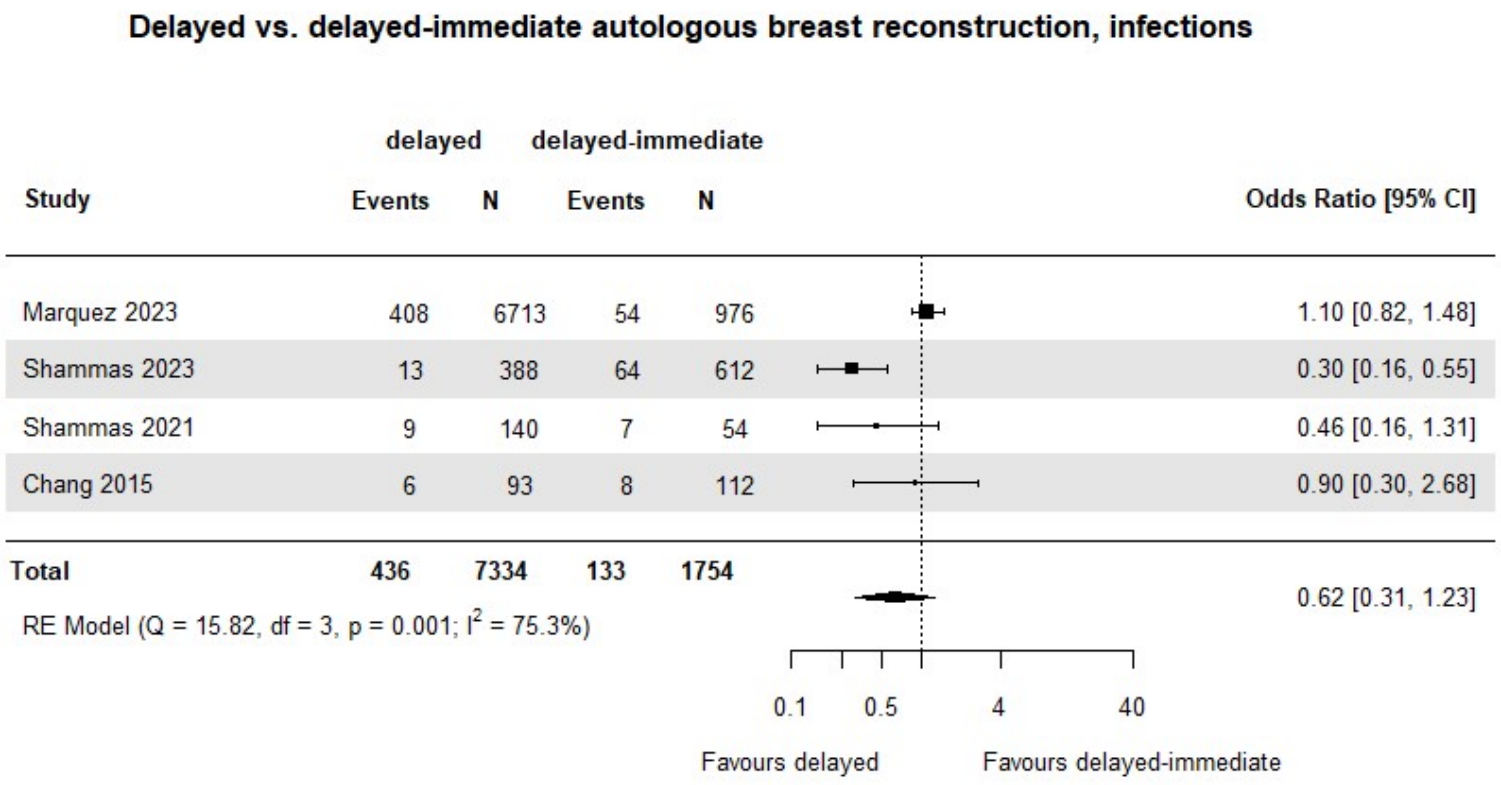
Heterogeneity: $Tau^2 = 0.5750$; $Chi^2 = 2.98$, df = 2 (P = 0.23); $I^2 = 33\%$

Test for overall effect: Z = -1.46 (P = 0.15)

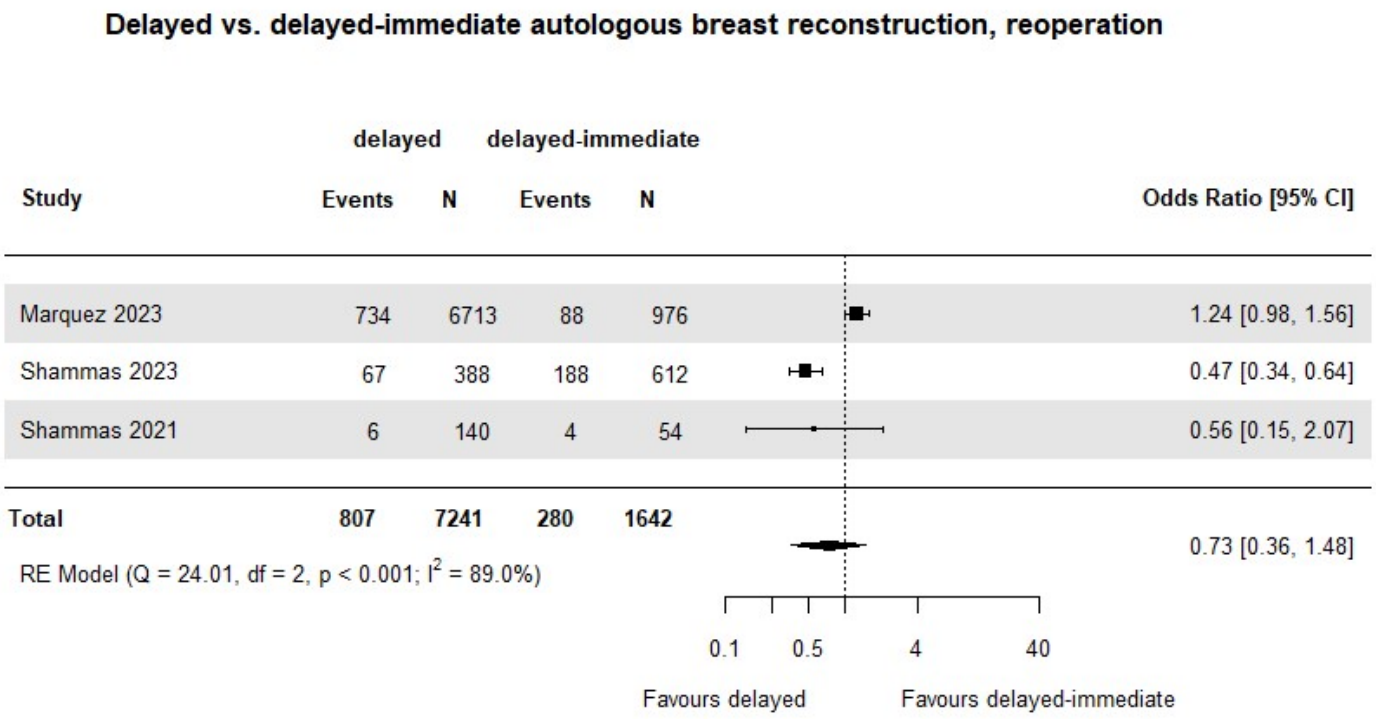


6.5.3.3 Delayed vs. Delayed-Immediate autologous breast reconstruction

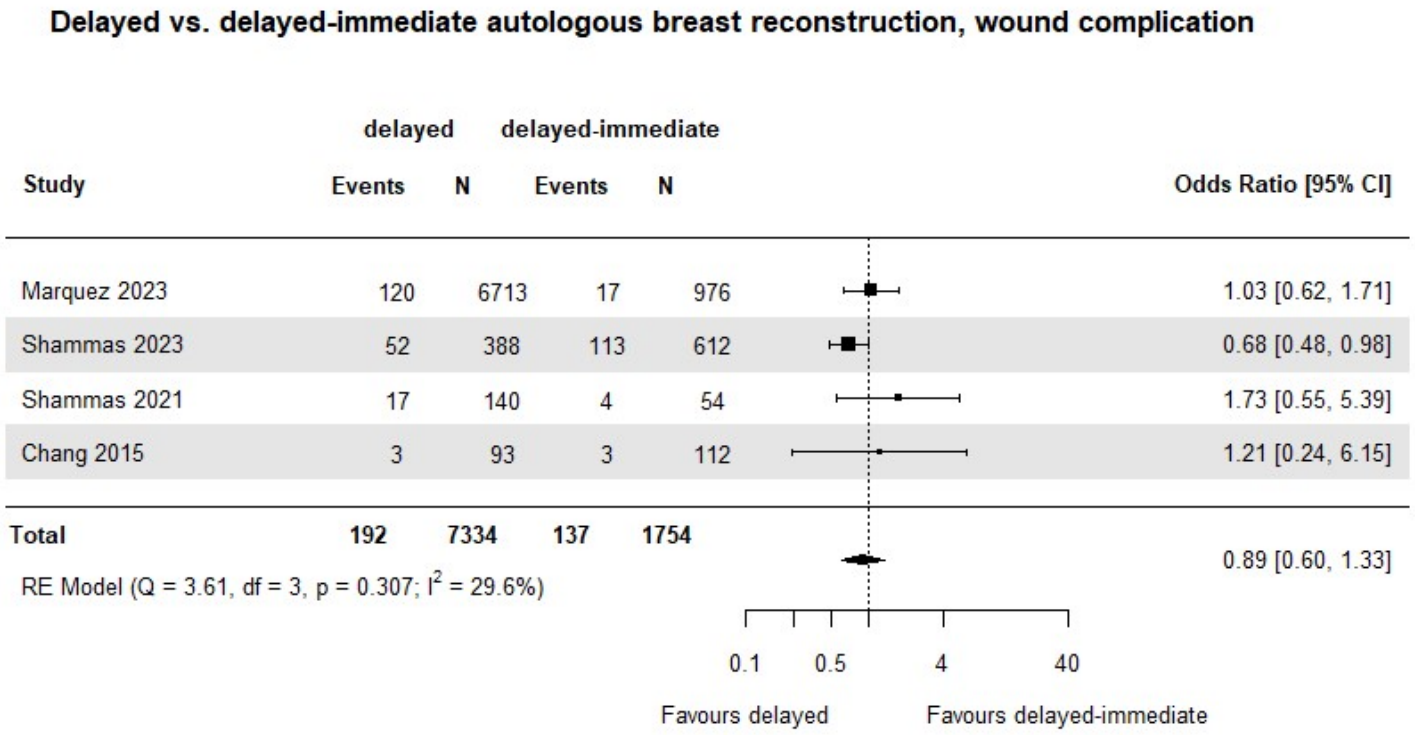
6.5.3.3.1 Infections



6.5.3.3.2 Reoperation

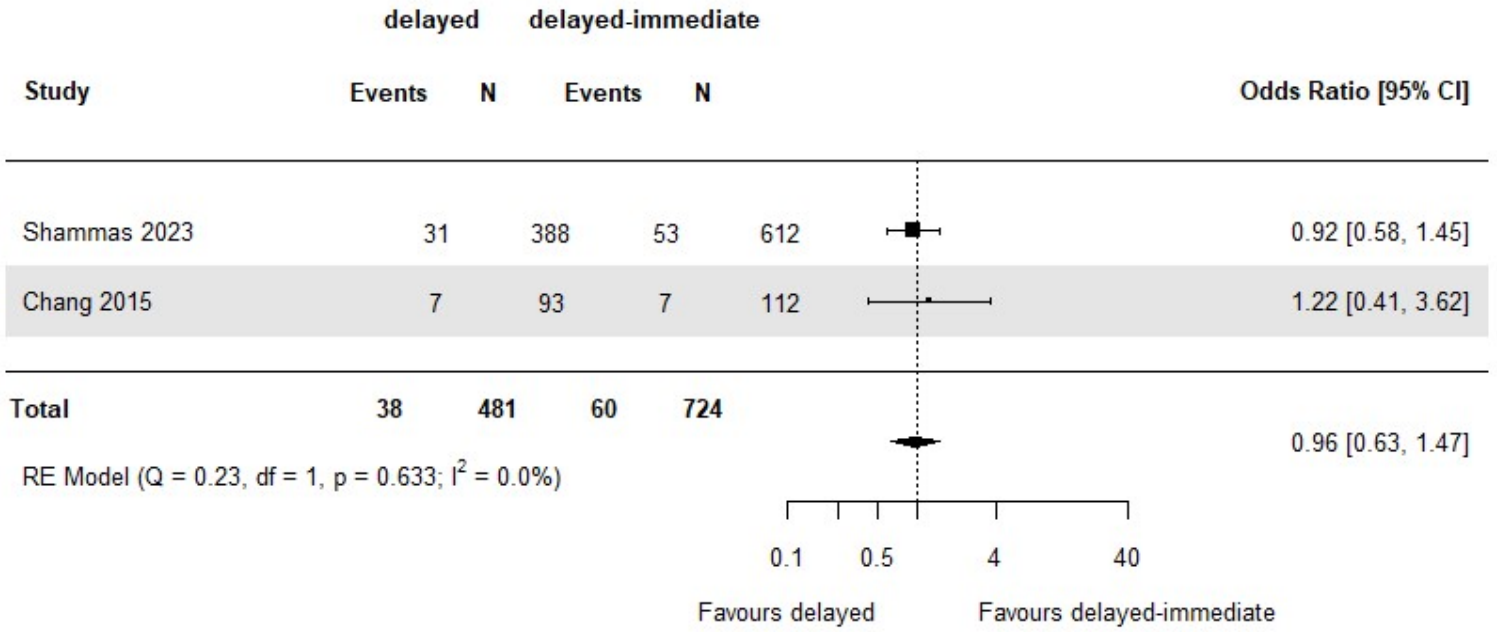


6.5.3.3.3 Wound complication



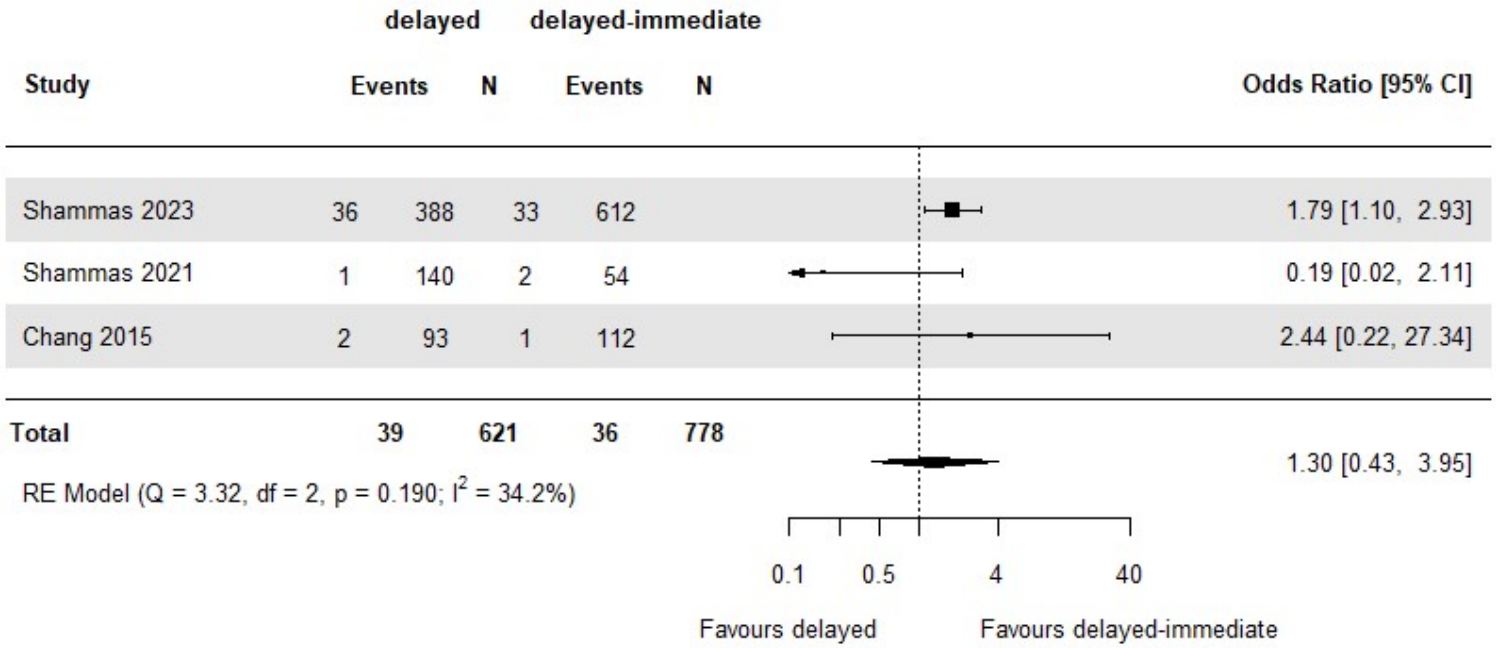
6.5.3.3.4 Fat necrosis

Delayed vs. delayed-immediate autologous breast reconstruction, fat necrosis

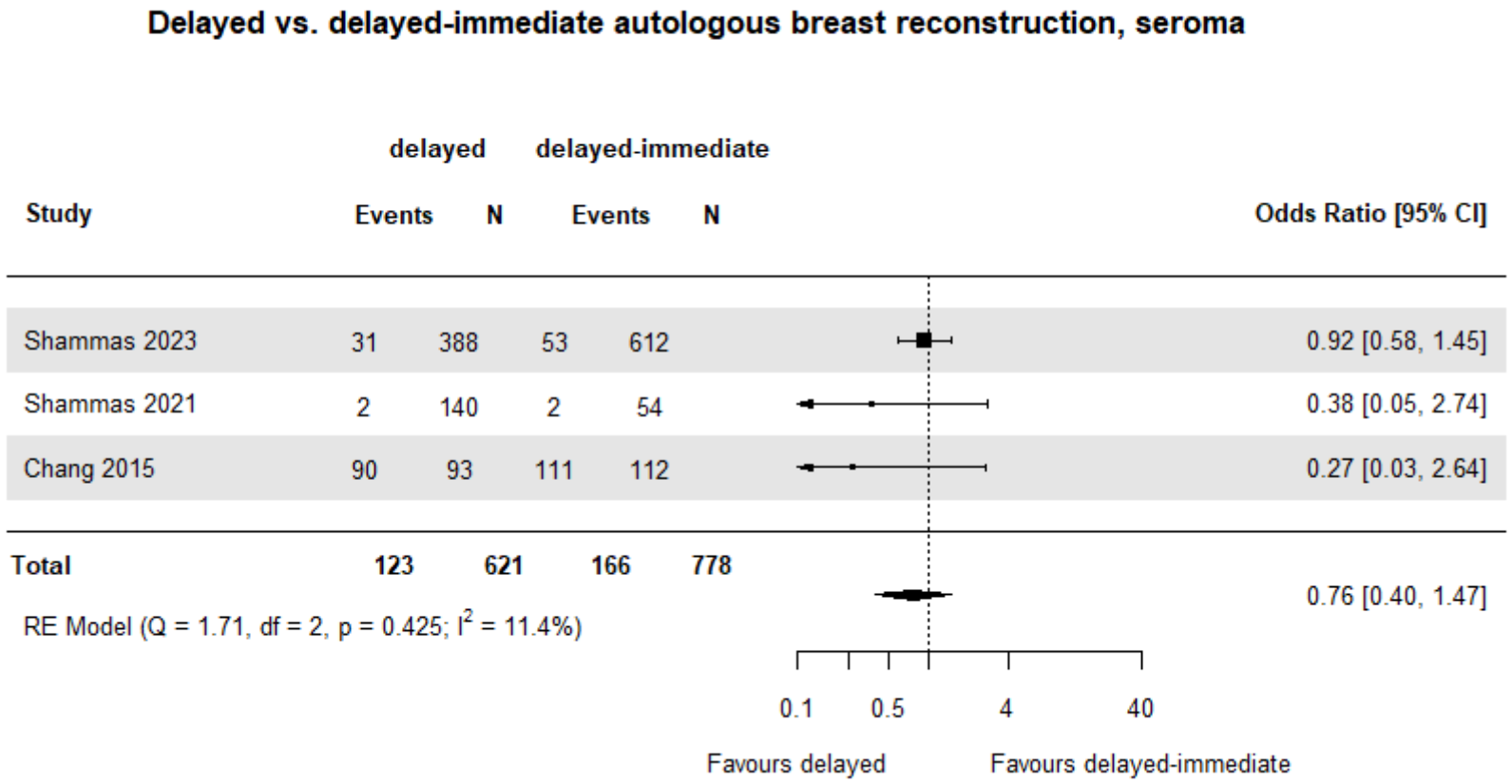


6.5.3.3.5 Hematoma

Delayed vs. delayed-immediate autologous breast reconstruction, hematoma



6.5.3.3.6 Seroma



6.5.4 Vertrauen in die Evidenz (nach GRADE)

6.5.4.1 Immediate vs. Delayed Comparison

Summary of findings:

Immediate compared to delayed for autologous breast reconstruction

Patient or population: breast cancer, autologous breast reconstruction

Intervention: immediate breast reconstruction

Comparison: delayed breast reconstruction

Outcomes	**Anticipated absolute effects*** (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with delayed	**Risk with immediate**				
Wound complication	26 per 1.000	**22 per 1.000** (18 to 27)	**OR 0.85** (0.69 to 1.04)	23712 (10 non-randomised studies)	⊕◯◯◯ Very low[a,b]	It is uncertain whether immediate compared to delayed autologous breast reconstruction increases or decreases the incidence of wound complications.
Fat necrosis	119 per 1.000	**165 per 1.000** (102 to 258)	**OR 1.46** (0.84 to 2.57)	4913 (11 non-randomised studies)	⊕◯◯◯ Very low[a,b,c]	It is uncertain whether immediate compared to delayed autologous breast reconstruction increases or decreases the incidence of fat necrosis.
Hematoma	39 per 1.000	**43 per 1.000** (21 to 85)	**OR 1.09** (0.53 to 2.27)	8987 (7 non-randomised studies)	⊕◯◯◯ Very low[a,b,c]	It is uncertain whether immediate compared to delayed autologous breast reconstruction increases or decreases the incidence of hematoma.
Infections	43 per 1.000	**45 per 1.000** (40 to 51)	**OR 1.05** (0.93 to 1.19)	25965 (13 non-randomised studies)	⊕◯◯◯ Very low[a,b]	Immediate autologous breast reconstruction may have little to no effect on the incidence of infections compared to delayed reconstruction.

Summary of findings:						
Seroma	126 per 1.000	**130 per 1.000** (39 to 362)	**OR 1.04** (0.28 to 3.93)	4048 (4 non-randomised studies)	⊕◯◯◯ Very low[a,b,c]	It is uncertain whether immediate compared to delayed autologous breast reconstruction increases or decreases the incidence of seroma.
Mastectomy flap necrosis	35 per 1.000	**114 per 1.000** (52 to 234)	**OR 3.51** (1.48 to 8.30)	416 (4 non-randomised studies)	⊕◯◯◯ Very low[a,d]	It is uncertain whether immediate compared to delayed autologous breast reconstruction increases or decreases the incidence of mastectomy flap necrosis.
Total flap loss	24 per 1.000	**24 per 1.000** (15 to 38)	**OR 0.99** (0.61 to 1.61)	10460 (7 non-randomised studies)	⊕◯◯◯ Very low[a,b]	It is uncertain whether immediate compared to delayed autologous breast reconstruction increases or decreases the incidence of total flap loss.
Partial flap loss	20 per 1.000	**14 per 1.000** (9 to 21)	**OR 0.69** (0.45 to 1.06)	6201 (8 non-randomised studies)	⊕◯◯◯ Very low[a,b]	It is uncertain whether immediate compared to delayed autologous breast reconstruction increases or decreases the incidence of partial flap loss.
Reoperation	113 per 1.000	**108 per 1.000** (84 to 138)	**OR 0.95** (0.72 to 1.25)	23546 (12 non-randomised studies)	⊕◯◯◯ Very low[a,b,c]	It is uncertain whether immediate compared to delayed autologous breast reconstruction increases or decreases the incidence of reoperation.
Local recurrence	18 per 1.000	**16 per 1.000** (6 to 45)	**OR 0.93** (0.33 to 2.60)	924 (2 non-randomised studies)	⊕◯◯◯ Very low[a,b]	It is uncertain whether immediate compared to delayed autologous breast reconstruction increases or decreases the incidence of local recurrence.
Regional recurrence	24 per 1.000	**37 per 1.000** (17 to 78)	**OR 1.54** (0.69 to 3.41)	862 (1 non-randomised study)	⊕◯◯◯ Very low[a,b]	It is uncertain whether immediate compared to delayed autologous breast reconstruction increases or decreases the incidence of regional recurrence.

Summary of findings:						
Distant metastatis	31 per 1.000	**100 per 1.000** (11 to 531)	**OR 3.44** (0.34 to 35.09)	62 (1 non-randomised study)	⊕◯◯◯ Very low[a,b]	It is uncertain whether immediate compared to delayed autologous breast reconstruction increases or decreases the incidence of distant metastasis.
Satisfaction with breast (BREAST-Q) assessed with: BREAST-Q	The mean satisfaction with breast was **51**	MD **8.14 higher** (11.76 lower to 28.04 higher)	-	1242 (2 non-randomised studies)	⊕◯◯◯ Very low[a,b,c]	It is uncertain whether immediate compared to delayed autologous breast reconstruction increases or decreases the satisfaction with breast, measured with the BREAST-Q questionnaire.
Sexual well-being assessed with: BREAST-Q	The mean sexual well-being was **64**	MD **7.5 higher** (7.79 lower to 22.8 higher)	-	1188 (2 non-randomised studies)	⊕◯◯◯ Very low[a,b,c]	It is uncertain whether immediate compared to delayed autologous breast reconstruction increases or decreases the sexual well-being, measured with the BREAST-Q questionnaire.
Physical well-being assessed with: BREAST-Q	The mean physical well-being was **71**	MD **6.38 higher** (6.33 lower to 19.09 higher)	-	1230 (2 non-randomised studies)	⊕◯◯◯ Very low[a,b,c]	It is uncertain whether immediate compared to delayed autologous breast reconstruction increases or decreases the physical well-being, measured with the BREAST-Q questionnaire.

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: confidence interval; **MD:** mean difference; **OR:** odds ratio

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

Explanations

a. Downgraded by two levels due to very serious risk of bias: Included studies were observational only, and the majority did not adjust at all for relevant baseline characteristics. Results are thus prone to confounding.
b. Downgraded one level due to serious inconsistency (high heterogeneity).
c. Downgraded by one level due to serious imprecision; the 95% confidence interval includes both in favor of immediate and in favor of delayed.
d. Downgraded one level due to indirectness of the outcome: imprecise definition of the outcome parameter (type and approach of mastectomy were not considered).

6.5.4.2 Immediate vs. Delayed-Immediate Comparison

Summary of findings:

Immediate compared to delayed-immediate for autologous breast reconstruction

Patient or population: breast cancer, autologous breast reconstruction

Intervention: immediate autologous breast reconstruction

Comparison: delayed-immediate autologous breast reconstruction

Outcomes	**Anticipated absolute effects*** (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with delayed-immediate	**Risk with immediate**				
Fat necrosis	78 per 1.000	**94 per 1.000** (41 to 200)	**OR 1.22** (0.50 to 2.95)	3678 (5 non-randomised studies)	⊕◯◯◯ Very low[a,b,c]	It is uncertain whether immediate compared to delayed-immediate autologous breast reconstruction increases or decreases the incidence of fat necrosis.
Mastectomy flap necrosis	0 per 1.000	**0 per 1.000** (0 to 0)	**OR 13.62** (2.49 to 74.60)	381 (3 non-randomised studies)	⊕◯◯◯ Very low[a,d]	It is uncertain whether immediate compared to immediate-delayed autologous breast reconstruction increases or decreases the incidence of mastectomy flap necrosis.

Summary of findings:						
Hematoma	45 per 1.000	**49 per 1.000** (34 to 69)	**OR 1.09** (0.76 to 1.58)	3678 (5 non-randomised studies)	⊕◯◯◯ Very low[a,c]	It is uncertain whether immediate compared to delayed-immediate autologous breast reconstruction increases or decreases the incidence of hematoma.
Infections	70 per 1.000	**49 per 1.000** (24 to 100)	**OR 0.69** (0.33 to 1.48)	12561 (6 non-randomised studies)	⊕◯◯◯ Very low[a,b,c]	It is uncertain whether immediate compared to delayed-immediate autologous breast reconstruction increases or decreases the incidence of infections.
Reoperation	185 per 1.000	**136 per 1.000** (31 to 431)	**OR 0.69** (0.14 to 3.33)	11805 (2 non-randomised studies)	⊕◯◯◯ Very low[a,b,c]	It is uncertain whether immediate compared to delayed-immediate autologous breast reconstruction increases or decreases the incidence of reoperations.
Seroma	73 per 1.000	**81 per 1.000** (21 to 272)	**OR 1.13** (0.27 to 4.78)	3283 (4 non-randomised studies)	⊕◯◯◯ Very low[a,c]	It is uncertain whether immediate compared to delayed-immediate autologous breast reconstruction increases or decreases the incidence of seroma.
Wound complication	77 per 1.000	**98 per 1.000** (48 to 191)	**OR 1.31** (0.61 to 2.84)	12483 (5 non-randomised studies)	⊕◯◯◯ Very low[a,b,c]	It is uncertain whether immediate compared to delayed-immediate autologous breast reconstruction increases or decreases the incidence of wound complications.
Total flap loss	155 per 1.000	**67 per 1.000** (20 to 203)	**OR 0.39** (0.11 to 1.39)	3283 (4 non-randomised study)	⊕◯◯◯ Very low[a,c]	It is uncertain whether immediate compared to delayed-immediate autologous breast reconstruction increases or decreases the incidence of total flap loss.
Partial flap loss	0 per 1.000	**0 per 1.000** (0 to 0)	**OR 2.12** (0.08 to 52.86)	151 (1 non-randomised study)	⊕◯◯◯ Very low[a,c]	It is uncertain whether immediate compared to delayed-immediate autologous breast reconstruction increases or decreases the incidence of partial flap loss.

Summary of findings:

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: confidence interval; **OR:** odds ratio

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

Explanations

a. Downgraded by two levels due to very serious risk of bias: Included studies were observational only, and the majority did not adjust at all for relevant baseline characteristics. Results are thus prone to confounding
b. Downgraded one level due to serious inconsistency above 70% (substantial heterogeneity).
c. Downgraded by one level due to serious imprecision; the 95% confidence interval includes both in favor of immediate and in favor of delayed-immediate.
d. Downgraded one level due to indirectness of the outcome: imprecise definition of the outcome parameter (type and approach of mastectomy were not considered).

6.5.4.3 Delayed vs. Delayed-Immediate comparison

Summary of findings:

Delayed compared to delayed-immediate for autologous breast reconstruction

Patient or population: breast cancer, autologous breast reconstruction

Intervention: delayed breast reconstruction

Comparison: delayed-immediate breast reconstruction

Outcomes	**Anticipated absolute effects*** (95% CI)				Comments

Summary of findings:

	Risk with delayed-immediate	Risk with delayed	Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	
infections	76 per 1.000	**48 per 1.000** (25 to 92)	**OR 0.62** (0.31 to 1.23)	9088 (4 non-randomised studies)	⊕◯◯◯ Very low[a,b,c]	It is uncertain whether delayed compared to delayed-immediate autologous breast reconstruction increases or decreases the incidence of infections.
reoperation	171 per 1.000	**130 per 1.000** (69 to 233)	**OR 0.73** (0.36 to 1.48)	8883 (3 non-randomised studies)	⊕◯◯◯ Very low[a,b,c]	It is uncertain whether delayed compared to delayed-immediate autologous breast reconstruction increases or decreases the incidence of reoperations.
wound complication	78 per 1.000	**70 per 1.000** (48 to 101)	**OR 0.89** (0.60 to 1.33)	9088 (4 non-randomised studies)	⊕◯◯◯ Very low[a,c]	It is uncertain whether delayed compared to delayed-immediate autologous breast reconstruction increases or decreases the incidence of wound complications.
fat necrosis	83 per 1.000	**80 per 1.000** (54 to 117)	**OR 0.96** (0.63 to 1.47)	1205 (2 non-randomised studies)	⊕◯◯◯ Very low[a,c]	It is uncertain whether delayed compared to delayed-immediate autologous breast reconstruction increases or decreases the incidence of fat necrosis.
hematoma	46 per 1.000	**59 per 1.000** (20 to 161)	**OR 1.30** (0.43 to 3.95)	1399 (3 non-randomised studies)	⊕◯◯◯ Very low[a,c]	It is uncertain whether delayed compared to delayed-immediate autologous breast reconstruction increases or decreases the incidence of hematoma.
Total flap loss	190 per 1.000	**68 per 1.000** (45 to 101)	**OR 0.31** (0.20 to 0.48)	1000 (1 non-randomised study)	⊕⊕◯◯ Low[a]	Delayed autologous breast reconstruction may decrease the incidence of total flap loss compared to delayed-immediate reconstruction.

Summary of findings:						
seroma	213 per 1.000	**171 per 1.000** (98 to 285)	**OR 0.76** (0.40 to 1.47)	1399 (3 non-randomised studies)	⊕◯◯◯ Very low[a,c]	It is uncertain whether delayed compared to delayed-immediate autologous breast reconstruction increases or decreases the incidence of seroma.

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: confidence interval; **OR:** odds ratio

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

Explanations

a. Downgraded by two levels due to very serious risk of bias: Included studies were observational only, and the majority did not adjust at all for relevant baseline characteristics. Results are thus prone to confounding
b. Downgraded one level due to serious inconsistency above 70% (substantial heterogeneity).
c. Downgraded by one level due to serious imprecision; the 95% confidence interval includes both in favor of delayed and in favor of delayed-immediate.

6.6 PICO 16B

6.6.1 PRSIMA Flowdiagramm

Not applicable.

6.6.2 Evidenztabellen

6.6.2.1 Systematisches Review

6.6.2.1.1 Evidenztabelle systematisches Review van der Wielen 2023

van der Wielen, A, Negenborn, V, Burchell, GL, Remmelzwaal, S, Lapid, O, Driessen, C, Less is more? One-stage versus two-stage implant-based breast reconstruction: A systematic review and meta-analysis of comparative studies. J Plast Reconstr Aesthet Surg, 2023. 86 (): p. 109-127., https://pubmed.ncbi.nlm.nih.gov/37716248/.

Reference/ Study type	Review description	Interventions	Study Population	Results of examined outcomes	Methodological comments	Included publications
van der Wielen, 2023 Systematic Review with meta-analysis	**Study design** ◆ Cohort studies **Search dates** ◆ Inception to 27.09.2022 **Databases** ◆ PubMed, Embase, The Cochrane Library, Web of Science **Inclusion criteria** ◆ Mastectomy ◆ Primary or secondary reconstruction **Exclusion criteria:** ◆ Reviews, case reports & series, and articles	**Question/ Aim** "This systematic review examines whether there is a difference in reported outcomes and complications between one- and two-staged implant-based breast reconstruction implant-based breast reconstruction in women undergoing breast	33 studies published up to September 2022, including 20,614 breasts that received implant-based reconstruction ◆ DTI: 5,201 ◆ TE: 15,413 * studies that were used for the re-analysis **Descriptive statistics** (see table 1 and 2 of van der Wielen 2023, copied below) ◆ Age: mean ages between 40 and 55 years old	Analysed as incidences, therefore, relevant outcomes were re-extracted and analysed for this guideline (OR).	**Risk of bias assessment of studies:** mostly fair rating, see table from van der Wielen 2023 below; although confounding may not have been assessed as strictly as we would have done with ROBINS-I or similar tools. **Overall confidence in results of SR (AMSTAR-2):** ◆ PICO elements: yes ◆ A priori design: not explicitly stated, no PROSPERO or protocol link provided. ◆ Justification for design: no ◆ Literature search >= 2 databases, search strategy + other sources: · 4 databases	Included and checked for additional outcomes: ◆ Aliotta 2021 ◆ Azouz 2017 ◆ Bennet 2018 ◆ Brunbjerg 2021 ◆ Caputo 2021 ◆ Carminati 2018 ◆ Casella 2019 ◆ Damen 2011 ◆ Davila 2013 ◆ Dikmans 2016 ◆ Dimovska 2021 ◆ Gao 2021 ◆ Han 2018 ◆ Hangge 2019 ◆ Hillberg 2018

van der Wielen, A, Negenborn, V, Burchell, GL, Remmelzwaal, S, Lapid, O, Driessen, C, Less is more? One-stage versus two-stage implant-based breast reconstruction: A systematic review and meta-analysis of comparative studies. J Plast Reconstr Aesthet Surg, 2023. 86 (): p. 109-127., https://pubmed.ncbi.nlm.nih.gov/37716248/.

with insufficient outcome reporting ◆ N < 20 ◆ Non-English publication	reconstruction after mastectomy." **Interventions:** A: Direct-to-implant (DTI, one-stage) B: Tissue expander (TE, two-stage)	◆ BMI: mean/median BMI values reported to be between 20.7 and 27.7 kg/m²	· String for all provided · Reference lists · No further resources searched ◆ Selection in duplicate: yes ◆ Data extraction in duplicate: · Probably yes ◆ List of excluded studies: no ◆ Sufficient detail on studies: yes, table 1 and 2 ◆ RoB assessed: yes, Study Quality Assessment Tools of the National Heart, Lung, and Blood Institute ◆ Funding of incl. studies: no ◆ MA appropriate: partly; proportions pooled, different from what we need regarding our PICO, therefore re-analysed. ◆ RoB considered in MA: NA (not the analysis we need) ◆ RoB in interpretation: NA (not the analysis we need) ◆ Heterogeneity explained: no ◆ Publication bias investigated: discussed, but not presented ◆ Sources of CoI: The authors have no conflict of interest to disclose. **Sources of funding**	◆ Hwang 2022 ◆ Innocenti 2021 ◆ Innocenti 2022 ◆ Meshulam-Derazon 2018 ◆ Negenborn 2018 ◆ Negenborn 2019 ◆ Pallara 2019 ◆ Riggio 2022 ◆ Rooostaeian 2012 ◆ Sgarzani 2021 ◆ Singh 2012 ◆ Singh 2021 ◆ Susarla 2015 ◆ Theunissen 2021 Excluded for this guideline, cost analysis only: ◆ Blacam 2012 (cost analysis only) ◆ Singh 2013 (duplicate to Singh 2012) ◆ Wendy 2017 (reference not identified) Excluded, delayed only: ◆ Hvilsom 2011

van der Wielen, A, Negenborn, V, Burchell, GL, Remmelzwaal, S, Lapid, O, Driessen, C, Less is more? One-stage versus two-stage implant-based breast reconstruction: A systematic review and meta-analysis of comparative studies. J Plast Reconstr Aesthet Surg, 2023. 86 (): p. 109-127., https://pubmed.ncbi.nlm.nih.gov/37716248/.

This systematic review and meta-analysis were not sponsored by external parties.

Characteristics of the systematic review chosen for this PICO 16B.

6.6.2.1.2 Characteristics of studies included in van der Wielen 2023

Study	Study design	Level of evidence	Number of patients	Number of breast	One-stage- (n. patients)	One-stage+ (n. patients)	Two-stage- (n. patients)	Two-stage+ (n. patients)	Follow-up (months)
Aliotta et al. 2021	Retrospective cohort	III	150	NA	0	50	50	50	17.2 + 14.8
Azouz et al. 2017	Retrospective cohort	III	119	196	69	0	50	0	14.7
Bennet et al. 2018	Prospective cohort	III	1637	2655	112	0	1525	0	24
Blacam et al. 2012	Prospective cohort	III	NA	NA	NA	NA	NA	NA	NA
Brunbjerg et al. 2021	Prospective cohort	III	44	61	0	21	23	0	24
Caputo et al. 2021	Retrospective cohort	III	192	NA	0	96	96	0	NA
Carminati et al. 2018	Retrospective cohort	III	393	450	NA	NA	NA	NA	12
Casella et al. 2019	Retrospective cohort	III	407	709	210	0	197	0	38
Damen et al. 2011	Prospective cohort	III	207	335	151	0	56	0	65
Davila et al. 2013	Prospective cohort	III	10561	13789	1528	0	9033	0	1

Study	Study design	Level of evidence	Number of patients	Number of breast	One-stage- (n. patients)	One-stage+ (n. patients)	Two-stage- (n. patients)	Two-stage+ (n. patients)	Follow-up (months)
Dikmans et al. 2016	RCT	I	121	183	0	59	62	0	24
Dimovska et al. 2021	Prospective cohort	III	223	223	187	0	36	0	NA
Gao et al. 2021	Retrospective cohort	III	124	125	0	79	45	0	NA
Han et al. 2018	Retrospective cohort	III	290	298	NA	0	NA	0	13.5
Hangge et al. 2019	Retrospective cohort	III	339	577	193	0	146	0	22.9
Hillberg et al. 2018	Prospective cohort	III	52	75	0	31	21	0	12
Hwang et al. 2022	Retrospective cohort	III	62	75	0	27	0	35	17.0 + 7.8
Innocenti et al. 2021	Retrospective cohort	III	81	92	0	29	52	0	NA
Innocenti et al. 2022	Retrospective cohort	III	72	78	0	32	40	0	NA
Meshulam-Derazon et al. 2018	Retrospective cohort	III	59	90	0	39	20	0	24.6 + 12,7
Negenborn et al. 2018	RCT	I	121	183	0	59	62	0	24
Negenborn et al. 2019	RCT	III	121	183	0	59	62	0	24
Pallara et al. 2019	Retrospective cohort	III	162	NA	104	2	56	0	35
Riggio et al. 2022	Retrospective cohort	III	120	NA	66	0	54	0	NA
Roostaeian et al. 2012	Retrospective cohort	III	85	149	35	0	50	0	14

Study	Study design	Level of evidence	Number of patients	Number of breast	One-stage- (n. patients)	One-stage+ (n. patients)	Two-stage- (n. patients)	Two-stage+ (n. patients)	Follow-up (months)
Sgarzani et al. 2021	Retrospective cohort	IV	54	NA	0	28	26	0	NA
Singh et al. 2012	Retrospective cohort	III	1316	NA	95	0	1221	0	NA
Singh et al. 2013	Retrospective cohort	III	1316	NA	95	0	1221	0	18
Singh er al. 2021	Retrospective cohort	III	1740	NA	870	0	870	0	NA
Susarla et al. 2015	Retrospective cohort	III	346	582	NA	0	NA	0	NA
Theunissen et al. 2021	Retrospective cohort	III	383	NA	56	0	327	0	NA
Wendy et al. 2017	Retrospective cohort	III	106	162	34	0	72	0	22.5 + 16.2

Characteristics of the studies included in van der Wielen. Information taken over and representation adapted from Table 1 of van der Wielen 2023.

Study	Mean age		Mean BMI		Smoke		RxT		CxT		Mean FIV (mL)	
	DTI	TE	DTI	TE	DTI	TE	DTI	TE	DTI	TE	DTI	TE
Aliotta et al. 2021	56.6 + 12.4*	50.9 + 10.9/ 48.4 I 10.9*	25.3 + 5.9*	27.7 + 6.3/ 25.3 + 5.5*	4*	4/8*	NA	NA	NA	NA	NA	NA
Azouz et al. 2017	NA	NA	27.6 I 6.2	26.2 # 4.8	15	17	8	5	38	29	NA	NA
Bennet et al. 2018	48.2 I 12.1	48.4 + 10.3	25.1 + 6.2	25.7 + 5.3	NA	40	23	398	13	518	NA	NA
Blacam et al. 2012	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA

Study	Mean age		Mean BMI		Smoke		RxT		CxT		Mean FIV (mL)	
Brunbjerg et al. 2021	48.3 = 10.7*	42.7 I 9.9	23.1 I 2.8*	24.7 + 3.8	2*	0	NA	NA	NA	NA	324 + 66	440 +- 138
Caputo et al. 2021	53.4 I 8.9*	53.6 I 9.5	NA	NA	NA	NA	0	0	2*	2	NA	NA
Carminati et al. 2018	40.2 = 14.2/	50.4 + 8.5	21.6 + 0.6/	24.4 + 4.0	2/4"	18	2/25	24	2/23*	39	NA	NA
	48.0 I 7.6*		22.4 + 3.5*									NA
Casella et al. 2019	56.1 + NA	55.5 + NA	24.1 + NA	24.9 + NA	36	24	78	53	NA	NA	NA	NA
Damen et al. 2011	42.4 + NA	39.2 + NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Davila et al. 2013	50.8 + 10.6	50.9 + 10.5	26.5 + 6.7	26.9 + 6.3	201	1276	7	28	53	380	NA	NA
Dikmans et al. 2016	43.5 + 11.7*	47.3 + 12.1	23.4 + 2.9"	22.9 + 2.5	12*	8	5*	6	22*	21	393.4 + 93.7*	408.0 +- 123.8
Dimovska et al. 2021	44.4 I 8.1	43.8 + 7.7	22.0 I 2.9	20.7 + 3.1	NA	NA	37	9	132	28	226.7 + 67.8*	256.1 +- 71.5
Gao et al. 2021	41.1 + 7.0*	38.6 + 7.3	21.7 + 2.2*	22.0 + 2.2	0*	0	0*	2	55*	41	231.58 + 53.27*	266.64 +- 38.64
Han et al. 2019	42 + NA	44 + NA	NA	NA	8	2	40	23	112	40	NA	NA
Hangge et al. 2019	50.9 + 11.0	51.5 + 11.3	25.0 + 5.0	25.4 + 5.1	3	10	NA	NA	46	34	NA	NA

Study	Mean age		Mean BMI		Smoke		RxT		CxT		Mean FIV (mL)	
Hillberg et al. 2018	40.8 + 12.2*	49.5 + 10.9	22.1 + 2.2*	21.8 + 2.5	4*	3	6*	4	NA	NA	353.8 + 88.3*	379-7 +- 85-8
Hwang et al. 2022	52.7 + 7.1*	49.0 + 8.7*	23.9 + 2.5*	22.4 + 3.0*	1*	2*	1*	0*	NA	NA	NA	NA
Innocenti et al. 2021	48.5 + 10.0*	50.1 + 9.3	NA	NA	NA	NA	4*	9	19*	33	NA	NA
Innocenti et al. 2022	48.9 # NA*	50.3 + NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Meshulam-Derazon et al. 2018	42.8 # 10.3*	53.1 + 10.24	NA	NA	3*	2	4*	5	NA	NA	375 + 105*	370 +- 100
Negenborn et al. 2018	43.5 # 11.6*	47.4 + 12.2	23.4 + 2.9*	22.9 + 2.5	12"	8	5*	6	22*	21	393.4 I 93.7*	408.0+ -123.8
Negenborn et al. 2019	43.5 # 11.6*	47.4 + 12.2	23.4 + 2.9*	22.9 + 2.5	12"	8	5*	6	22*	21	393.4 I 93.7*	408.0+ -123.8
Pallara et al. 2019	48 # NA	50 + NA	22.7 + NA	23.0 + NA	14	21	1	8	46	30	NA	NA
Riggio et al. 2022	45.6 # 8.4	46.28 # 6.5	21.5 + 2.7	21.9 + 2.7	NA	NA	5	9	39	32	351.2 + 94.3	462-8 +- 116.6
Roostaeian et al. 2012	45 + NA	47 + NA	22 + NA	22.6 + NA	1	3	6	8	6	16	397 + 93	386 +- 128
Sgarzani et al. 2021	46 I NA*	48 + NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Singh et al. 2012	49.3 + NA	49.1 + NA	NA	NA	NA	NA	18	NA	NA	NA	NA	NA
Singh et al. 2013	49.3 + NA	49.1 + NA	NA	NA	NA	NA	18	NA	NA	NA	NA	NA

Study	Mean age		Mean BMI		Smoke		RxT		CxT		Mean FIV (mL)	
Susarla et al. 2015	47.2 + 10.3	47.6 + 10.2	24.6 + 5.0	25.4 + 4.9	16	33	38	112	NA	NA	NA	NA
Theunissen et al. 2021	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Wendy et al. 2017	46.6 + 8.5	47.8 + 9.1	NA	NA	4	12	11	24	11	4	376.4 + 116.2	483.3 +- 133.9

Characteristics of the included study populations from van der Wielen 2023. Information taken over and representation adapted from Table 2 of van der Wielen.

6.6.2.1.3 Risk of Bias assessment of Studies included in Van der Wielen 2023

Study	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15 (Overall quality)
Aliotta et al. 2021	Yes	Yes	CD	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Good
Azouz et al. 2017	Yes	Yes	CD	Yes	Yes	No	Yes	NA	Yes	Yes	Yes	No	CD	Yes	Fair
Bennet et al. 2018	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Good
Blacam et al. 2012	Yes	Yes	NA	Yes	NA	NA	NA	NA	NA	NA	Yes	No	NA	Yes	Fair
Brunbjerg et al. 2021	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	No	CD	Yes	Fair
Caputo et al. 2021	Yes	Yes	Yes	Yes	No	Yes	Yes	NA	Yes	Yes	Yes	No	CD	Yes	Fair
Carminati et al. 2018	Yes	Yes	Yes	Yes	No	Yes	Yes	NA	Yes	Yes	Yes	No	CD	Yes	Fair

Study	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15 (Overall quality)
Casella et al. 2019	Yes	Yes	CD	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	No	CD	Yes	Fair
Damen et al. 2011	Yes	Yes	CD	Yes	No	Yes	Yes	NA	Yes	Yes	Yes	No	NR	No	Fair
Davila et al. 2013	Yes	Yes	No	Yes	Yes	Yes	Yes	NA	Yes	No	Yes	No	CD	Yes	Fair
Dimovska et al. 2021	Yes	Yes	CD	Yes	No	Yes	Yes	NA	Yes	Yes	Yes	No	CD	Yes	Fair
Gao et al. 2021	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Good
Han et al. 2018	Yes	Yes	CD	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	No	CD	Yes	Fair
Hangge et al. 2019	Yes	Yes	Yes	Yes	No	Yes	Yes	NA	Yes	Yes	Yes	No	CD	Yes	Fair
Hillberg et al. 2018	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	No	CD	Yes	Good
Hwang et al. 2022.	Yes	Yes	Yes	Yes	No	Yes	Yes	NA	Yes	Yes	No	No	Yes	Yes	Fair
Innocenti et al. 2021	Yes	Yes	Yes	Yes	No	Yes	Yes	NA	Yes	Yes	Yes	No	CD	Yes	Fair
Innocenti et al. 2022	Yes	Yes	CD	Yes	Yes	Yes	Yes	NA	Yes	No	Yes	No	CD	Yes	Good
Meshulam-Derazon et al. 2018	Yes	Yes	Yes	Yes	Yes	Yes	Yes	NA	Yes	No	Yes	No	No	No	Fair
Pallara et al. 2019	Yes	Yes	Yes	Yes	No	Yes	Yes	NA	Yes	Yes	Yes	No	CD	Yes	Fair
Riggio et al. 2022	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	No	No	Yes	Good

Study	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15 (Overall quality)
Roostaeian et al. 2012	Yes	Yes	Yes	Yes	No	Yes	Yes	NA	Yes	No	Yes	No	CD	Yes	Fair
Sgarzani et al. 2021	Yes	Yes	Yes	Yes	No	Yes	Yes	NA	Yes	No	Yes	No	CD	No	Fair
Singh et al. 2012	Yes	Yes	Yes	Yes	Yes	Yes	Yes	NA	Yes	Yes	Yes	No	Yes	No	Fair
Singh et al. 2013	Yes	Yes	Yes	Yes	Yes	Yes	Yes	NA	Yes	No	Yes	No	Yes	No	Fair
Singh et al. 2021	Yes	Yes	Yes	Yes	Yes	Yes	CD	NA	Yes	Yes	Yes	No	CD	Yes	Fair
Susarla et al. 2015	Yes	Yes	Yes	Yes	Yes	Yes	CD	NA	Yes	Yes	Yes	No	CD	Yes	Fair
Theunissen et al. 2021	Yes	Yes	Yes	Yes	No	Yes	CD	NA	Yes	Yes	Yes	No	CD	Yes	Fair
Wendy et al. 2017	Yes	Yes	Yes	Yes	Yes	Yes	Yes	NA	Yes	CD	Yes	No	Yes	No	Fair

Risk of bias assessment of non-randomised studies of interventions, table taken over from van der Wielen 2023 (using the Study Quality Assessment Tools of the National Heart, Lung, and Blood Institute)

Study	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
Negenborn et al. 2018	Yes	Yes	No	No	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Good

Risk of bias assessment of randomised studies of interventions, table taken over from van der Wielen 2023 (using the Study Quality Assessment Tools of the National Heart, Lung, and Blood Institute)

Study Quality Assessment Tools of the National Heart, Lung, and Blood Institute (Link)

Cohort / cross-sectional studies:

Criteria per question: Yes, No, Other (CD, NR, NA)*

1. Was the research question or objective in this paper clearly stated?

2. Was the study population clearly specified and defined?

3. Was the participation rate of eligible persons at least 50%?

4. Were all the subjects selected or recruited from the same or similar populations (including the same time period)? Were inclusion and exclusion criteria for being in the study prespecified and applied uniformly to all participants?

5. Was a sample size justification, power description, or variance and effect estimates provided?

6. For the analyses in this paper, were the exposure(s) of interest measured prior to the outcome(s) being measured?

7. Was the timeframe sufficient so that one could reasonably expect to see an association between exposure and outcome if it existed?

8. For exposures that can vary in amount or level, did the study examine different levels of the exposure as related to the outcome (e.g., categories of exposure, or exposure measured as continuous variable)?

9. Were the exposure measures (independent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?

10. Was the exposure(s) assessed more than once over time?

11. Were the outcome measures (dependent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?

12. Were the outcome assessors blinded to the exposure status of participants?

13. Was loss to follow-up after baseline 20% or less?

14. Were key potential confounding variables measured and adjusted statistically for their impact on the relationship between exposure(s) and outcome(s)?

Randomised controlled trials:

Criteria: Yes, No, Other (CD, NR, NA)*

1. Was the study described as randomized, a randomized trial, a randomized clinical trial, or an RCT?

2. Was the method of randomization adequate (i.e., use of randomly generated assignment)?

3. Was the treatment allocation concealed (so that assignments could not be predicted)?

4. Were study participants and providers blinded to treatment group assignment?

5. Were the people assessing the outcomes blinded to the participants' group assignments?

6. Were the groups similar at baseline on important characteristics that could affect outcomes (e.g., demographics, risk factors, co-morbid conditions)?

7. Was the overall drop-out rate from the study at endpoint 20% or lower of the number allocated to treatment?

8. Was the differential drop-out rate (between treatment groups) at endpoint 15 percentage points or lower?

9. Was there high adherence to the intervention protocols for each treatment group?

10. Were other interventions avoided or similar in the groups (e.g., similar background treatments)?

11. Were outcomes assessed using valid and reliable measures, implemented consistently across all study participants?

12. Did the authors report that the sample size was sufficiently large to be able to detect a difference in the main outcome between groups with at least 80% power?

13. Were outcomes reported or subgroups analyzed prespecified (i.e., identified before analyses were conducted)?

14. Were all randomized participants analyzed in the group to which they were originally assigned, i.e., did they use an intention-to-treat analysis?

Quality Rating (Good, Fair, or Poor)

Additional Comments (If POOR, please state why):

6.6.3 Meta-analysen

Erklärungen: Mit * markierte Studien haben einen adjustierten Effektschätzer berichtet, der hier verwendet wurde.

Weiteres zu Studien eingeschlossen in van der Wielen 2023:

- Wendy 2017: Was not cited in van der Wielen, reference not found. No outcomes extracted.
- Blacam 2012: Cost analysis only, no extraction for this guideline.
- Singh 2013: Duplicate study population with Singh 2012, no full-text accessible. We therefore only used the publication by Singh 2012.
- Dikman 2017, Negenborn 2018 and Negenborn 2019 are three publications of the same RCT (BRIOS). In der Publikation wurden auch adjustierte Daten berichtet und hier zusätzlich aufgeführt* ("Adjusted for age, body-mass index, smoking, diabetes mellitus, chemotherapy (before and after surgery), radiotherapy (postoperative), hormone therapy, and targeted therapy").

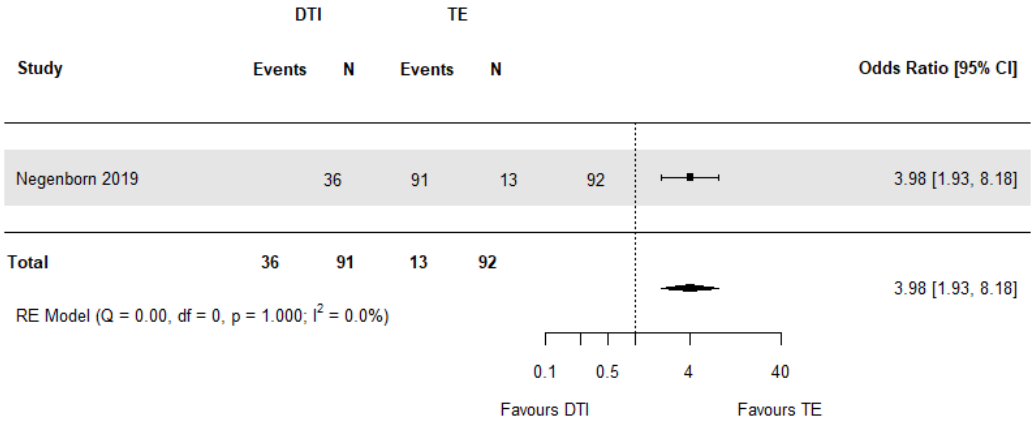
6.6.3.1 Overall complications

Overall complications were analysed in van der Wielen 2023 as incidences. Where we could not reproduce the numbers from the primary studies, we excluded this study from meta-analysis, or corrected numbers as necessary:

- Azouz 2017: we used the unit of analysis breast instead of person whenever possible. Van der Wielen used mixed units (N persons, e breasts).
- Bennett 2018: we used the adjusted OR reported in the study.
- Caminati 2018: numbers not reproducible.
- Damen 2011: slightly inconsistent numbers.
- Davila 2013: numbers in table 2 differ from van der Wielen 2023, Table 2, Total complications.
- Hillberg 2018: we used the unit of analysis breast instead of person whenever possible. Van der Wielen used mixed units (N persons, e breasts).
- Innocenti 2022: we used the unit of analysis breast instead of person whenever possible. Van der Wielen used mixed units (N persons, e breasts).

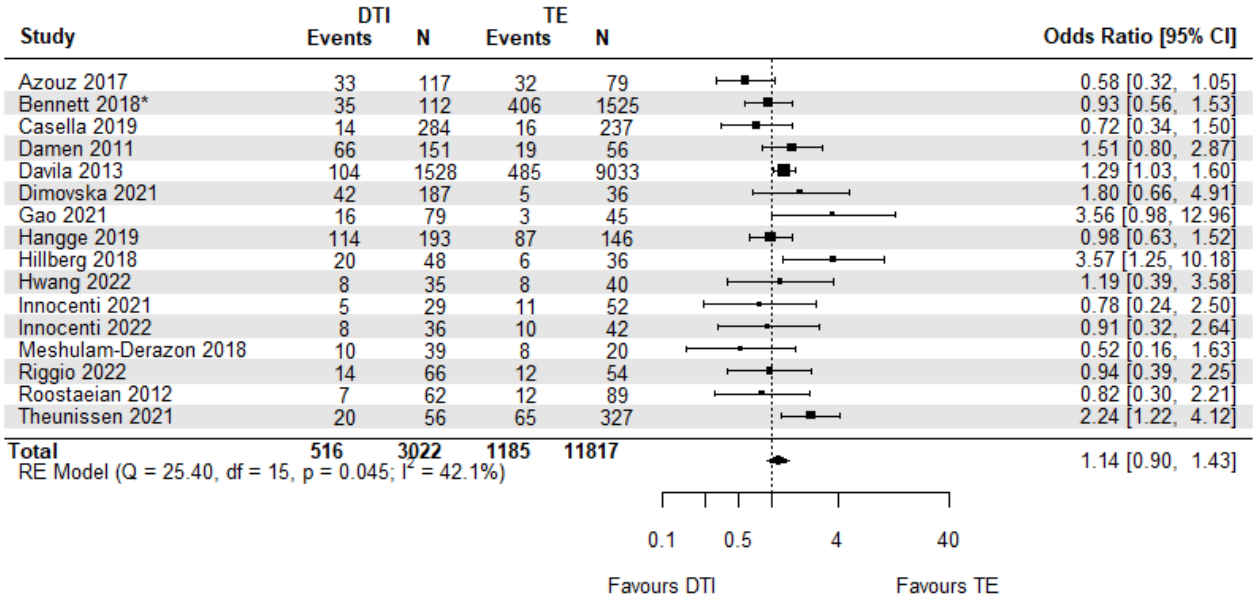
- Roostaeian 2012: we used the unit of analysis breast instead of person whenever possible. Van der Wielen used mixed units (N persons, e breasts).
- Wendy 2017: reference could not be identified (not cited), excluded for all outcomes.

RCT: DTI vs. TE implant-based breast reconstruction, overall complications

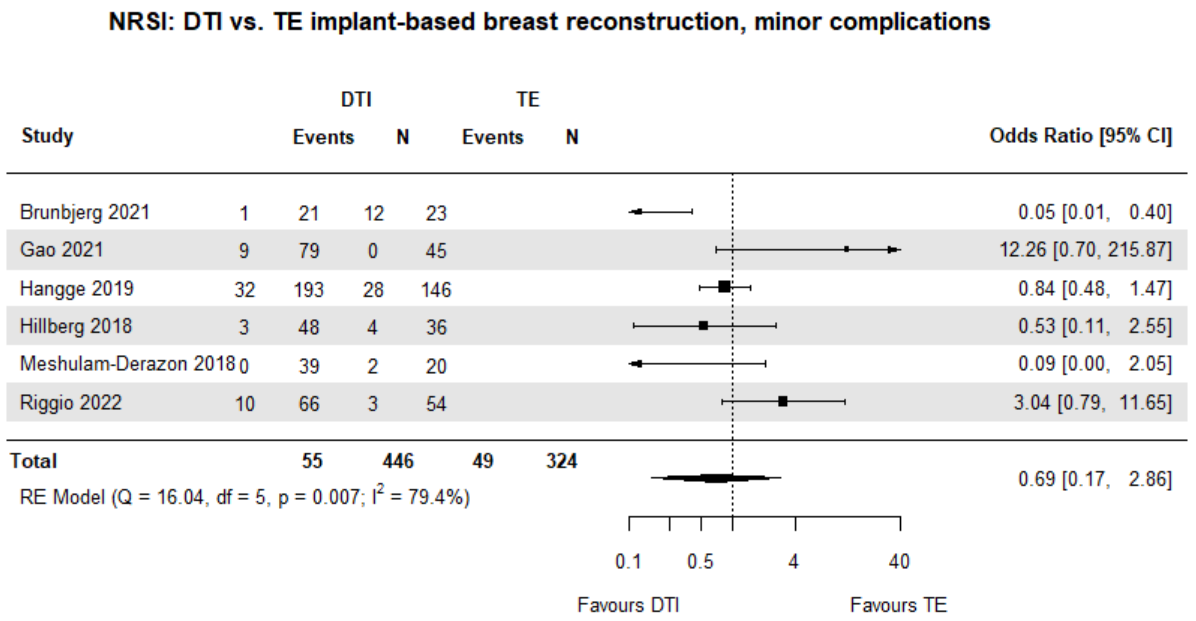


*Adjusted OR: 3.42 (95% CI: 2.28-5.12)

NRSI: DTI vs. TE implant-based breast reconstruction, overall complications

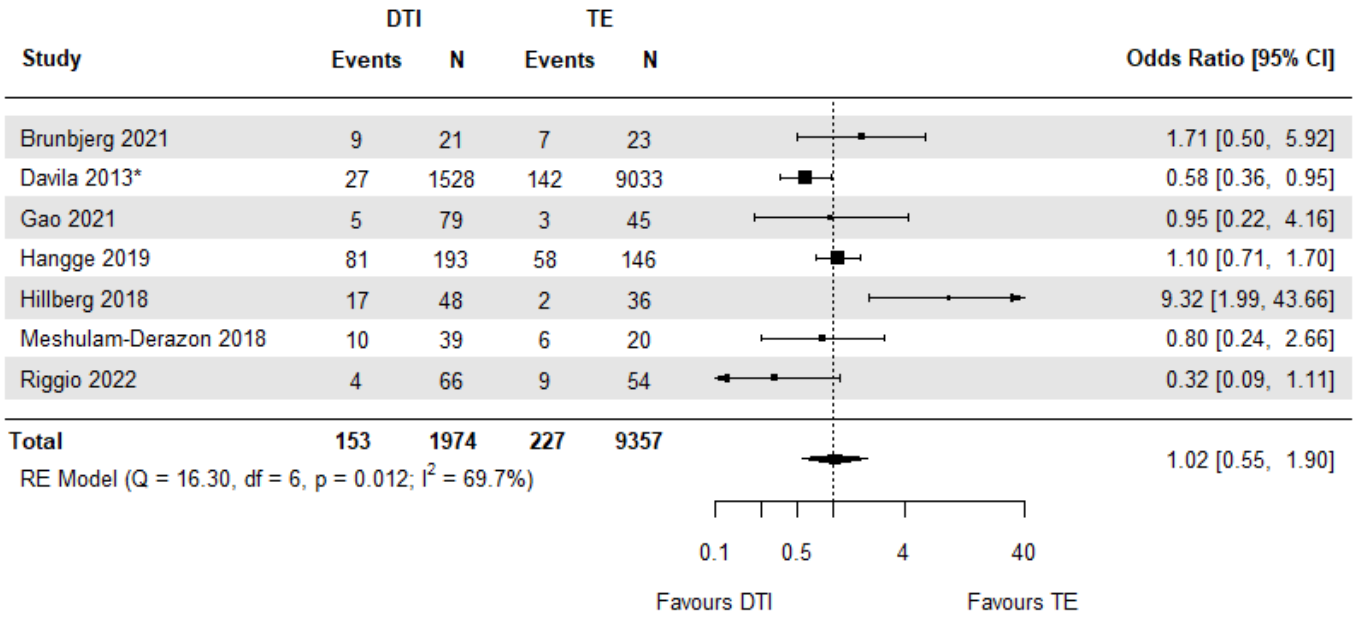


6.6.3.2 Minor complications

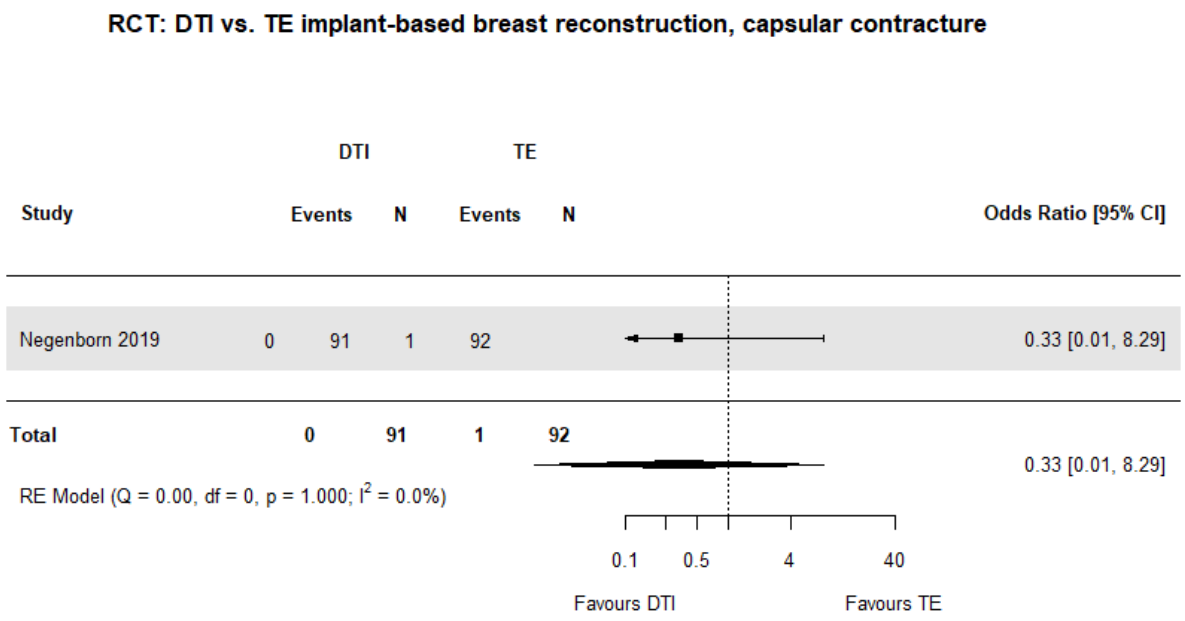


6.6.3.3 Major complications

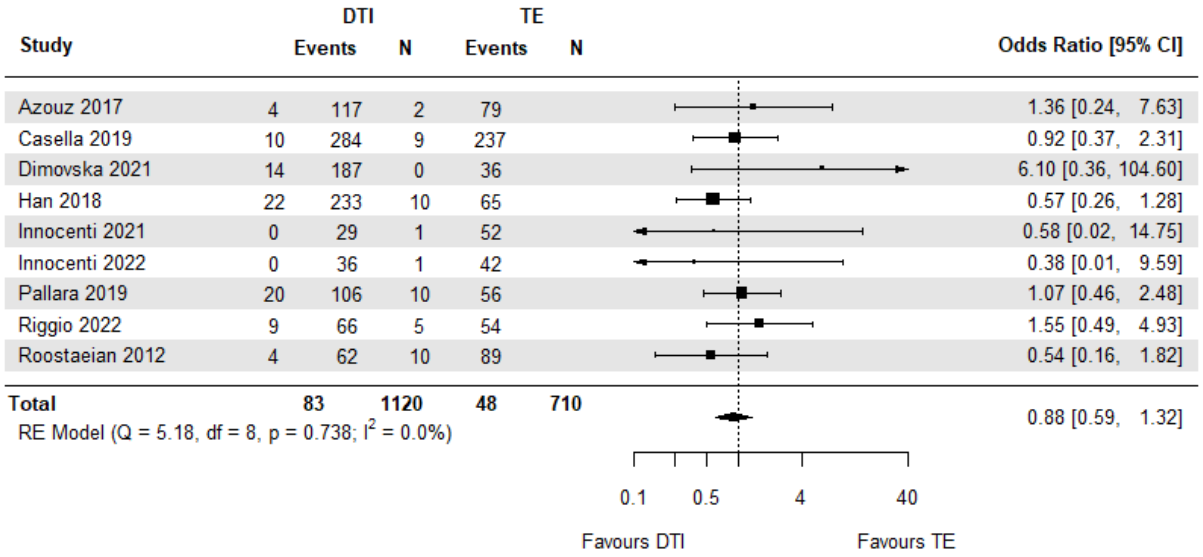
DTI vs. TE implant-based breast reconstruction, major complications



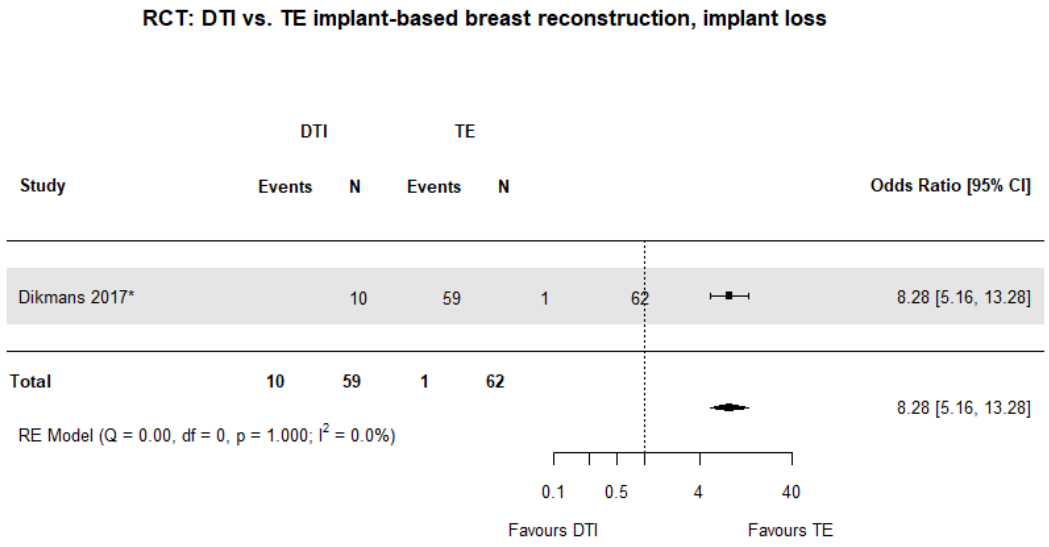
6.6.3.4 Capsular contracture



NRSI: DTI vs. TE implant-based breast reconstruction, capsular contracture

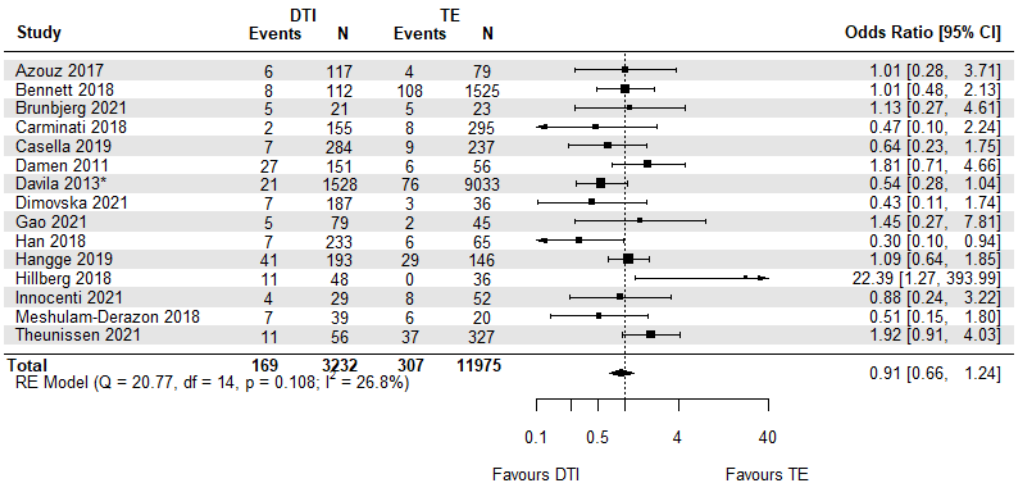


6.6.3.5 Implant loss

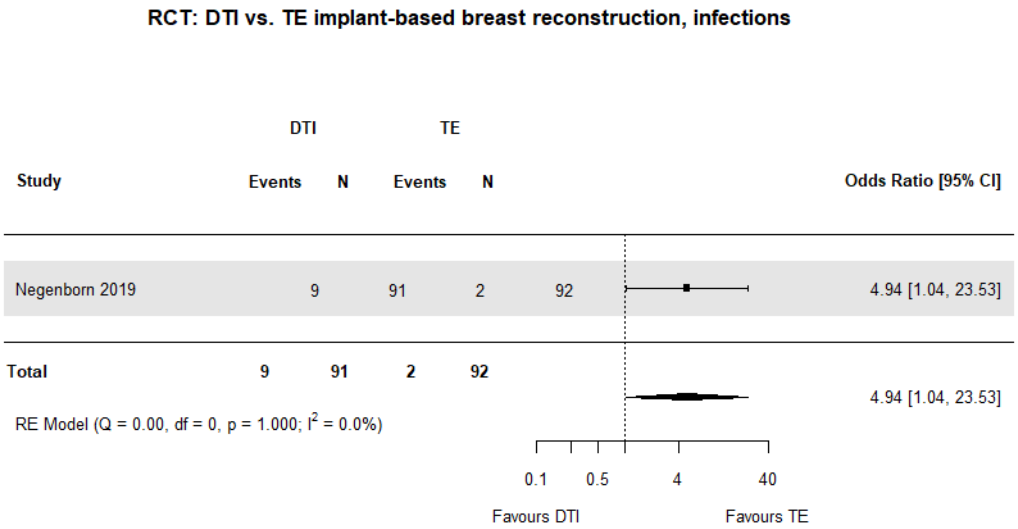


*Adjusted OR: 8.28 (95% CI: 5.22-13.14)

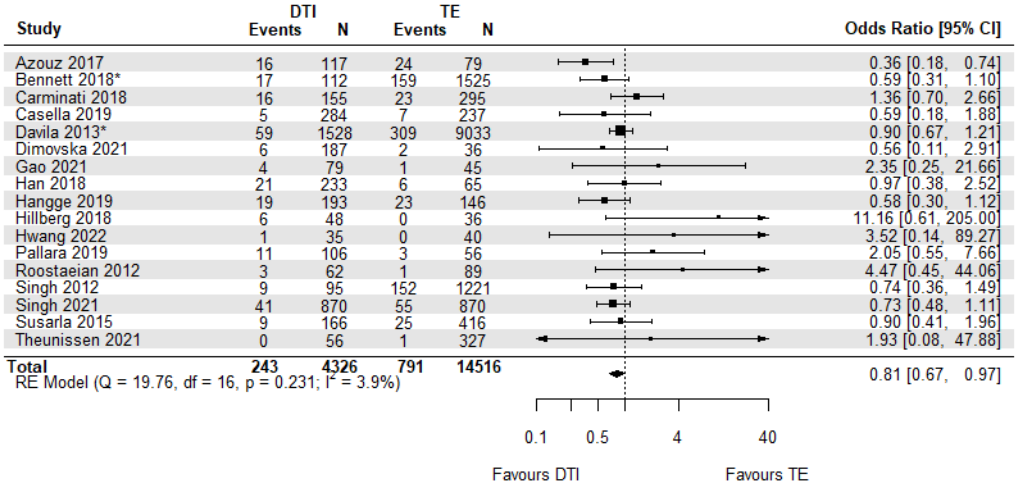
NRSI: DTI vs. TE implant-based breast reconstruction, implant loss



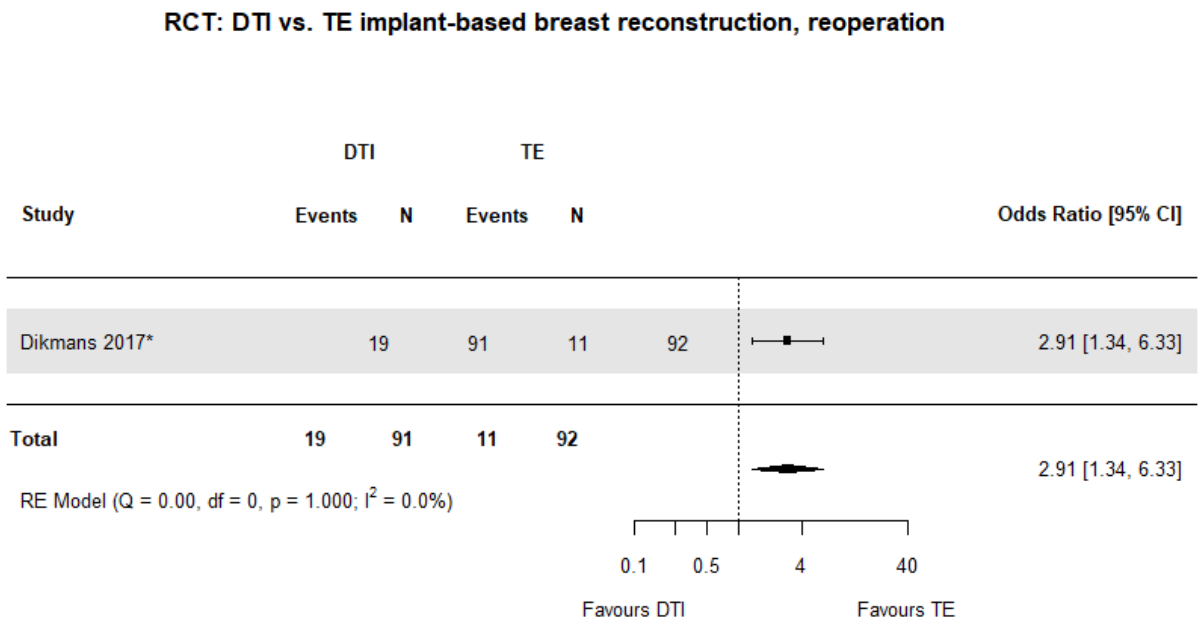
6.6.3.6 Infections



NRSI: DTI vs. TE implant-based breast reconstruction, infections

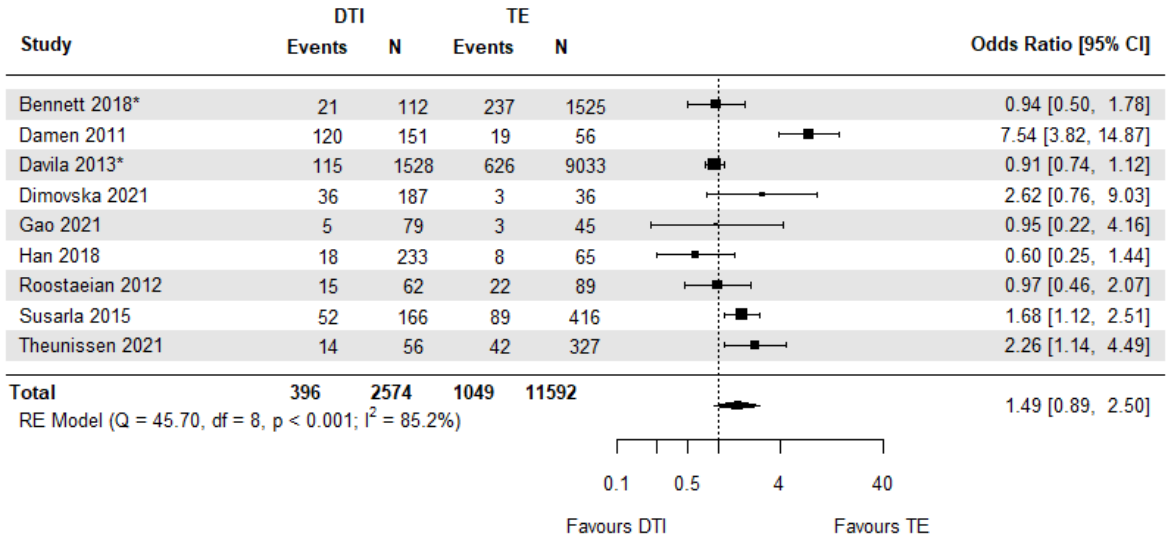


6.6.3.7 Reoperation

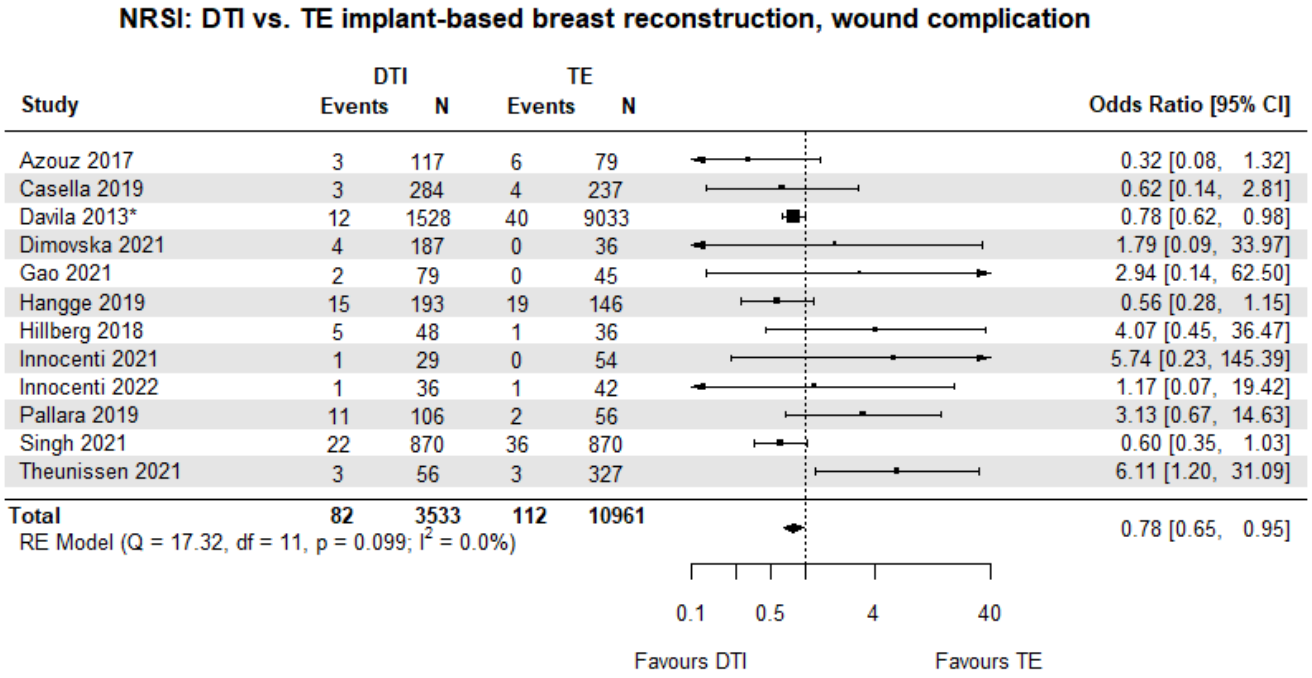


*Adjusted OR: 2.91 (95% CI: 1.34- 6.34)

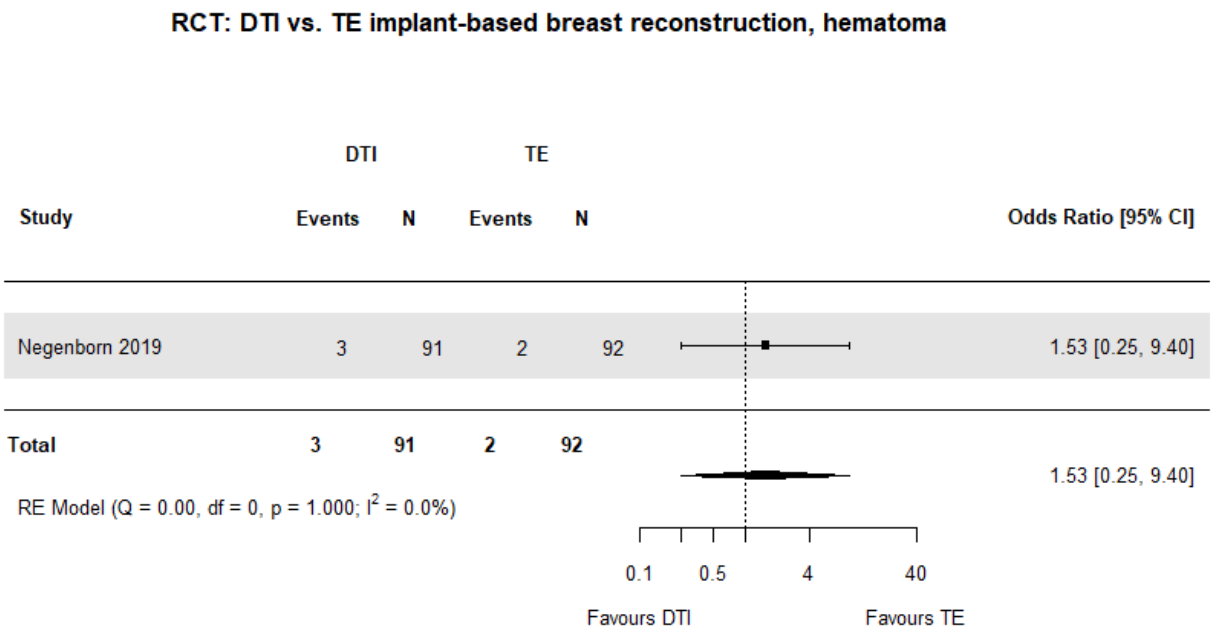
NRSI: DTI vs. TE implant-based breast reconstruction, reoperation



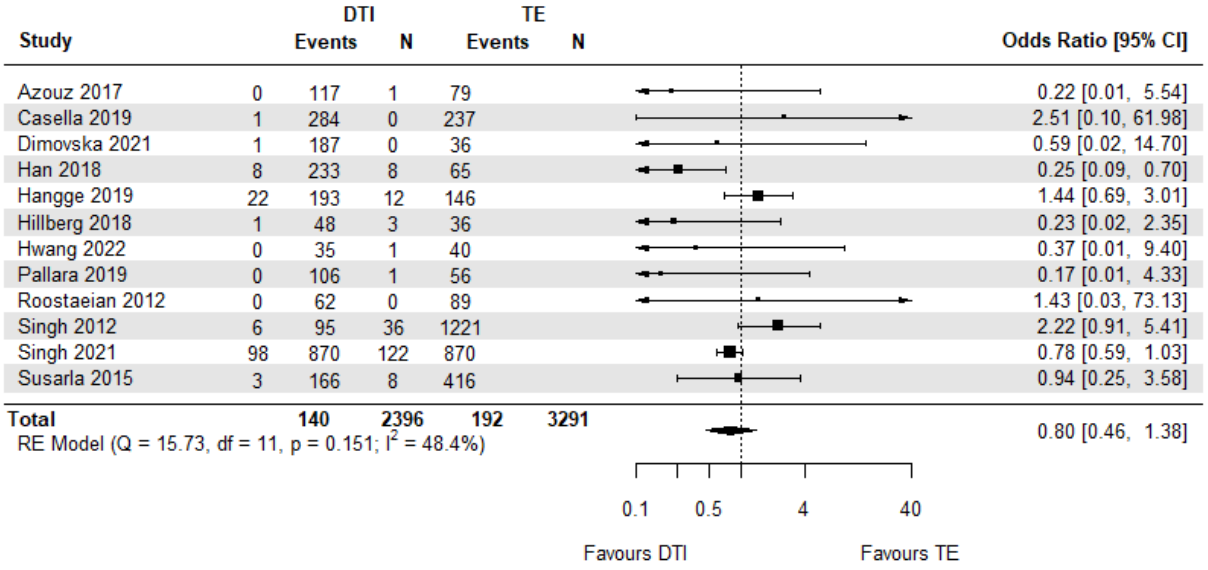
6.6.3.8 Wound complications



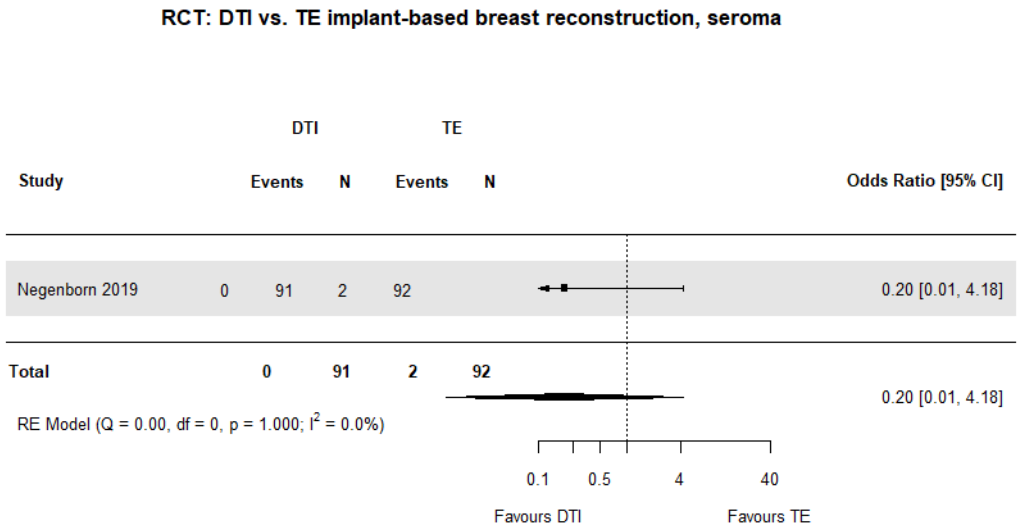
6.6.3.9 Hematoma



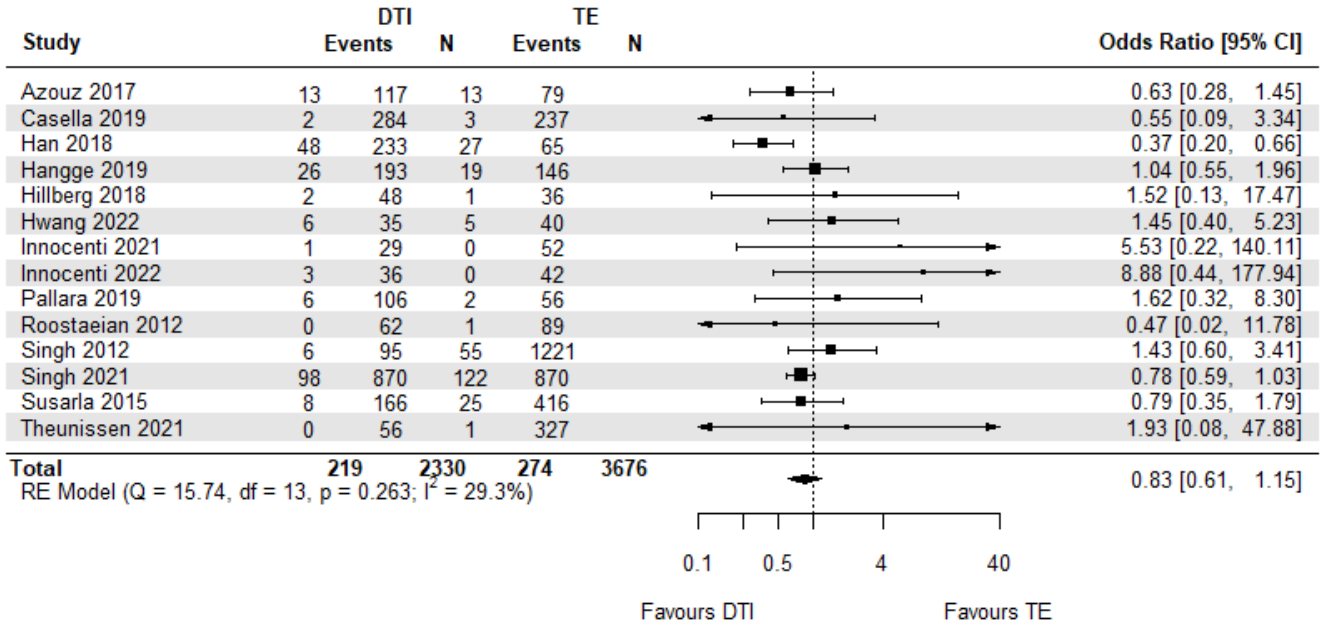
NRSI: DTI vs. TE implant-based breast reconstruction, hematoma



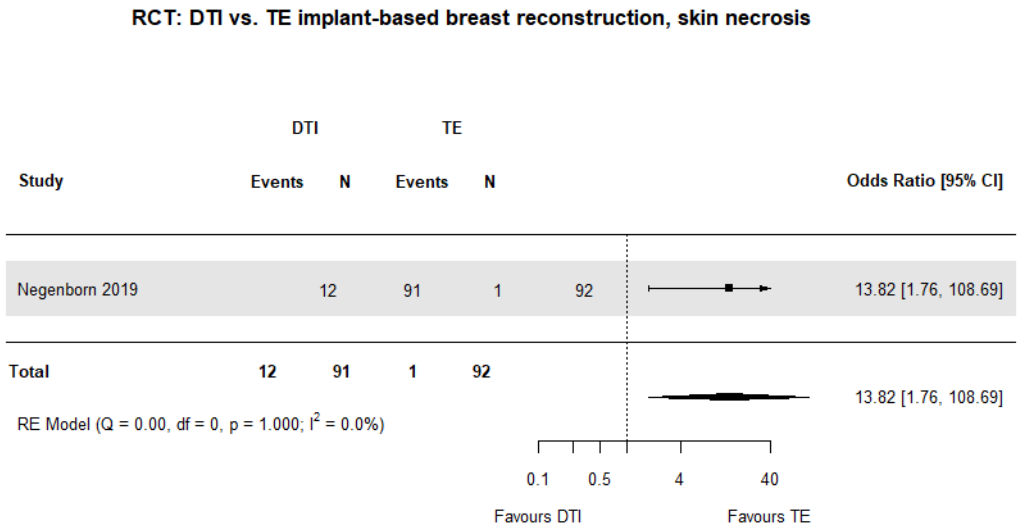
6.6.3.10 Seroma



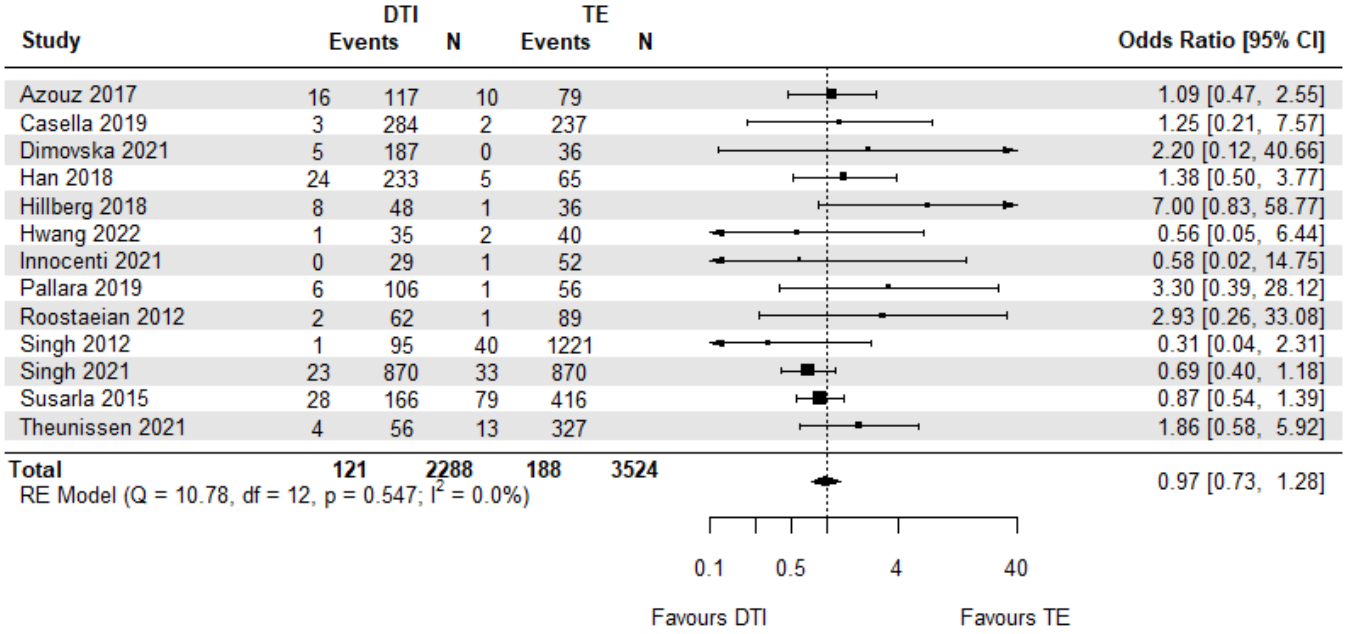
NRSI: DTI vs. TE implant-based breast reconstruction, seroma



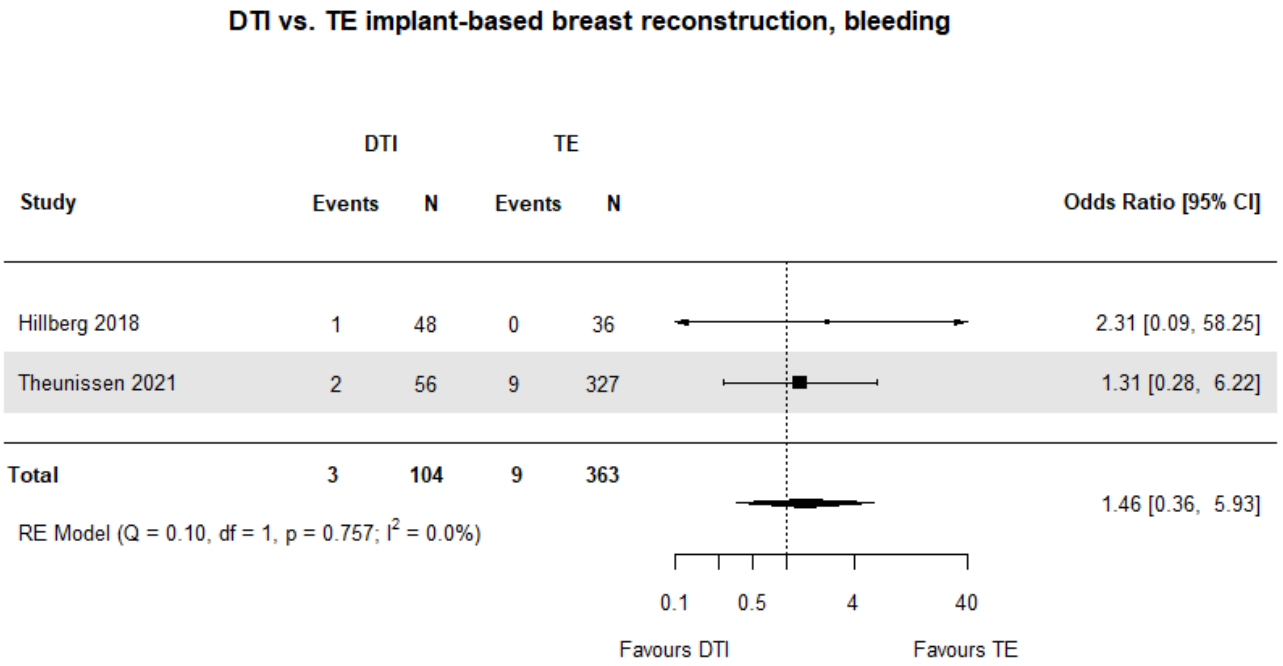
6.6.3.11 Skin Necrosis



NRSI: DTI vs. TE implant-based breast reconstruction, skin necrosis



6.6.3.12 Bleeding



6.6.3.13 Local recurrence

No data reported.

6.6.3.14 Metastatic disease

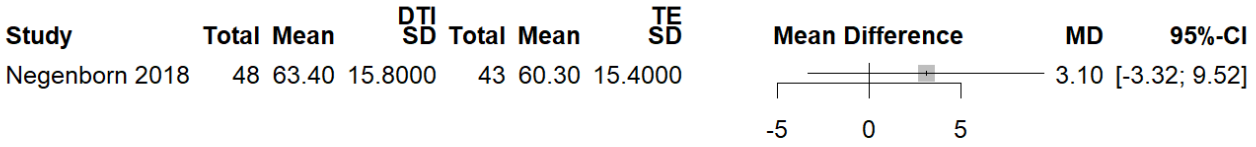
No data reported.

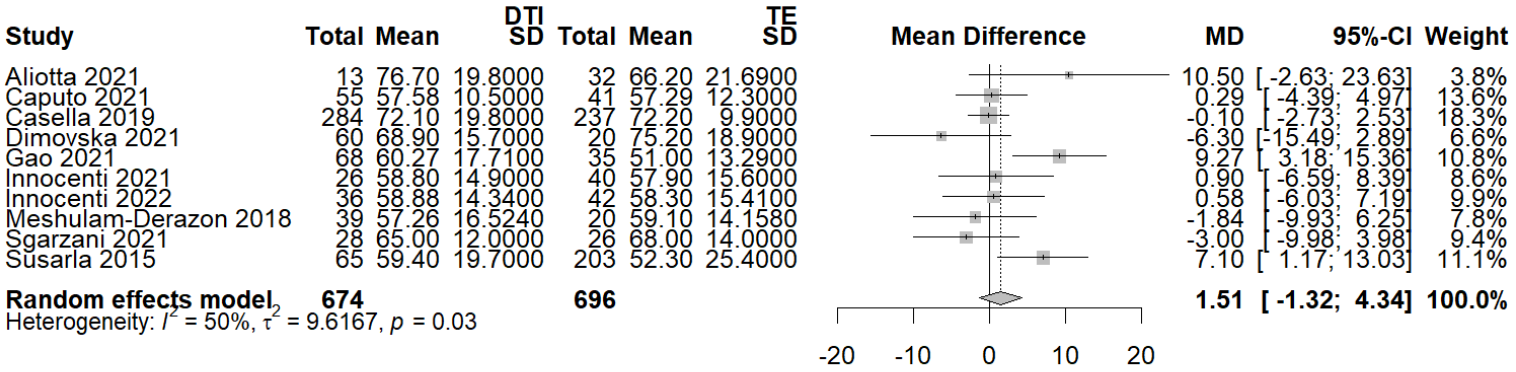
6.6.3.15 BREAST-Q dimensions, only measurements from 2 years onwards after reconstruction (according to median follow-up or time point of QoL measurement)

Notes: In Aliotta 2021, BREAST-Q scores were reported separately for tissue expander groups with and without ADM (read from graph). For the analysis in this report, groups were combined using this resource / formula by Cochrane (Practical 2 on how to include multi-arm studies in meta-analysis) by Emma Axon.

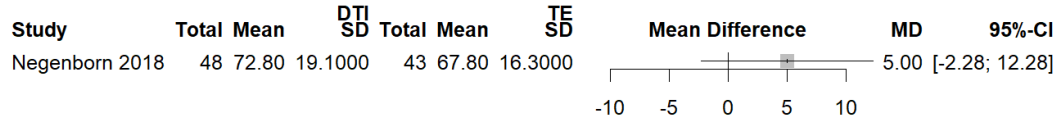
Alle Beobachtungszeiträume für die BREAST-Q Skalen liegen zwischen medianen/durchschnittlichen 6 Monaten und 36 Monaten; häufig mit einem längeren Abstand der Messung zur Operation für die DTI-Gruppe.

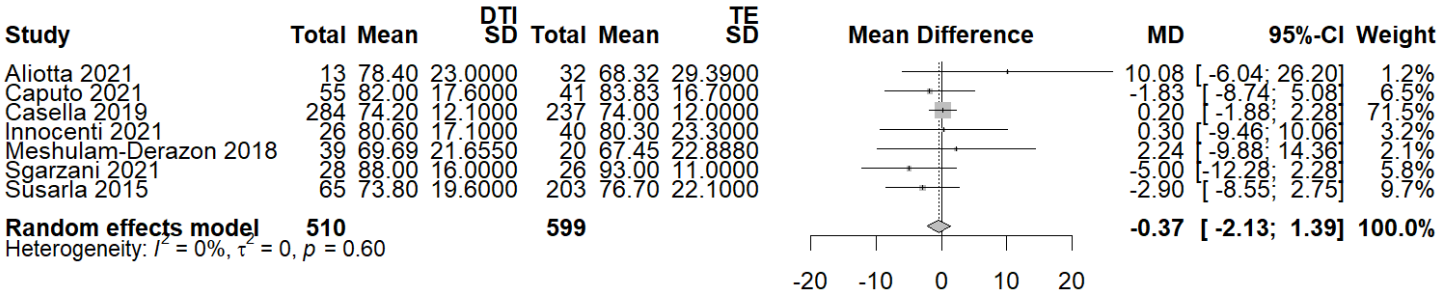
6.6.3.15.1 Satisfaction with breast



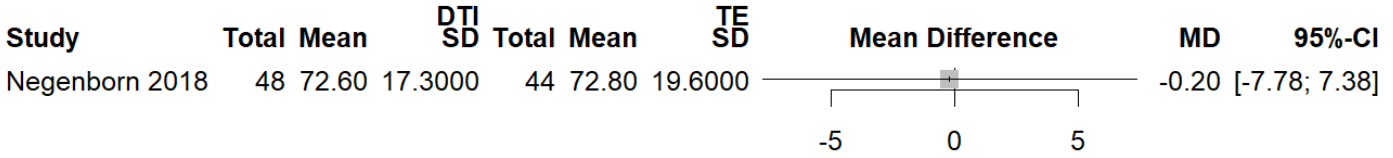

Study
DTI Total Mean SD
TE Total Mean SD
Mean Difference
MD 95%-CI Weight
Aliotta 2021 13 76.70 19.8000 32 66.20 21.6900 10.50 [-2.63; 23.63] 3.8%
Caputo 2021 55 57.58 10.5000 41 57.29 12.3000 0.29 [-4.39; 4.97] 13.6%
Casella 2019 284 72.10 19.8000 237 72.20 9.9000 -0.10 [-2.73; 2.53] 18.3%
Dimovska 2021 60 68.90 15.7000 20 75.20 18.9000 -6.30 [-15.49; 2.89] 6.6%
Gao 2021 68 60.27 17.7100 35 51.00 13.2900 9.27 [3.18; 15.36] 10.8%
Innocenti 2021 26 58.80 14.9000 40 57.90 15.6000 0.90 [-6.59; 8.39] 8.6%
Innocenti 2022 36 58.88 14.3400 42 58.30 15.4100 0.58 [-6.03; 7.19] 9.9%
Meshulam-Derazon 2018 39 57.26 16.5240 20 59.10 14.1580 -1.84 [-9.93; 6.25] 7.8%
Sgarzani 2021 28 65.00 12.0000 26 68.00 14.0000 -3.00 [-9.98; 3.98] 9.4%
Susarla 2015 65 59.40 19.7000 203 52.30 25.4000 7.10 [1.17; 13.03] 11.1%
Random effects model 674 696 1.51 [-1.32; 4.34] 100.0%
Heterogeneity: I^2 = 50%, τ^2 = 9.6167, p = 0.03
-20
-10
0
10
20

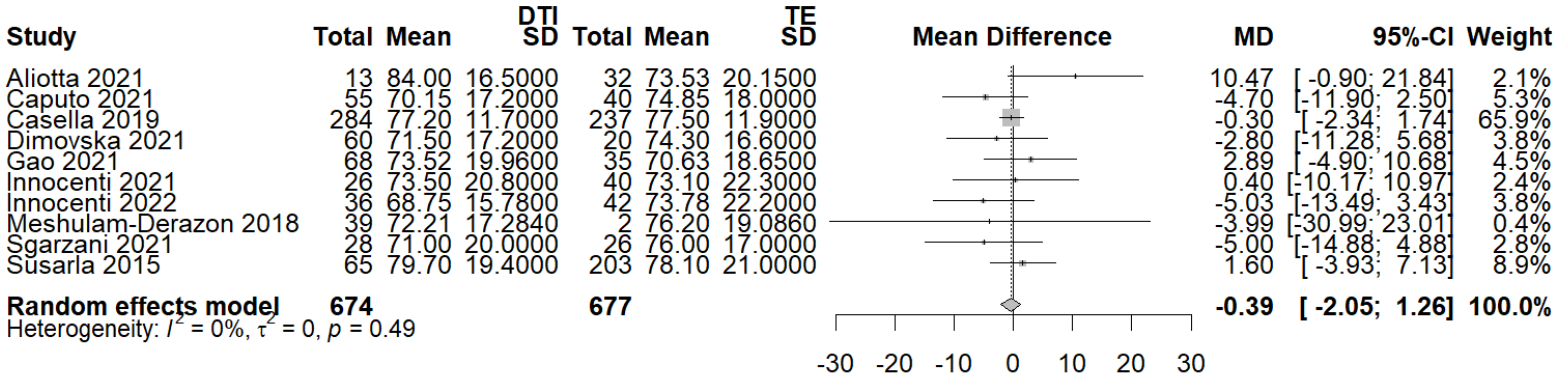
6.6.3.15.2 Satisfaction with overall outcome



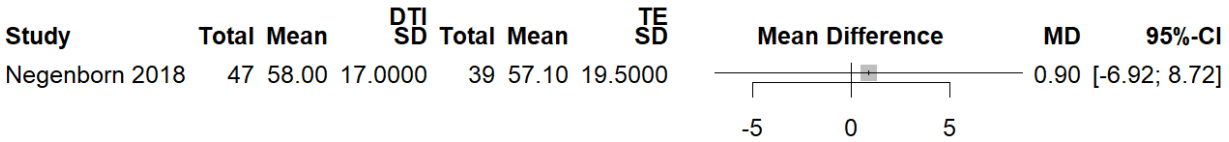

Study
DTI
Total Mean SD
TE
Total Mean SD
Mean Difference
MD
95%-CI
Weight
Aliotta 2021 13 78.40 23.0000 32 68.32 29.3900 10.08 [-6.04; 26.20] 1.2%
Caputo 2021 55 82.00 17.6000 41 83.83 16.7000 -1.83 [-8.74; 5.08] 6.5%
Casella 2019 284 74.20 12.1000 237 74.00 12.0000 0.20 [-1.88; 2.28] 71.5%
Innocenti 2021 26 80.60 17.1000 40 80.30 23.3000 0.30 [-9.46; 10.06] 3.2%
Meshulam-Derazon 2018 39 69.69 21.6550 20 67.45 22.8880 2.24 [-9.88; 14.36] 2.1%
Sgarzani 2021 28 88.00 16.0000 26 93.00 11.0000 -5.00 [-12.28; 2.28] 5.8%
Susarla 2015 65 73.80 19.6000 203 76.70 22.1000 -2.90 [-8.55; 2.75] 9.7%
Random effects model 510 599 -0.37 [-2.13; 1.39] 100.0%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.60
-20
-10
0
10
20

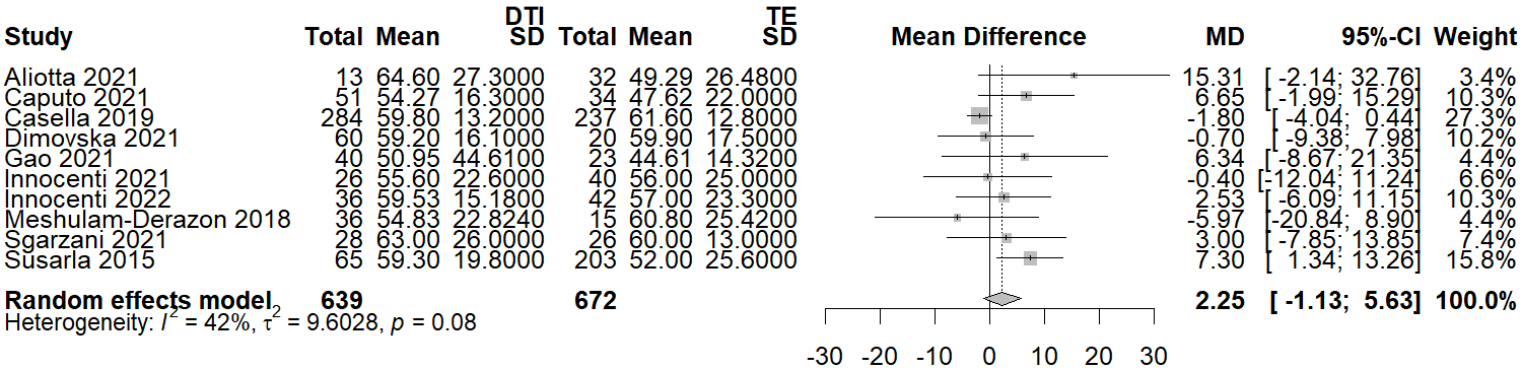
6.6.3.15.3 Psychosocial well-being



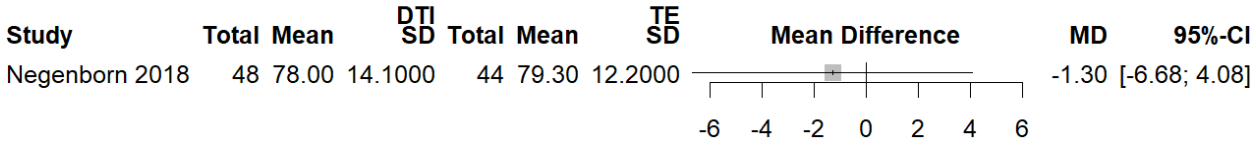

Study
DTI Total Mean SD
TE Total Mean SD
Mean Difference
MD 95%-CI Weight
Aliotta 2021 13 84.00 16.5000 32 73.53 20.1500 10.47 [-0.90; 21.84] 2.1%
Caputo 2021 55 70.15 17.2000 40 74.85 18.0000 -4.70 [-11.90; 2.50] 5.3%
Casella 2019 284 77.20 11.7000 237 77.50 11.9000 -0.30 [-2.34; 1.74] 65.9%
Dimovska 2021 60 71.50 17.2000 20 74.30 16.6000 -2.80 [-11.28; 5.68] 3.8%
Gao 2021 68 73.52 19.9600 35 70.63 18.6500 2.89 [-4.90; 10.68] 4.5%
Innocenti 2021 26 73.50 20.8000 40 73.10 22.3000 0.40 [-10.17; 10.97] 2.4%
Innocenti 2022 36 68.75 15.7800 42 73.78 22.2000 -5.03 [-13.49; 3.43] 3.8%
Meshulam-Derazon 2018 39 72.21 17.2840 2 76.20 19.0860 -3.99 [-30.99; 23.01] 0.4%
Sgarzani 2021 28 71.00 20.0000 26 76.00 17.0000 -5.00 [-14.88; 4.88] 2.8%
Susarla 2015 65 79.70 19.4000 203 78.10 21.0000 1.60 [-3.93; 7.13] 8.9%
Random effects model 674 677 -0.39 [-2.05; 1.26] 100.0%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.49
-30 -20 -10 0 10 20 30

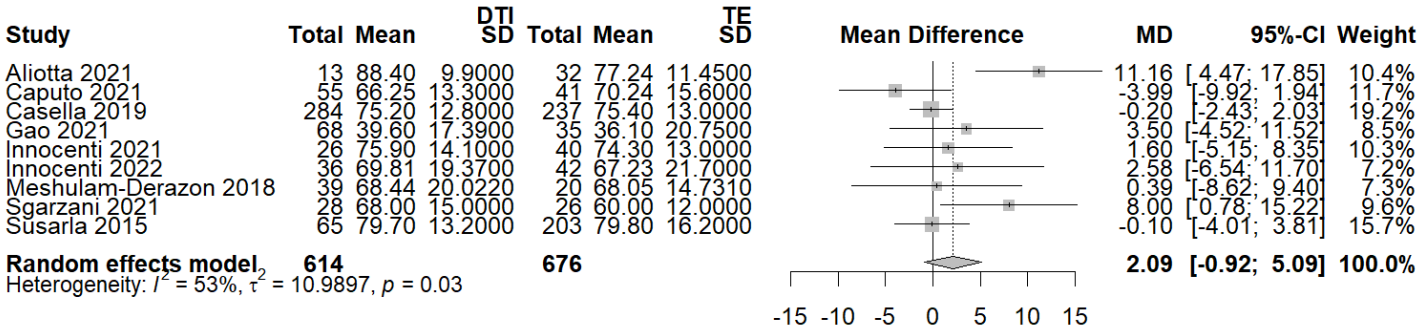
6.6.3.15.4 Sexual well-being




Study
DTI Total Mean SD
TE Total Mean SD
Mean Difference
MD 95%-CI Weight
Aliotta 2021 13 64.60 27.3000 32 49.29 26.4800 15.31 [-2.14; 32.76] 3.4%
Caputo 2021 51 54.27 16.3000 34 47.62 22.0000 6.65 [-1.99; 15.29] 10.3%
Casella 2019 284 59.80 13.2000 237 61.60 12.8000 -1.80 [-4.04; 0.44] 27.3%
Dimovska 2021 60 59.20 16.1000 20 59.90 17.5000 -0.70 [-9.38; 7.98] 10.2%
Gao 2021 40 50.95 44.6100 23 44.61 14.3200 6.34 [-8.67; 21.35] 4.4%
Innocenti 2021 26 55.60 22.6000 40 56.00 25.0000 -0.40 [-12.04; 11.24] 6.6%
Innocenti 2022 36 59.53 15.1800 42 57.00 23.3000 2.53 [-6.09; 11.15] 10.3%
Meshulam-Derazon 2018 36 54.83 22.8240 15 60.80 25.4200 -5.97 [-20.84; 8.90] 4.4%
Sgarzani 2021 28 63.00 26.0000 26 60.00 13.0000 3.00 [-7.85; 13.85] 7.4%
Susarla 2015 65 59.30 19.8000 203 52.00 25.6000 7.30 [1.34; 13.26] 15.8%
Random effects model 639 672 2.25 [-1.13; 5.63] 100.0%
Heterogeneity: I^2 = 42%, τ^2 = 9.6028, p = 0.08
-30 -20 -10 0 10 20 30

6.6.3.15.5 Physical well-being




Study
DTI Total Mean SD
TE Total Mean SD
Mean Difference
MD 95%-CI Weight
Aliotta 2021 13 88.40 9.9000 32 77.24 11.4500 11.16 [4.47; 17.85] 10.4%
Caputo 2021 55 66.25 13.3000 41 70.24 15.6000 -3.99 [-9.92; 1.94] 11.7%
Casella 2019 284 75.20 12.8000 237 75.40 13.0000 -0.20 [-2.43; 2.03] 19.2%
Gao 2021 68 39.60 17.3900 35 36.10 20.7500 3.50 [-4.52; 11.52] 8.5%
Innocenti 2021 26 75.90 14.1000 40 74.30 13.0000 1.60 [-5.15; 8.35] 10.3%
Innocenti 2022 36 69.81 19.3700 42 67.23 21.7000 2.58 [-6.54; 11.70] 7.2%
Meshulam-Derazon 2018 39 68.44 20.0220 20 68.05 14.7310 0.39 [-8.62; 9.40] 7.3%
Sgarzani 2021 28 68.00 15.0000 26 60.00 12.0000 8.00 [0.78; 15.22] 9.6%
Susarla 2015 65 79.70 13.2000 203 79.80 16.2000 -0.10 [-4.01; 3.81] 15.7%
Random effects model 614 676 2.09 [-0.92; 5.09] 100.0%
Heterogeneity: I^2 = 53%, τ^2 = 10.9897, p = 0.03
-15 -10 -5 0 5 10 15

6.6.4 Vertrauen in die Evidenz (nach GRADE)

Die Means für die Berechnung der absoluten Risiken sind aus den Kontrollgruppen (TE) Means abgeschätzt, nicht präzise berechnet.

Summary of findings:

Direct-to-implant breast reconstruction compared to tissue expander breast reconstruction in women with mastectomy for implant-based reconstruction

Patient or population: women with mastectomy for implant-based reconstruction

Intervention: direct-to-implant breast reconstruction

Comparison: tissue expander breast reconstruction

Outcomes	**Anticipated absolute effects*** (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with tissue expander breast reconstruction	**Risk with direct-to-implant breast reconstruction**				
Overall complications						
RCT: Overall complications	141 per 1 000	**396 per 1 000** (246 to 574)	**OR 3.42** (2.28 to 5.12)	183 (1 RCT)	⊕⊕◯◯ Low[a,b]	Direct-to-implant breast reconstruction may increase the incidence of overall complications compared with tissue expander breast reconstruction. .
NRSI: Overall complications	100 per 1 000	**113 per 1 000** (91 to 137)	**OR 1.14** (0.90 to 1.43)	14839 (16 non-randomised studies)	⊕◯◯◯ Very low[c,d]	
Minor complications						
NRSI: Minor complications	151 per 1 000	**109 per 1 000** (29 to 338)	**OR 0.69** (0.17 to 2.86)	770 (6 non-randomised studies)	⊕◯◯◯ Very low[c,d,e]	Direct-to-implant breast reconstruction may reduce the incidence of minor complications but the evidence is very uncertain.
Major complications						

Summary of findings:						
NRSI: Major complications	24 per 1 000	**25 per 1 000** (13 to 45)	**OR 1.02** (0.55 to 1.90)	11331 (7 non-randomised studies)	⊕◯◯◯ Very low[c,f]	Direct-to-implant breast reconstruction may have little effect on the incidence of major complications but the evidence is very uncertain.
Capsular contracture						
RCT: Capsular contracture	11 per 1 000	**4 per 1 000** (0 to 83)	**OR 0.33** (0.01 to 8.29)	183 (1 RCT)	⊕◯◯◯ Very low[a,g]	Direct-to-implant breast reconstruction may reduce capsular contracture but the evidence is very uncertain.
NRSI: Capsular contracture	68 per 1 000	**59 per 1 000** (43 to 81)	**OR 0.87** (0.62 to 1.22)	1830 (9 non-randomised studies)	⊕◯◯◯ Very low[c,d]	
Implant loss						
RCT: Implant loss	16 per 1 000	**120 per 1 000** (78 to 179)	**OR 8.28** (5.22 to 13.14)	121 (1 RCT)	⊕⊕◯◯ Low[a,b]	Direct-to-implant breast reconstruction may increase the incidence of implant loss, however, data from observational studies shows little to no difference (very low evidence).
NRSI: Implant loss	26 per 1 000	**23 per 1 000** (17 to 32)	**OR 0.91** (0.66 to 1.24)	15207 (15 non-randomised studies)	⊕◯◯◯ Very low[c,d,e]	
Infections						
RCT: Infections	22 per 1 000	**99 per 1 000** (23 to 343)	**OR 4.94** (1.04 to 23.53)	183 (1 RCT)	⊕◯◯◯ Very low[a,h]	Direct-to-implant breast reconstruction may increase the incidence of infections but the evidence is very uncertain and contradictory from observational studies.
NRSI: Infections	54 per 1 000	**45 per 1 000** (37 to 53)	**OR 0.81** (0.67 to 0.97)	18842 (17 non-randomised studies)	⊕◯◯◯ Very low[c,d]	
Reoperations						

Summary of findings:						
RCT: Reoperation	120 per 1 000	**283 per 1 000** (154 to 462)	**OR 2.91** (1.34 to 6.34)	183 (1 RCT)	⊕⊕◯◯ Low[a,b]	Direct-to-implant breast reconstruction may increase the number of unplanned reoperations.
NRSI: Reoperation	90 per 1 000	**129 per 1 000** (81 to 199)	**OR 1.49** (0.89 to 2.50)	14166 (9 non-randomised studies)	⊕◯◯◯ Very low[c,e]	
Wound complications						
NRSI: Wound complications	10 per 1 000	**8 per 1 000** (7 to 10)	**OR 0.78** (0.65 to 0.95)	14494 (12 non-randomised studies)	⊕⊕◯◯ Low[c]	Direct-to-implant breast reconstruction may decrease the incidence of wound complications.
Hematoma						
RCT: Hematoma	22 per 1 000	**33 per 1 000** (6 to 173)	**OR 1.53** (0.25 to 9.40)	183 (1 RCT)	⊕◯◯◯ Very low[a,h]	We are uncertain whether DTI increases the incidence of hematoma.
NRSI: Hematoma	58 per 1 000	**47 per 1 000** (28 to 79)	**OR 0.80** (0.46 to 1.38)	5687 (12 non-randomised studies)	⊕◯◯◯ Very low[c,d]	
Seroma						
RCT: Seroma	22 per 1 000	**4 per 1 000** (0 to 85)	**OR 0.20** (0.01 to 4.18)	183 (1 RCT)	⊕◯◯◯ Very low[a,g]	Direct-to-implant breast reconstruction may decrease the incidence of seroma but the evidence is very uncertain.
NRSI: Seroma	75 per 1 000	**63 per 1 000** (47 to 85)	**OR 0.83** (0.61 to 1.15)	6006 (14 non-randomised studies)	⊕◯◯◯ Very low[c,d]	
Skin necrosis						

Summary of findings:						
RCT: Skin necrosis	11 per 1 000	**132 per 1 000** (19 to 544)	**OR 13.82** (1.76 to 108.69)	183 (1 RCT)	⊕◯◯◯ Very low[a,h]	Direct-to-implant breast reconstruction may increase the incidence of skin necrosis but the evidence is very uncertain. Very low certainty evidence from observational studies shows little to no effect.
NRSI: Skin necrosis	53 per 1 000	**52 per 1 000** (40 to 67)	**OR 0.97** (0.73 to 1.28)	5812 (13 non-randomised studies)	⊕◯◯◯ Very low[c,e]	
Bleeding						
NRSI: Bleeding	25 per 1 000	**36 per 1 000** (9 to 131)	**OR 1.46** (0.36 to 5.93)	467 (2 non-randomised studies)	⊕◯◯◯ Very low[c,d]	Direct-to-implant breast reconstruction may increase the incidence of perioperative bleeding but the evidence is very uncertain.
Satistfaction with breasts						
RCT: Satisfaction with breast assessed with: BRAST-Q	The mean RCT: Satisfaction with breast was **79.3**	MD **1.3 lower** (6.68 lower to 4.08 higher)	-	92 (1 RCT)	⊕⊕⊕◯ Moderate[a]	Direct-to-implant breast reconstruction probably results in little to no difference in satisfaction with breasts.
NRSI: Satisfaction with breast assessed with: BREAST-Q Scale from: 0 to 100	The mean NRSI: Satisfaction with breast was **60**	MD **1.51 higher** (1.32 lower to 4.34 higher)	-	1370 (10 non-randomised studies)	⊕⊕◯◯ Low[c]	
Satisfaction with outcome						
RCT: Satisfaction with outcome	The mean RCT: Satisfaction with outcome was **67.8**	MD **5 higher** (2.28 lower to 12.28 higher)	-	91 (1 RCT)	⊕⊕◯◯ Low[a,b]	Direct-to-implant breast reconstruction may result in a slight increase in physical well-being, however, data from observational studies shows little to no difference.
NRSI: Satisfaction with outcome assessed with: BREAST-Q Scale from: 0 to 100	The mean NRSI: Satisfaction with outcome was **75**	MD **0.37 lower** (2.13 lower to 1.39 higher)	-	1109 (7 non-randomised studies)	⊕⊕◯◯ Low[c]	

Summary of findings:						
Psychosocial well-being						
RCT: Psychosocial well-being assessed with: BREAST-Q	The mean RCT: Psychosocial well-being was **71.8**	MD **0.2 lower** (7.78 lower to 7.38 higher)	-	92 (1 RCT)	⊕⊕⊕◯ Moderate[a]	Direct-to-implant breast reconstruction probably results in little to no difference in psychosocial well-being
NRSI: Psychosocial well-being assessed with: BREAST-Q Scale from: 0 to 100	The mean NRSI: Psychosocial well-being was **75**	MD **0.39 lower** (2.05 lower to 1.26 higher)	-	1351 (10 non-randomised studies)	⊕⊕◯◯ Low[c]	
Sexual well-being						
RCT: sexual well-being assessed with: BREAST-Q	The mean RCT: sexual well-being was **57.10**	MD **0.9 higher** (6.92 lower to 8.72 higher)	-	86 (1 RCT)	⊕⊕⊕◯ Moderate[a]	Direct-to-implant breast reconstruction probably results in little to no difference in sexual well-being.
NRSI: Sexual well-being assessed with: BREAST-Q Scale from: 0 to 100	The mean NRSI: Sexual well-being was **55**	MD **2.25 higher** (1.13 lower to 5.63 higher)	-	1311 (10 non-randomised studies)	⊕⊕◯◯ Low[c]	
Physical well-being						
RCT: Physical well-being assessed with: BREAST-Q	The mean RCT: Physical well-being was **79.3**	MD **1.3 lower** (6.68 lower to 4.08 higher)	-	92 (1 RCT)	⊕⊕⊕◯ Moderate[a]	Direct-to-implant breast reconstruction probably results in little to no difference in physical well-being.
NRSI: Physical well-being assessed with: BREAST-Q Scale from: 0 to 100	The mean NRSI: Physical well-being was **70**	MD **2.09 higher** (0.92 lower to 5.09 higher)	-	1290 (9 non-randomised studies)	⊕⊕◯◯ Low[c]	

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: confidence interval; **MD:** mean difference; **OR:** odds ratio

Summary of findings:

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

Explanations

a. Downgraded by one level due to serious risk of bias (unclear allocation concealment, per protocol analysis, unclear reporting bias)

b. Downgraded by one level due to serious imprecision; large confidence intervals and small sample size.

c. Downgraded by two levels due to very serious risk of bias: Included studies were observational only, and the majority did not adjust at all for relevant baseline characteristics. Results are thus prone to confounding / bias by indication.

d. Downgraded by one level due to serious imprecision; the 95% confidence interval includes both favorable and unfavorable effect of DTI reconstruction.

e. Downgraded by one level due to serious inconsistency; the heteorgeneity across studies is high.

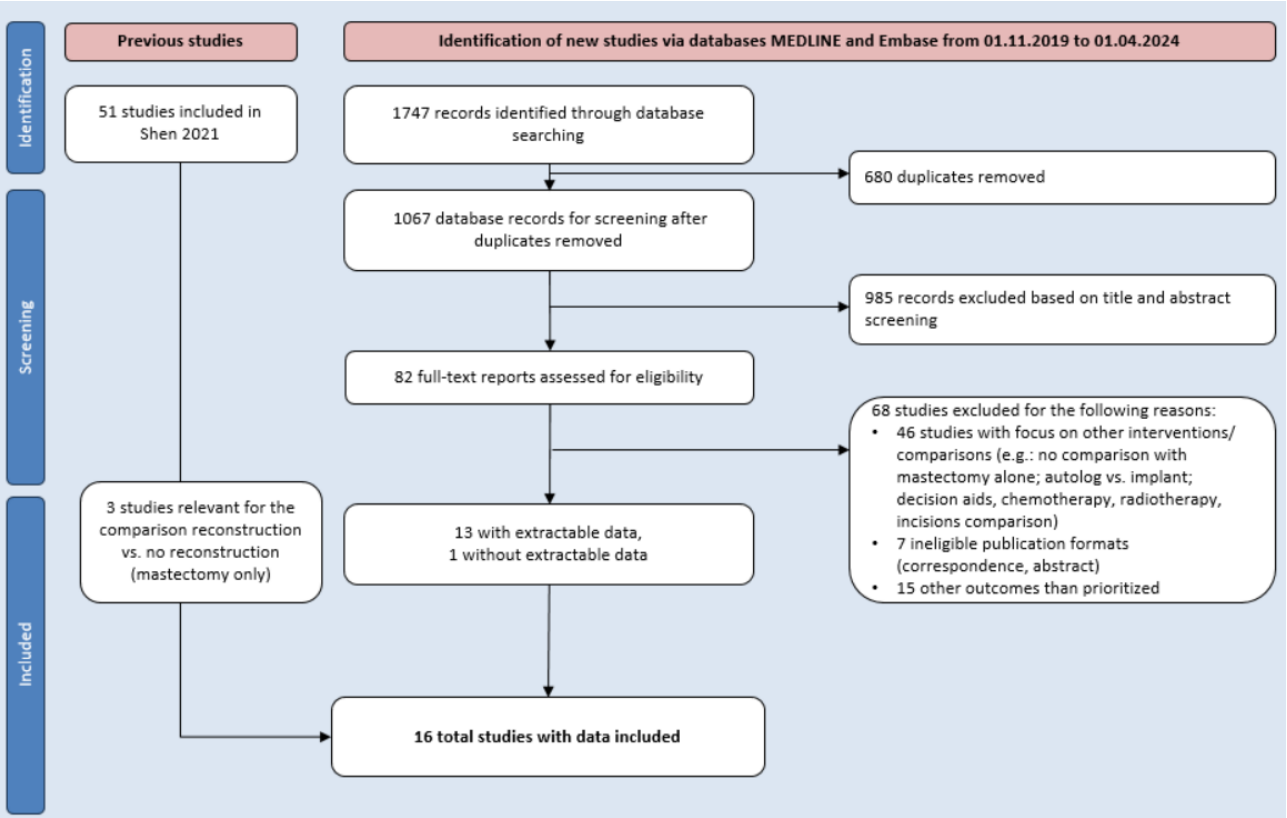
f. Downgraded by one level due to inconsistency across studies and imprecision.

g. Downgraded by two levels due to very serious imprecision: very large confidence intervals crossing the line of no effect, small number of events, small sample size.

h. Downgraded by two levels due to very serious imprecision, very large confidence intervals, small number of events and small sample size.

6.7 PICO 23

6.7.1 PRISMA Flowdiagramm



Correction: 12 studies with extractable data; 15 total included.

6.7.2 Evidenztabellen

6.7.2.1 Systematisches Review

6.7.2.1.1 Evidenztabelle systematisches Review Shen 2021 (Characteristics of the systematic review chosen for this systematic review)

Shen, Z, Sun, J, Yu, Y, Chiu, C, Zhang, Z, Zhang, Y, et.al. Oncological safety and complication risks of mastectomy with or without breast reconstruction: A Bayesian analysis.. J Plast Reconstr Aesthet Surg, 2021. 74 (2)(2): p. 290-299., https://pubmed.ncbi.nlm.nih.gov/33093010/.

Reference/ Study type	Review description	Interventions	Study Population	Ergebnisse der untersuchten Endpunkte	Methodological comments	Included publications
Shen 2021 Systematisches Review mit Meta-Analyse	**Study design** ◆ Cohort studies, case control studies **Search dates** ◆ November 2019 **Databases** ◆ Cochrane library ◆ PubMed/MEDLINE ◆ EMBASE ◆ China National Knowledge Infrastructure **Inclusion criteria** ◆ prospective or retrospective studies that enrolled breast cancer patients with MA alone or breast re- construction (IBR and DBR) after MA ◆ comparisons of any two or three surgical	**Question/ Aim** "surgeons and researchers remain uncertain about the oncological safety of breast reconstruction. 13 Which surgical choice offers the greatest balance of benefits and risks is still unclear. Therefore, a systematic review of the current literature with a Bayesian network meta-analysis was con- ducted to	51 studies published, including 265,522 breast cancer patients undergoing MA with or with- out reconstruction ◆ IBR: 58418 ◆ DBR: 5500 ◆ No reconstruction: 201604 **Descriptive statistics** ◆ Age: · NR ◆ BMI: · NR ◆ Reconstruction type (N studies) · NR	**Complications** *IBR vs. no reconstruction* ◆ 6 studies ◆ OR: 0.78 (95%-CI: 0.43 – 1.44) ◆ I^2: 97.6%	**Risk of bias assessment of studies:** not assessed, reassessed for the current clinical guideline **Overall confidence in results of SR (AMSTAR-2): moderate** ◆ PICO elements: yes ◆ A priori design: partial yes ◆ Justification for design: no ◆ Literature search >= 2 databases, search strategy + other sources: · 3 databases · String for PubMed provided · No further resources searched ◆ Selection in duplicate: yes ◆ Data extraction in duplicate: yes ◆ List of excluded studies: no ◆ sufficient detail on studies: partial yes ◆ RoB assessed: no (NOS was used to assess the quality of the	**Included and checked for additional outcomes:** ◆ Browne 2017 ◆ Eriksen 2011 ◆ O'Connell 2019 ◆ Ryu 2011 **Excluded for this guideline, comparison RT on TE versus final implant only:** ◆ Alderman 2002 ◆ Aurilio 2015 ◆ Avraham 2010 ◆ Baek 2019 ◆ Baker 2013 ◆ Beugels 2018 ◆ Bezuhly 2009 ◆ Cheng 2006 ◆ Dillekas 2016 ◆ Gerber 2009

Shen, Z, Sun, J, Yu, Y, Chiu, C, Zhang, Z, Zhang, Y, et.al. Oncological safety and complication risks of mastectomy with or without breast reconstruction: A Bayesian analysis.. J Plast Reconstr Aesthet Surg, 2021. 74 (2)(2): p. 290-299., https://pubmed.ncbi.nlm.nih.gov/33093010/.

options (MA, IBR, or DBR)
- report on at least one of the outcomes for oncological safety (disease- free survival (DFS), overall survival, local recurrence, and distant metastases) and complication risks (overall compli- cations, surgical site infection, and lymphedema)

Exclusion criteria:
- studies enrolling participants with prophylactic MA or primary breast augmentation or the ones published be- fore 2000

compare data on oncological safety and compli- cation risks among the MA, IBR, and DBR groups.

Interventions:

A: IBR

B: DBR

C: No reconstruction (Mastectomy only)

cohorts, but no results reported on each study included)
- Funding of incl. studies: no
- MA appropriate: yes
- RoB considered in MA: no
- RoB in interpretation: no
- Heterogeneity explained: no
- Publication bias investigated: yes
- Sources of CoI: The authors report no conflicts of interest.

Sources of funding

NR

- Giacalone 2010
- He 2017
- Holmich 2008
- Hsieh 2014
- Huang 2006
- Huang 2016
- Jabo 2018
- Jagsi 2016
- Jeevan 2014
- Juhl 2017
- Le 2005
- Lee 2018
- Lim 2010
- Liu 2017
- McCarthy 2008
- Murphy 2003
- Nedumpara 2011
- Nguyen 2012
- Ota 2014
- Park 2016
- Patel 2018
- Petit 2008
- Qin 2018
- Quan 2011
- Reddy 2011
- Scuderi 2011
- Seidel 2017
- Sullivan 2008
- Van Huizum 2016
- Vandeweyer 2016

Shen, Z, Sun, J, Yu, Y, Chiu, C, Zhang, Z, Zhang, Y, et.al. Oncological safety and complication risks of mastectomy with or without breast reconstruction: A Bayesian analysis.. J Plast Reconstr Aesthet Surg, 2021. 74 (2)(2): p. 290-299., https://pubmed.ncbi.nlm.nih.gov/33093010/.

- Wu 2018
- Yoon 2018
- Zhang 2016
- Zhong 2016

Characteristics of the systematic review chosen for this PICO 7.

6.7.2.1.2 Characteristics of studies included in Shen 2021 (see Table 1 in Review)

Author, year	Country	Study design	Patients (n)	Age, median (years)	Stage (I/II/III/IV)	Lymph node (+)	Estrogen receptor (+)	Chemo-therapy	Radio-therapy	Follow (years) up, median	Quality Scores (NOS)
Browne 2017	Ireland	Prospective	BR: 2226 No BR: 4179	NR	NR	NR	NR:	NR	NR	1.5	Selection: 4 Comparability: 2 Exposure: 2
Eriksen 2011	Sweden	Retrospective (pre-post)	BR: 300 No BR: 300	BR: 46 No BR: 46	NR	BR: 36.70% No BR: 79.90%	BR: NR No BR: 68.6%	BR: NR No BR: 34.20%	BR: NR No BR: 24.80%	BR: NR No BR: 11.5	Selection: 3 Comparability: 2 Exposure: 3
Ryu 2017	Korea	Retrospective	BR: 580 No BR: 878	BR: 43.9 No BR: 47.3	BR: 348/196/36/0	NR	BR: 79.10% No BR: 76%	BR: 50.50% No BR: 60%	BR: 13.50% No BR: 19.10%	BR: 3.44 No BR: 3.62	Selection: 3 Comparability: 2 Exposure: 2

Author, year	Country	Study design	Patients (n)	Age, median (years)	Stage (I/II/III/IV)	Lymph node (+)	Estrogen receptor (+)	Chemo-therapy	Radio-therapy	Follow (years) up, median	Quality Scores (NOS)
					No BR: 435/ 375/ 68/0						

Characteristics of the studies included in Shen 2021 (only those revelant to PICO 23 are presented). Information taken over and representation adapted from Table 1 of Shen 2021.

6.7.2.1.3 Risk of Bias assessment of Studies included in Shen 2021 (RoB assessment adapted from SIGN for cohort studies)

First author Year	Study Design	Bias due to confounding	Selection bias	Assessment reliable: • Assessed more than once: • Possibly affected by knowledge of outcome status?	Attrition Bias	Outcome • well-defined, valid and reliable: • Blind outcome assessment to exposure	CI reported?	Reporting Bias
Browne 2017	prospective cohort study	High risk: adjustment but no results reported	Low risk: "There were 18,216 eligible women registered within the inclusion period, of whom 17,844 had a complete record of any complications suffered during the perioperative period."	yes/no/no	High risk: not reported	Reliable outcome measure; no blind outcome assessment	no	no protocol accessible.
Eriksen 2011	matched retrospective cohort study	Moderate risk: no adjustment, but matching	Unclear: no information provided	yes/no/no (retrospective cohort study)	High risk: not reported	Reliable outcome measure; no blind outcome assessment	no	no protocol accessible.
Ryu 2017	matched retrospective case-control study	Moderate risk: no adjustment, but matching	Low risk: …we excluded patients who underwent NAC (n=309), those with a follow-up	yes/no/no (retrospective case-control study)	High risk: not reported	Reliable outcome measure; no blind outcome assessment	no	no protocol accessible.

First author Year	Study Design	Bias due to confounding	Selection bias	Assessment reliable: • Assessed more than once: • Possibly affected by knowledge of outcome status?	Attrition Bias	Outcome • well-defined, valid and reliable: • Blind outcome assessment to exposure	CI reported?	Reporting Bias
			duration <12 months (n=147), those with incomplete data (n=24), and those who underwent palliative surgery (n=11)"					

Risk of bias assessment of studies included in Shen 2021 that were eligible for PICO 23.

6.7.3 Primärstudien – neu identifiziert

Reference/ Study type	Population	Interventions	Main results	Methodological evaluation
Afshar-Bakshloo 2023 Prospective cohort study	**Inclusion criteria (for analysis):** ◆ First clinic visit at Charité breast center between 11/17/2016 and 10/31/2019 ◆ written consent for PRO collection ◆ received BCS, mastectomy without or with immediate breast reconstruction for invasive breast cancer or DCIS. **Exclusion criteria (for analysis):** ◆ no consent ◆ no e-mail-address ◆ no therapeutic breast surgery ◆ cM1 at first clinic visit ◆ palliative treatment (for reasons other than cM1) ◆ missing information on postoperative therapeutic course ◆ no PRO-measurement from at least two time points **Enrolment period** ◆ 17.11.2016 – 31.09.2019 **Follow-up (overall population)** ◆ Median: 370 days ◆ Maximum: 41.5 months **Descriptive statistics** ◆ Age (median, range) · Reconstruction: 47.05 (10.90) · No reconstruction: 65.19 (12.01) ◆ BMI (Median (25%-, 75%-quartile))	**Interventions** A: reconstruction · N = 86 B: no reconstruction (mastectomy only) · N = 27 **Analysis** ◆ Frequencies ◆ linear mixed regression model ◆ Matching: no ◆ Adjustment: no	**Reoperation:** · Reconstruction: 33/86 · No reconstruction: 3/27 · p = 0.022	**General information** ◆ **Follow-up**: median 370 days ◆ **Funding:** Open Access funding enabled and organized by Projekt DEAL. The study as part of the patient-reported outcome program at Charité breast center was funded by Charité – Universitätsmedizin Berlin. ◆ **CoI**: OB: Employee and stockholder at Takeda Pharma (financial interests). MMK: Speaker fee from Roche, Gilead, Astra Zeneca, Sysmex (financial interests). MAB, SA, CR, JUB, RR, DS declare that they have no competing interests. **Risk of bias considerations (adapted from SIGN cohort study checklist)** ◆ Study type: prospective cohort study ◆ Confounding: yes ◆ Rate of participation/Exclusions reported (selection bias into the study): yes ◆ Exposure/Intervention · Assessment reliable: yes · Assessed more than once: no · Possibly affected by knowledge of outcome status: no ◆ Drop-out rate & reasons reported: no

Reference/ Study type	Population	Interventions	Main results	Methodological evaluation
	· Reconstruction: 22.86 (20.66, 25.91) · No reconstruction: 25.47 (21.64, 27.78) ◆ Stadium (TNM) · NR ◆ Chemotherapy (% yes) (previous) · NR ◆ Reconstruction type (flap type) (%) · NR			◆ Outcome · Outcome measure is well-defined, valid and reliable: yes · Blind outcome assessment to exposure: (→If not, Knowledge of exposure status likely to influence the outcome?: possible ◆ Main cofounders taken into account: no ◆ Confidence intervals reported: no ◆ Selective reporting (comparison with protocol): yes **Other limitations or comments**: ◆ real-world data?
Delenne 2024 retrospective, descriptive and unicentric study	**Inclusion criteria (for analysis):** ◆ Patients who received a mastectomy for their breast cancer between 2016 and 2020 ◆ Patients who automatically received a bilateral mastectomy for a bilateral breast cancer **Exclusion criteria (for analysis):** ◆ Male patients ◆ prophylactic mastectomies ◆ history of breast surgery ◆ mastectomies for non-breast cancer or recurrence of breast cancer after autologous reconstruction	**Interventions** A: reconstruction · N = 32 B: no reconstruction (mastectomy only) · N = 153 **Analysis** ◆ frequencies, secondary univariate analysis ◆ Matching: no	**Post-operative complications** ◆ Grade IIIa · Reconstruction: 6/32 · No reconstruction: 72/153 ◆ Grade IIIb · Reconstruction: 4/32 · No reconstruction: 21/153 ◆ IVA complications · Reconstruction: 0/32 · No reconstruction: 0/153 ◆ IVB complications · Reconstruction: 0/32	**General information** ◆ Follow-up: NR ◆ **Funding:** This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors. ◆ **CoI**: The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Reference/ Study type	Population	Interventions	Main results	Methodological evaluation
	Enrolment period ◆ 2016 - 2020 **Follow-up** · NR **Descriptive statistics** ◆ Age (median, range) · Reconstruction: below or equal to 70: 28/32 (88%); above 70: 4/32 (12%) · No reconstruction: below or equal to 70: 101/153 (66%); above 70: 52/153 (34%) ◆ BMI (median, range) · Reconstruction: below or equal to 25: 23/32 (72%); above 25: 9/32 (28%) · No reconstruction: below or equal to 25: 100/153 (65%); above 25: 53/153 (35%) ◆ Stadium (TNM) · Reconstruction: <T3: 32 (100%); T3: 0; T4: 0; T4D: 0; N+: 2 (7.1%); M+: 0 · No reconstruction: <T3: 118 (77%); T3: 16 (10%); T4: 7 (4.6%); T4D: 12 (7.8%); N+: 70 (54%); M+: 16 (10%) ◆ Chemotherapy (% yes) (previous) · Reconstruction: 5/32 (16%) · No reconstruction: 105/153 (69%) ◆ Reconstruction type (flap type) (%) · Immediate breast reconstruction	◆ Adjustment: no	· No reconstruction: 0/153	**Risk of bias considerations (adapted from SIGN cohort study checklist)** ◆ Study type: retrospective, descriptive and unicentric study ◆ Confounding: yes ◆ Rate of participation/Exclusions reported (selection bias into the study): yes ◆ Exposure/Intervention · Assessment reliable: yes · Assessed more than once: no · Possibly affected by knowledge of outcome status: no ◆ Drop-out rate & reasons reported: no ◆ Outcome · Outcome measure is well-defined, valid and reliable: yes · Blind outcome assessment to exposure: (→If not, Knowledge of exposure status likely to influence the outcome?: no (retrospective) ◆ Main cofounders taken into account: no ◆ Confidence intervals reported: no ◆ Selective reporting (comparison with protocol): yes **Other limitations or comments**: ◆ retrospective design

Reference/ Study type	Population	Interventions	Main results	Methodological evaluation
Grigor 2021 Retrospective study	**Inclusion criteria (for analysis):** ◆ Any type of MO (total mastectomy, skin-sparing mastectomy, or nipple-sparing mastectomy) and MIBR (mastectomy and direct-to- implant [MIBRi1], mastectomy and 2-stage reconstruction [MIBRi2], and mastectomy and autologous flap reconstruction [MIBRf]) **Exclusion criteria (for analysis):** ◆ Risk-reduction mastectomy ◆ Mammoplasty ◆ partial mastectomy ◆ distant metastatic disease ◆ de novo stage IV cancer ◆ recurrent breast cancer ◆ a history of neoadjuvant radiochemotherapy, or delayed breast reconstruction **Enrolment period** ◆ 01.01.2013 - 31.05.2019 **Follow-up (mean (SD))** ◆ mastectomy with 1-stage direct to implant IBR: 3.40 (1.75) ◆ mastectomy with 2-stage tissue expander to implant IBR: 3.48 (1.60) ◆ mastectomy with autologous flap IBR: 2.14 (1.05) ◆ no reconstruction: 3.33 (1.28) **Descriptive statistics**	**Interventions** A: reconstruction · N = 277 Subgroups: · Mastectomy with 1-stage direct to implant IBR: N = 140 · mastectomy with 2-stage tissue expander to implant IBR: N = 96 · mastectomy with autologous flap IBR: N = 41 B: no reconstruction (mastectomy only) · N = 443 **Analysis** ◆ frequencies, multivariable cox regression analysis ◆ Matching: no ◆ Adjustment: no	**Any complications** · Reconstruction: 109/277 · No reconstruction: 201/443 **Major complications** · Reconstruction: 58/277 No reconstruction: 30/443 **Minor complications** · Reconstruction: 76/277 · No reconstruction: 193/443	**General information** ◆ **Follow-up**: mean 3.30 (±1.44) ◆ Funding: NR ◆ **CoI**: The authors have no conflict of interest to disclose. **Risk of bias considerations (adapted from SIGN cohort study checklist)** ◆ Study type: retrospective study ◆ Confounding: yes ◆ Rate of participation/Exclusions reported (selection bias into the study): yes ◆ Exposure/Intervention · Assessment reliable: yes · Assessed more than once: no · Possibly affected by knowledge of outcome status: no ◆ Drop-out rate & reasons reported: no ◆ Outcome · Outcome measure is well-defined, valid and reliable: yes · Blind outcome assessment to exposure: (→If not, Knowledge of exposure status likely to influence the outcome: no (retrospective) ◆ Main cofounders taken into account: no

Reference/ Study type	Population	Interventions	Main results	Methodological evaluation
	◆ Age (mean (SD)) · masetctomy with 1-stage direct to implant IBR: 50.3 (11.3) · mastectomy with 2-stage tissue expander to implant IBR: 48.6 (10.2) · mastectomy with autologous flap IBR: 51.9 (7.46) · No reconstruction: 66.2 (13.8) ◆ BMI (mean (SD)) · mastectomy with 1-stage direct to implant IBR: 24.6 (4.45) · mastectomy with 2-stage tissue expander to implant IBR: 24.6 (5.53) · mastectomy with autologous flap IBR: 26.4 (3.90) · No reconstruction: 26.3 (5.30) ◆ Stadium (TNM) · Mastectomy with 1-stage direct to implant IBR: Tis: 22 (15.7); T1: 16 (11.4); T1b: 30 (21.4); T1c: 35 (25.0); T2: 6 (4.28); T3: 0 (0); T4: 21 (15.0); Not reported: 9 (7.14) · mastectomy with 2-stage tissue expander to implant IBR: Tis: 7 (7.29); T1: 15 (15.6) ; T1b: 18 (18.8) ;T1c: 32 (33.3);T2: 13 (13.5);T3: 2 (2.08);T4: 8 (8.33);Not reported: 9 (7.14) · mastectomy with autologous flap: Tis: 6 (14.6); T1: 4 (9.76); T1b: 9 (22.0); T1c: 3 (7.32); T2: 2 (4.88); T3: 0 (0); T4: 14 (34.1); Not reported: 3 (7.32) · no reconstruction: Tis: 54 (7.44); T1: 60 (8.26); T1b: 165 (22.7) T1c: 260 (35.9);			◆ Confidence intervals reported: no ◆ Selective reporting (comparison with protocol): unclear **Other limitations or comments**: ◆ retrospective design

Reference/ Study type	Population	Interventions	Main results	Methodological evaluation
	T2: 81 (11.2); T3: 6 (0.826); T4: 77 (10.6); Not reported: 17 (2.36) ◆ Chemotherapy (% yes) (previous) · NR ◆ Reconstruction type (flap type) · 1-stage direct to implant IBR: 140/720 · 2-stage tissue expander to implant IBR: 96/720 · autologous flap IBR: 41/720			
Ho 2022 Retrospective observational study	**Inclusion criteria (for analysis):** ◆ All women above 18 years-old ◆ Women who had unilateral mastectomy with subsequent development of new contralateral breast cancer **Exclusion criteria (for analysis):** ◆ Male ◆ under 18 years of age ◆ underwent palliative mastectomy ◆ women who had prophylactic mastectomies ◆ those who had previous oncologic surgery prior to the study date or outside of the hospital service **Enrolment period** ◆ 01.01.2016 – 31.12.2021 **Follow-up (median (range))** ◆ 36-months (2 - 74 months) **Descriptive statistics**	**Interventions** A: reconstruction · N = 311 B: no reconstruction (mastectomy only) · N = 618 **Analysis** ◆ frequencies ◆ Matching: no ◆ Adjustment: no	**General complications requiring return to theatre within follow-up period** · Reconstruction: 39/311 · No reconstruction: 44/618	**General information** ◆ **Follow-up**: median 36-months (range: 2 to 74 months) ◆ Funding: NR ◆ **CoI**: None declared. **Risk of bias considerations (adapted from SIGN cohort study checklist)** ◆ Study type: Retrospective observational study ◆ Confounding: yes ◆ Rate of participation/Exclusions reported (selection bias into the study): no ◆ Exposure/Intervention · Assessment reliable: yes · Assessed more than once: no · Possibly affected by knowledge of outcome status: no

Reference/ Study type	Population	Interventions	Main results	Methodological evaluation
	◆ Age (median (range)) · Reconstruction: 48 (23-83) · No reconstruction: 64 (30-92) ◆ BMI (mean) · Reconstruction: 26.0 · No reconstruction: 28.6S ◆ Stadium (TNM) · NR ◆ Chemotherapy (% yes) (previous) · NR ◆ Reconstruction type (flap type) (%) · Immediate: 278/311 (89.4%) · autologous: 17% · implant: 80% · deep inferior epigastric perforator (DIEP) flap: 74.2%) · transverse rectus abdominis musculocutaneous (TRAM) flap: 3.2% · latissimus dorsi flap: 16.1%) · mixed autologous reconstruction, including DIEP and TRAM flaps: 6.5% · mixed (implant and autologous): 3.2% · delayed implant BR: 19 (6.1%) · delayed autologous BR: 9 (2.9%)			◆ Drop-out rate & reasons reported: no ◆ Outcome · Outcome measure is well-defined, valid and reliable: yes · Blind outcome assessment to exposure: (→If not, Knowledge of exposure status likely to influence the outcome: no (retrospective) ◆ Main cofounders taken into account: no ◆ Confidence intervals reported: no ◆ Selective reporting (comparison with protocol): yes **Other limitations or comments**: ◆ retrospective design

Reference/ Study type	Population	Interventions	Main results	Methodological evaluation
Nickel 2022 retrospective cohort study	**Inclusion criteria (for analysis):** ◆ all mastectomy operations among women aged ≥ 21 years **Exclusion criteria (for analysis):** ◆ NR **Enrolment period** ◆ 01.07.2010 – 31.12.2015 **Follow-up** ◆ 180 days **Descriptive statistics** ◆ Age (median, IQR) · Overall: 53 years (45–63) ◆ BMI (median, range) · NR ◆ Stadium (TNM) · NR ◆ Chemotherapy (% yes) (previous) · NR ◆ Reconstruction type (flap type) (%) · subpectoral implant reconstruction: 1271/2159 (58.9%) - of those with a tissue expander: 1080/1271 (85%) · flap reconstruction: 108/2159 (5.0%) · flap plus implant reconstruction: 31/2159 (1.4%)	**Interventions** A: reconstruction (implant and/or flap) · N = 1410 Subgroups: · Implant reconsruction: N = 1271 · Flap reconstruction: N = 139 B: no reconstruction (mastectomy only) · N = 749 **Analysis** ◆ Frequencies, multivariable analysis ◆ Matching: no ◆ Adjustment: no	**Any serious wound complications** · Reconstruction (implant and/or flap): 237/1410 · Implant reconstruction: 199/1271 · Flap reconstruction: 38/139 · No reconstruction: 30/749	**General information** ◆ **Follow-up**: 180 days ◆ Funding: NR ◆ **CoI**: Margaret A. Olsen reports consultant work and grant funding from Pfizer for work outside the submitted manuscript. Victoria J. Fraser reports that her spouse is the Chief Clinical Officer at Cigna Corporation. Terence M. Myckatyn reports advisory board membership, investigator-initiated grant, and device development royalties for RTI Surgical. He reports former investigator-initiated grants and advisory board work with Allergan, and an unencumbered research award from Sientra. Clara N. Lee was supported by a grant from the Agency for Healthcare Research and Quality (R18 HS026699-01A1). The remaining authors have no conflicts of interest. **Risk of bias considerations (adapted from SIGN cohort study checklist)** ◆ Study type: retrospective cohort study ◆ Confounding: yes

Reference/ Study type	Population	Interventions	Main results	Methodological evaluation
				◆ Rate of participation/Exclusions reported (selection bias into the study): no ◆ Exposure/Intervention · Assessment reliable: yes · Assessed more than once: no · Possibly affected by knowledge of outcome status: no ◆ Drop-out rate & reasons reported: no ◆ Outcome · Outcome measure is well-defined, valid and reliable: yes · Blind outcome assessment to exposure: (→If not, Knowledge of exposure status likely to influence the outcome?: no (retrospective) ◆ Main cofounders taken into account: no ◆ Confidence intervals reported: no ◆ Selective reporting (comparison with protocol): yes **Other limitations or comments**: ◆ retrospective design

Reference/ Study type	Population	Interventions	Main results	Methodological evaluation
O'Connell 2019 Prospective multicentre cohort study	**Inclusion criteria (for analysis):** ◆ Consecutive women aged 18 or over ◆ undergoing mastectomy with or without IBR using any technique for invasive or preinvasive (ductal carcinoma in situ, DCIS) breast cancer with curative intent at participating centres **Exclusion criteria (for analysis):** ◆ patients undergoing risk-reducing surgery (without a therapeutic mastectomy for breast cancer) ◆ partial mastectomy including wide local excision with volume replacement (latissimus dorsi miniflaps; lateral intercostal perforator (LICAP) or thoracodorsal artery perforator (TDAP) flaps) ◆ displacement techniques (therapeutic mammaplasty), ◆ those with distant metastatic disease **Enrolment period** ◆ 01.07.2016 – 31.12.2016 **Follow-up** ◆ NR **Descriptive statistics** ◆ Age (median (IQR) (range)) · Implant reconstruction: 50 (43-57) (23-82) · Pedicled flap reconstruction: 52 (47-60) (25-74)	**Interventions** A: reconstruction · N = 1126 procedures Subgroups: · Implant reconstruction: N = 773 · Pedicled flap reconstruction: N = 106 · Free flap reconstruction: N = 247 B: no reconstruction (mastectomy only) · N = 1606 procedures **Analysis** ◆ frequencies, univariable and multivariable logistic regression analysis ◆ Matching: no ◆ Adjustment: yes (age, BMI, smoking and ASA grade)	**Any complications** · Implant reconstruction: 223/667 · Pedicled flap reconstruction: 42/105 · Free flap reconstruction: 94/228 · No reconstruction: 570/1517 **Major complications** · Implant reconstruction: 100/675 · Pedicled flap reconstruction: 7/105 · Free flap reconstruction: 38/228 · No reconstruction: 76/1532	**General information** ◆ Follow-up: NR ◆ Funding: NR ◆ **CoI**: The authors declare no competing interests. **Risk of bias considerations (adapted from SIGN cohort study checklist)** ◆ Study type: Prospective multicentre cohort study ◆ Confounding: yes ◆ Rate of participation/Exclusions reported (selection bias into the study): no ◆ Exposure/Intervention · Assessment reliable: yes · Assessed more than once: no · Possibly affected by knowledge of outcome status: no ◆ Drop-out rate & reasons reported: no ◆ Outcome · Outcome measure is well-defined, valid and reliable: yes · Blind outcome assessment to exposure: (→If not, Knowledge of exposure status likely to influence the outcome: no (possible) ◆ Main cofounders taken into account:

Reference/ Study type	Population	Interventions	Main results	Methodological evaluation
	· Free-flap reconstruction: 50 (44.5-56) (21-72) · No reconstruction: 65 (54-75) (26-96) ◆ BMI (median (IQR) (range)) · Implant reconstruction: 24.4 (21.9-27.6) (16.0-61.4) · Pedicled flap reconstruction: 26.6 (23.3-30.6) (18.5-39.2) · Free-flap reconstruction: 27.4 (24.2-30.19 (15.6-31.1) · No reconstruction: 27.3 (23.7-32.2) (13.4-80.7) ◆ Stadium (TNM) · implant-based reconstruction: Tis: 163/707 (71.7%), T1a: 71/707 (10.0%), T1b: 63/707 (8.9%), T1c: 156/707 (22.1%), T2: 185/707 (26.2%), T3: 55/707 (7.8%), Not reported:14/707 (2.0%) · pedicled flap: Tis: 26/105 (24.8%), T1a: 9/105 (8.6%), T1b: 13/105 (12.4%), T1c: 17/105 (16.2%), T2: 28/105 (26.7%), T3: 9/105 (8.6%), Not reported:3/105 (2.9%) · free-flap: Tis: 58/231 (25.1%), T1a: 19/231 (8.2%), T1b: 14/231 (6.1%), T1c: 46/231 (19.9%), T2: 63/231 (27.3%), T3: 18/231 (7.8%), Not reported:13/231 (5.6%) · no reconstruction: Tis: 141/1564 (9.0%), T1a: 88/1564 (5.6%), T1b: 89/1564 (5.7%), T1c: 359/1564 (23.0%), T2:			◆ Confidence intervals reported: no ◆ Selective reporting (comparison with protocol): unclear **Other limitations or comments**: ◆ NR

Reference/ Study type	Population	Interventions	Main results	Methodological evaluation
	672/1564 (43.0%), T3: 190/1564 (12.2%), Not reoprted: 25/1564 (1.6%) ◆ Chemotherapy (% yes) (previous) · NR ◆ Reconstruction type (flap type) (%) · implant: 675/2540 (26.6%) (157 subpectoral expanders; 410 subpectoral reconstructions with biological or synthetic mesh; 105 dermal-sling procedures and 98 prepectoral reconstructions) · pedicled flap: 105/2540 (4.1%) (62 autologous LD, 39 LD with implant, 2 pedicled TRAM and 2 other) · free-flap: 228/2540 (8.9%) (19 DIEPs, 16 free TRAMs, 4 SIEA, 7 TUG flaps and 1 other)			
Palmquist 2023 retrospective cohort study	**Inclusion criteria (for analysis):** ◆ patients with a diagnosis of clinical stage T4 breast cancer but no evidence of distant metastatic disease **Exclusion criteria (for analysis):** ◆ NR **Enrolment period** ◆ 2014 - 2021 **Follow-up** ◆ 2 years	**Interventions** A: reconstruction · N = 73 Subgroups: · Delayed reconstruction: N = 36 · Immediate reconstruction: N = 37	**QoL-outcomes: Breast -Q (median, IQR)** *Satisfaction with breast* ◆ 6 months post-score: · Delayed reconstruction: 57 (53-71) · Immediate reconstruction: 58 (41-58) · No reconstruction: NA · p = 0.2 ◆ 1 year post-score:	**General information** ◆ **Follow-up**: 2 years ◆ Funding: NR ◆ **CoI**: Dr. Monica Morrow has received honoraria from Exact Sciences and Roche. The remaining authors have no conflicts of interest. **Risk of bias considerations (adapted from SIGN cohort study checklist)**

Reference/ Study type	Population	Interventions	Main results	Methodological evaluation
	Descriptive statistics ◆ Age (median) · Delayed reconstruction: 51 · Immediate reconstruction: 47 · No reconstruction: 55 ◆ BMI (median) · Delayed reconstruction: 30.0 · Immediate reconstruction: 27.7 · No reconstruction: 26.4 ◆ Stadium (TNM) · Delayed reconstruction: - Clinical N: N0: 5 (14%), N1: 24 (67%), N2: 2 (5.6%), N3: 5 (14%) - Pathologic T: T0: 21 (58%), T1: 4 (11%), T2: 4 (11%), T3: 2 (5.6%), T4: 5 (14%) - Pathologic N: N0: 20 (56%), N1: 8 (22%), N2: 7(19%), N3: 1 (2.8%) · Immediate reconstruction: - Clinical N: N0: 8 (22%), N1: 23 (62%), N2: 3 (8.1%), N3: 3 (8.1%) - Pathologic T: T0: 7 (19%), T1: 15 (41%), T2: 9 (24%), T3: 1 (2.7%), T4: 5 (14%) - Pathologic N: N0: 16 (43%), N1: 12 (32%), N2: 5 (14%), N3: 4 (11%) · No reconstruction: - Clinical N: N0: 4 (5.6%), N1: 51 (72%), N2: 7 (9.9%), N3: 9 (13%) - Pathologic T: T0: 20 (28%), T1: 20 (28%), T2: 14 (20%), T3: 4 (5.6%), T4: 13 (18%)	B: no reconstruction (mastectomy only) · N = 71 **Analysis** ◆ Matching: no ◆ Adjustment: no	· Delayed reconstruction: 65 (54–82) · Immediate reconstruction: 57 (47–61) · No reconstruction: NA · p = 0.079 ◆ 2 years post-score: · Delayed reconstruction: 64 (52–82) · Immediate reconstruction: 58 (45–70) · No reconstruction: NA · p = 0.3 *Physical well-being of the chest* ◆ 6 months post-score: · Delayed reconstruction: 60 (55–74) · Immediate reconstruction: 72 (50–78) · No reconstruction: 60 (50–68) · p = 0.3 ◆ 1 year post-score: · Delayed reconstruction: 72 (64–80) · Immediate reconstruction: 68 (55–76) · No reconstruction: 68 (63–76) · p = 0.5 ◆ 2 years post-score:	◆ Study type: retrospective cohort study ◆ Confounding: yes ◆ Rate of participation/Exclusions reported (selection bias into the study): no ◆ Exposure/Intervention · Assessment reliable: yes · Assessed more than once: no · Possibly affected by knowledge of outcome status: no ◆ Drop-out rate & reasons reported: no ◆ Outcome · Outcome measure is well-defined, valid and reliable: yes · Blind outcome assessment to exposure: (→If not, Knowledge of exposure status likely to influence the outcome?: no (retrospective) ◆ Main cofounders taken into account: no ◆ Confidence intervals reported: no ◆ Selective reporting (comparison with protocol): yes **Other limitations or comments**: ◆ retrospective design

Reference/ Study type	Population	Interventions	Main results	Methodological evaluation
	- Pathologic N: N0: 29 (41%), N1: 17 (24%), N2: 13 (18%), N3: 12 (17%) ◆ Chemotherapy (% yes) (previous) · Delayed reconstruction: 0 (0.0%) · Immediate reconstruction: 0 (0.0%) · No reconstruction: 1 (1.4%) ◆ Reconstruction type (flap type) (%) · Delayed reconstruction: TE/implant: 0 (0.0%); autologous: 36 (100%) · Immediate reconstruction: TE/implant: 24 (64.9%); autologous: 13 (35.1%)		· Delayed reconstruction: 76 (76–80) · Immediate reconstruction: 66 (51–80) · No reconstruction: 64 (55–80) · p = 0.4	
Van Bommel 2020 retrospective study	**Inclusion criteria (for analysis):** ◆ female breast cancer patients ◆ age of 18 years ◆ surgically treated for primary breast cancer or DCIS by mastectomy either with or without IBR **Exclusion criteria (for analysis):** ◆ Patients with distant metastases **Enrolment period** ◆ January 2013 - October 2014 **Follow-up** ◆ mean: 17.5 months (range 3-34 months) **Descriptive statistics** ◆ Age (median, range)	**Interventions** A: immediate reconstruction · N = 164 B: no reconstruction (mastectomy only) · N = 281 **Analysis** ◆ Mean (SD), multivariate linear regression analysis ◆ Matching: no ◆ Adjustment: no	**QoL-outcomes: Breast -Q (mean, SD)** ◆ Satisfaction with breast · Reconstruction: 64 ± 18.08 · No reconstruction: 62 ± 18.46 ◆ Psychosocial well-being · Reconstruction: 75 ± 18.76 · No reconstruction: 67 ± 18.97 ◆ Sexual well-being · Reconstruction: 62 ± 20.70 · No reconstruction: 52 ± 24.28 ◆ Physical well-being: chest · Reconstruction: 77 ± 16.08 · No reconstruction: 74 ± 16.44 ◆ Satisfaction with outcome · Reconstruction: 71 ± 21.15	**General information** ◆ **Follow-up**: mean: 17.5 months (range 3-34 months) ◆ **Funding:** This work has been funded by the Dutch Cancer Society, grant number: IKNL-2013-6501. The funding body did not play a role in the analysis and interpretation of data and in the writing of the manuscript. ◆ **CoI**: The authors declare that they have no conflict of interest. None of the authors has a financial interest in any of the products, devices, or drugs mentioned in this manuscript.

Reference/ Study type	Population	Interventions	Main results	Methodological evaluation
	· Reconstruction: <50: 51/164 (31%); 50-65: 98/164 (60%); ≥65. 15/164 (9%) · No reconstruction: <50: 47/281 (17%); 50-65: 126/281 (45%); ≥65: 108/281 (38%) ◆ BMI (median, range) · Reconstruction: <25: 118/164 (72%); >25: 46/164 (28%) · No reconstruction: <25: 126/281 (45%); >25: 155/281 (55%) ◆ Stadium (TNM) · Reconstruction: 0: 42/164 (26%); I: 68/164 (42%); II: 50/164 (31%); III: 4/164 (2%) · No reconstruction: 0: 55/281 (20%); I: 61/281 (22%); II: 103/281 (37%); III: 62/281 (22%) ◆ Chemotherapy (% yes) (previous) · NR ◆ Reconstruction type (flap type) (%) · Tissue expander or immediate implant: 146/164 (89%) · Latissimus dorsi flap with implant: 9/164 (6%) · autologous reconstruction: 9/164 (6%)		· No reconstruction: NA ◆ Satisfaction with nipples · Reconstruction: 67 ± 22.51 · No reconstruction: NA	**Risk of bias considerations (adapted from SIGN cohort study checklist)** ◆ Study type: retrospective study ◆ Confounding: yes ◆ Rate of participation/Exclusions reported (selection bias into the study): no ◆ Exposure/Intervention · Assessment reliable: yes · Assessed more than once: no · Possibly affected by knowledge of outcome status: no ◆ Drop-out rate & reasons reported: no ◆ Outcome · Outcome measure is well-defined, valid and reliable: yes · Blind outcome assessment to exposure: (→If not, Knowledge of exposure status likely to influence the outcome: no (retrospective) ◆ Main cofounders taken into account: no ◆ Confidence intervals reported: no ◆ Selective reporting (comparison with protocol): yes **Other limitations or comments**: ◆ retrospective design

Reference/ Study type	Population	Interventions	Main results	Methodological evaluation
Simon 2020 retrospective, monocentric, cohort study	**Inclusion criteria (for analysis):** ◆ patients who required a total mastectomy ◆ Mastectomies performed for ILBLR after initial BCT **Exclusion criteria (for analysis):** ◆ NR **Enrolment period** ◆ January 2016 – April 2019 **Follow-up** ◆ median: 198 months (95%-CI: 175-207) from initial breast cancer diagnosis ◆ median 21 months (95%-CI: 21-25) from the date of mastectomy for recurrence **Descriptive statistics** ◆ Age (n, (%)) · Reconstruction: ≤ 40: 2/68 (2.9%); 41-50: 12/68 (17.6%); 51-74: 47/68 (69.1%); ≥75: 7/68 (10.3%) · No reconstruction: ≤ 40: 0/139 (0.0%); 41-50: 12/139 (8.6%); 51-74: 88/139 (63.3%); ≥75: 39/139 (28.1%) ◆ BMI (n, (%))) · Reconstruction: <25: 51/68 (75.0%); 25.0-29.9: 14/68 (20.6%); ≥30: 3/68 (4.4%) · No reconstruction: <25: 74/139 (53.2%); 25.0-29.9: 35/139 (25.2%); ≥30: 30/139 (21.6%)	**Interventions** A: immediate reconstruction · N = 68 B: no reconstruction (mastectomy only) · N = 139 **Analysis** ◆ Frequencies, Multivariate analyses using binary logistic regression ◆ Matching: no ◆ Adjustment: no	**Reoperation** · Reconstruction: 8/68 · No reconstruction: 9/139 · p = 0.151	**General information** ◆ **Follow-up**: median 198 months (95%-CI: 175-207) from initial breast cancer diagnosis; 21 months (95%-CI: 21-25) from the date of mastectomy for recurrence ◆ Funding: NR ◆ **CoI**: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest. **Risk of bias considerations (adapted from SIGN cohort study checklist)** ◆ Study type: retrospective, monocentric, cohort study ◆ Confounding: yes ◆ Rate of participation/Exclusions reported (selection bias into the study): no ◆ Exposure/Intervention · Assessment reliable: yes · Assessed more than once: no · Possibly affected by knowledge of outcome status: no ◆ Drop-out rate & reasons reported: no ◆ Outcome

Reference/ Study type	Population	Interventions	Main results	Methodological evaluation
	◆ Stadium (TNM) · NR ◆ Chemotherapy (% yes) (previous) · Reconstruction: 12/68 (17.6%) · No reconstruction: 37/139 (26.6%) ◆ Reconstruction type (flap type) (%) · implant alone: 31/68 (45.6%) · LDF: 37/68 (54.4%)			· Outcome measure is well-defined, valid and reliable: yes · Blind outcome assessment to exposure: (→If not, Knowledge of exposure status likely to influence the outcome: no (retrospective) ◆ Main cofounders taken into account: no ◆ Confidence intervals reported: no ◆ Selective reporting (comparison with protocol): yes **Other limitations or comments**: ◆ retrospective design
Taqi 2021 retrospective study	**Inclusion criteria (for analysis):** ◆ patients with clinically locally advanced breast cancer on presentation who underwent mastectomy ◆ patients who were treated with neoadjuvant therapy (NAT) or upfront surgery **Exclusion criteria (for analysis):** ◆ Patients with inflammatory breast cancer or who had mastectomy for recurrent breast cancer or with palliative intent **Enrolment period** ◆ 01.01.2012 – 31.12.2017 **Follow-up**	**Interventions** A: reconstruction · N = 112 B: no reconstruction (mastectomy only) · N = 155 **Analysis** ◆ Matching: no ◆ Adjustment: no	**Reoperation** · Reconstruction: 9/112 · No reconstruction: 2/155 · p = 0.559	**General information** ◆ **Follow-up**: median 50.7 ± 23.4 months (0–107) ◆ **Funding:** The authors received no funding for the project. ◆ **CoI**: The authors report no proprietary or commercial interest in any product mentioned or concept discussed in this article. **Risk of bias considerations (adapted from SIGN cohort study checklist)** ◆ Study type: retrospective study

Reference/ Study type	Population	Interventions	Main results	Methodological evaluation
	◆ Median: 50.7 ± 23.4 months (0–107) **Descriptive statistics** ◆ Age (mean ± SD) · Reconstruction: 48.82 ± 10.08 · No reconstruction: 61.42 ± 13.50 ◆ BMI (median, range) · NR ◆ Stadium (TNM) · Reconstruction: T1N2: 2/112 (1.8%); T2N1: 36/112 (32.1%); T2N2: 8/112 (7.1%); T2N3: 3/112 (2.7%); T3N0: 15/112 (13.4%); T3N1: 33/112 (29.5%); T3N2: 8/112 (7.1%); T3N3: 2/112 (1.8%); T4N0: 2/112 (1.8%); T4N1: 2/112 (1.8%); T4N2: 1/112 (0.9%) · No Reconstruction: T1N2: 3/155 (1.9%); T2N1: 69/155 (44.5%=; T2N2: 7/155 (4.5%); T2N3: 3/155 (1.9%); T3N0: 13/155 (8.4%); T3N1: 27/155 (17.5%); T3N2: 4/155 (2.6%); T3N3: 4/155 (2.6%); T4N0: 6/155 (3.9%); T4N1: 16/155 (10.3%); T4N2: 3/155 (1.9%) ◆ Chemotherapy (% yes) (previous) · NR ◆ Reconstruction type (flap type) (%) · tissue expander: 53/112 (47.3%) · implant with bioplrosthesis: 36/112 (32.1%) · TRAM flap: 16/112 (14.3%)			◆ Confounding: yes ◆ Rate of participation/Exclusions reported (selection bias into the study): no ◆ Exposure/Intervention · Assessment reliable: yes · Assessed more than once: no · Possibly affected by knowledge of outcome status: no ◆ Drop-out rate & reasons reported: no ◆ Outcome · Outcome measure is well-defined, valid and reliable: yes · Blind outcome assessment to exposure: (→If not, Knowledge of exposure status likely to influence the outcome: no (retrospective) ◆ Main cofounders taken into account: no ◆ Confidence intervals reported: no ◆ Selective reporting (comparison with protocol): yes **Other limitations or comments**: ◆ retrospective design

Reference/ Study type	Population	Interventions	Main results	Methodological evaluation
	· DIEP flap: 7/112 (6.3%)			
Tang 2024 prospective cohort study	**Inclusion criteria (for analysis):** ◆ 18 years of age or older ◆ patients who did not reside in a conjugate living setting such as a nursing home ◆ able to communicate in English ◆ Patients who have a first diagnosis of breast cancer by core needle biopsy ◆ scheduled for surgery as their initial treatment **Exclusion criteria (for analysis):** ◆ Patients scheduled for a second breast cancer surgical procedure ◆ Patients who were receiving neoadjuvant systemic therapy, had stage 4 disease, or were diagnosed with recurrence or a second primary tumor **Enrolment period** ◆ September 2017 - August 2020 **Follow-up**	**Interventions** A: reconstruction · N = 84 B: no reconstruction (mastectomy only) · N = 46 **Analysis** ◆ frequencies, mean (SD) ◆ Matching: no ◆ Adjustment: no	**QoL-outcomes: Breast –Q (mean, SD)** ◆ Breast satisfaction · Reconstruction: 64.00 (20.23) · No reconstruction: 61.48 (24.76) ◆ Psychosocial well-being · Reconstruction: 67.23 (21.70) · No reconstruction: 68.41 (23.78) ◆ Physical well-being · Reconstruction: 75.39 (15.46) · No reconstruction: 70.93 (16.18) ◆ Sexual well-being · Reconstruction: 54.52 (28.34) · No reconstruction: 56.65 (25.04)	**General information** ◆ Follow-up: NR ◆ **Funding:** This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors. ◆ **CoI**: The authors of this manuscript declare no conflicts of interest for this publication. **Risk of bias considerations (adapted from SIGN cohort study checklist)** ◆ Study type: prospective cohort study ◆ Confounding: yes ◆ Rate of participation/Exclusions reported (selection bias into the study): no ◆ Exposure/Intervention · Assessment reliable: yes

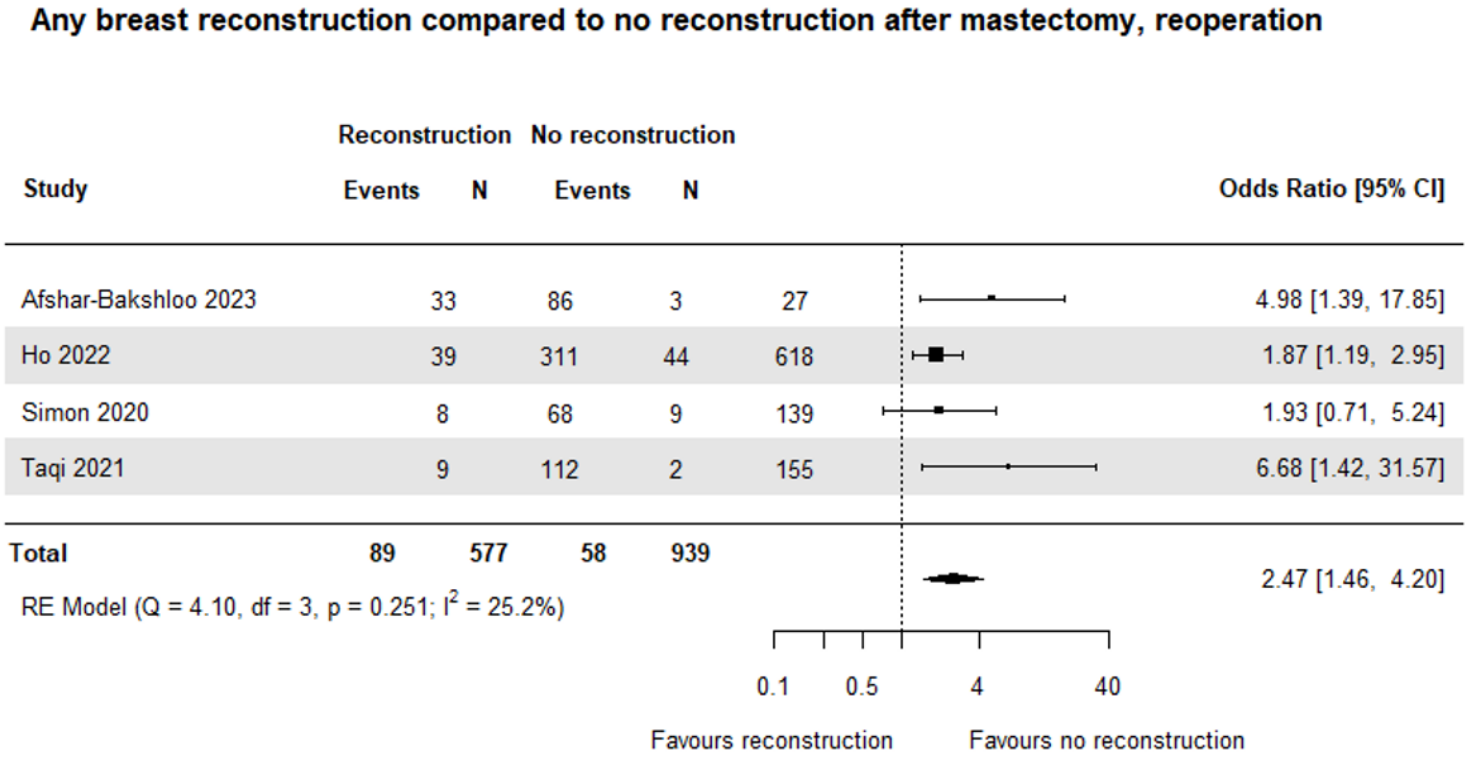
Reference/ Study type	Population	Interventions	Main results	Methodological evaluation
	◆ NR **Descriptive statistics** ◆ Age (median, range) · Reconstruction: ≤49: 46/84 (55%); 50-59: 21/84 (25%); 60-69: 12/84 (14%); ≥70: 5/84 (6%) · No reconstruction: ≤49: 9/46 (20%); 50-59: 8/46 (17%); 60-69: 13/46 (28%); ≥70: 16/46 (35%) ◆ BMI (median, range) · NR ◆ Stadium (TNM) · NR ◆ Chemotherapy (% yes) (previous) · Reconstruction: 35/84 (42%) · No reconstruction: 21/46 (46%) ◆ Reconstruction type (flap type) (%) · tissue expander placement: 38/84 · direct to implant: 33/84 · DIEP flap: 5/84 · TRAM flap: 5/84 · unspecified: 3/84			· Assessed more than once: no · Possibly affected by knowledge of outcome status: no ◆ Drop-out rate & reasons reported: no ◆ Outcome · Outcome measure is well-defined, valid and reliable: yes · Blind outcome assessment to exposure: (→If not, Knowledge of exposure status likely to influence the outcome?: no (possible) ◆ Main cofounders taken into account: no ◆ Confidence intervals reported: no ◆ Selective reporting (comparison with protocol): yes **Other limitations or comments**: ◆ NR

Reference/ Study type	Population	Interventions	Main results	Methodological evaluation
Vohra 2023 Prospective cohort study	**Inclusion criteria (for analysis):** ◆ NR **Exclusion criteria (for analysis):** ◆ Patients who had died ◆ those who had undergone breast reconstruction following BCS and were unwilling to participate or refused to give informed consent were excluded from the study **Enrolment period** ◆ 01.01.2015 – 31.12.2021 **Follow-up** ◆ NR **Descriptive statistics** ◆ Age (median, range) · Reconstruction: <46: 29/69 (42%); 46-55: 32/69 (46.4%); >56: 8/69 (11.6%) · No reconstruction: <46: 18/71 (25.3%); 46-55: 31/71 (43.6%); >56:22/71 (31%) ◆ BMI (median, range) · NR ◆ Stadium (TNM) · NR ◆ Chemotherapy (% yes) (previous) · NR ◆ Reconstruction type (flap type) (%)	**Interventions** A: reconstruction · N = 69 B: no reconstruction (mastectomy only) · N = 71 **Analysis** ◆ Mean (SD), Kruskal-Wallis Test ◆ Matching: no ◆ Adjustment: no	**QoL-outcomes: Breast -Q (mean, SD not reported)** ◆ Satisfaction with breast · Reconstruction: 70.0 · No reconstruction: 52.0 ◆ Psychosocial well-being · Reconstruction: 79.9 · No reconstruction: 54.8 ◆ Sexual well-being · Reconstruction: 61.0 · No reconstruction: 45.0 As SD was not reported, it was not possible to be introduced in the analysis.	**General information** ◆ Follow-up: NR ◆ **Funding:** No funding was received to perform this study. ◆ **CoI**: The authors have no conflicts of interest to declare. **Risk of bias considerations (adapted from SIGN cohort study checklist)** ◆ Study type: Prospective cohort study ◆ Confounding: yes ◆ Rate of participation/Exclusions reported (selection bias into the study): no ◆ Exposure/Intervention · Assessment reliable: yes · Assessed more than once: no · Possibly affected by knowledge of outcome status: no ◆ Drop-out rate & reasons reported: no ◆ Outcome · Outcome measure is well-defined, valid and reliable: yes · Blind outcome assessment to exposure: (→If not, Knowledge of exposure status likely to influence the outcome?: no (possible)

Reference/ Study type	Population	Interventions	Main results	Methodological evaluation
	· NR			◆ Main cofounders taken into account: no ◆ Confidence intervals reported: no ◆ Selective reporting (comparison with protocol): yes **Other limitations or comments**: ◆ NR

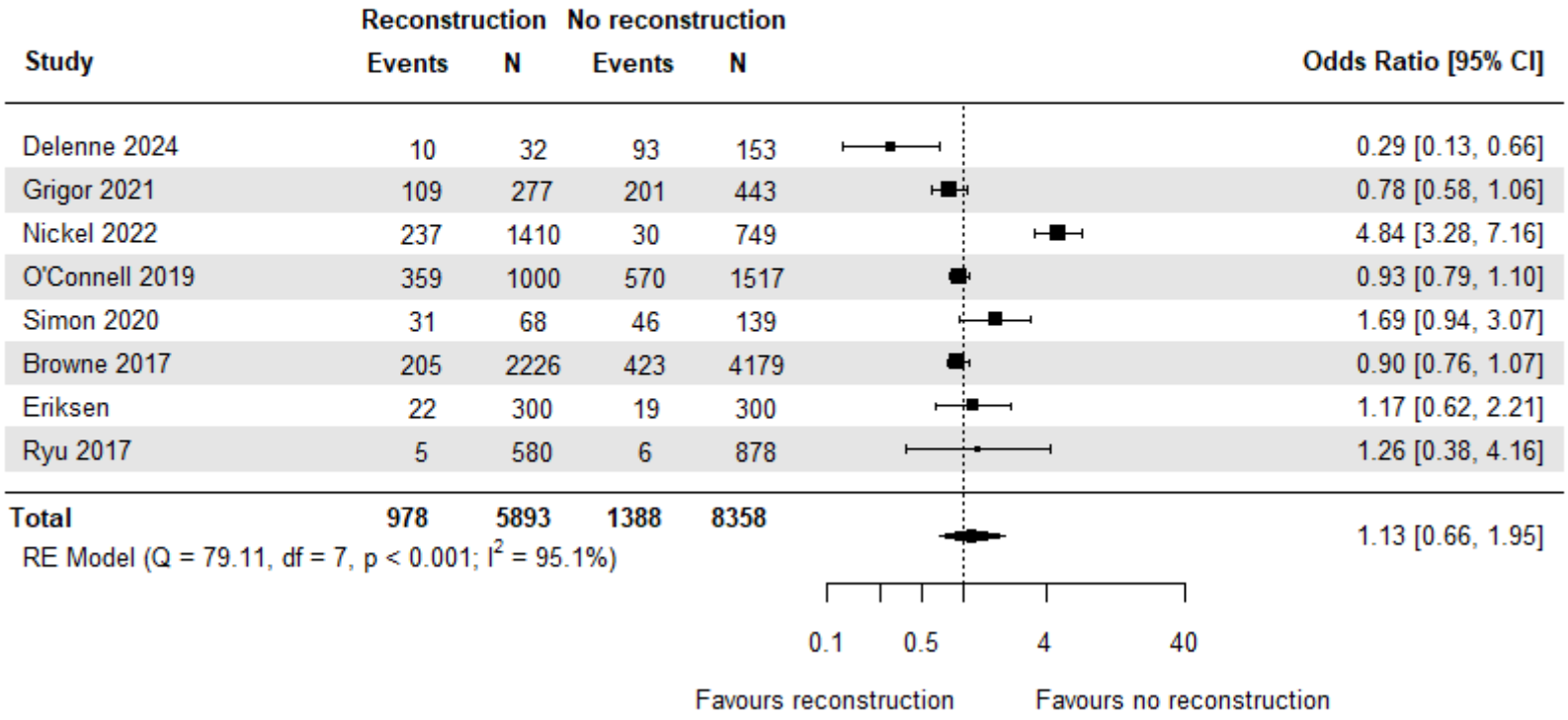
6.7.4 Meta-analysen

6.7.4.1 Reoperation



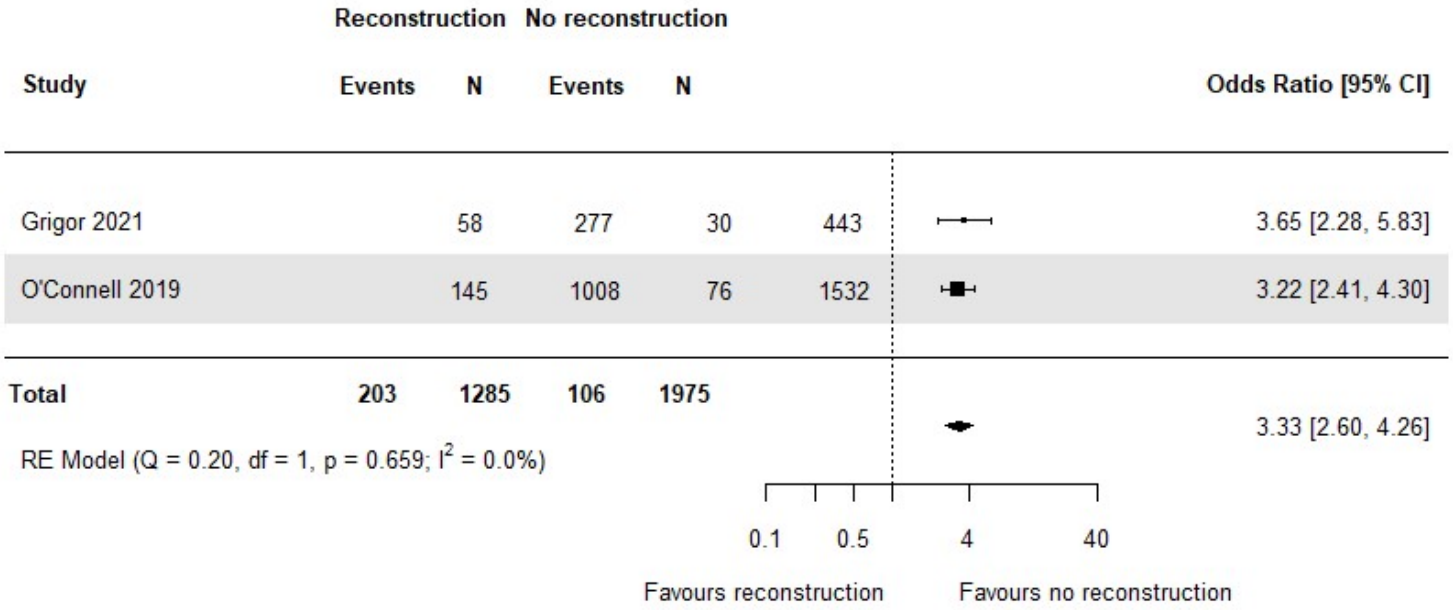
6.7.4.2 Any complications

ny breast reconstruction compared to no reconstruction after mastectomy, any complications



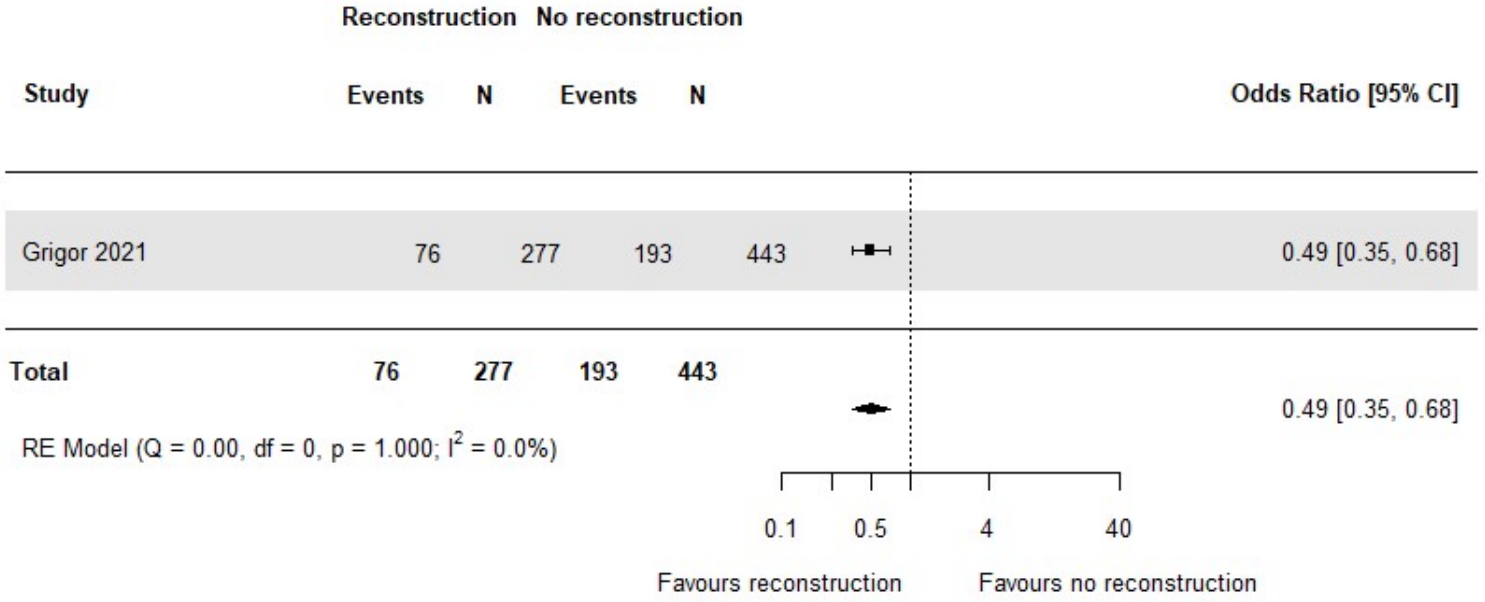
6.7.4.3 Major complications

y breast reconstruction compared to no reconstruction after mastectomy, major complications



6.7.4.4 Minor complications

y breast reconstruction compared to no reconstruction after mastectomy, minor complications



6.7.5 Vertrauen in die Evidenz (nach GRADE)

Summary of findings:

Any breast reconstruction compared to no reconstruction (mastectomy alone) after mastectomy

Patient or population: after mastectomy

Intervention: any breast reconstruction

Comparison: no reconstruction (mastectomy alone)

Outcomes	**Anticipated absolute effects*** (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with no reconstruction (mastectomy alone)	**Risk with any breast reconstruction**				
Any complications	166 per 1.000	**184 per 1.000** (116 to 280)	**OR 1.13** (0.66 to 1.95)	14251 (8 non-randomised studies)	⊕◯◯◯ Very low[a,b,c]	It is uncertain whether any breast reconstruction compared to no reconstruction (mastectomy alone) increases or decreases the incidence of any complications.
Reoperation	62 per 1.000	**140 per 1.000** (88 to 217)	**OR 2.47** (1.46 to 4.20)	1516 (4 non-randomised studies)	⊕⊕⊕◯ Moderate[a]	Mastectomy alone or no reconstruction likely reduces the incidence of reoperations compared to any breast reconstruction.
Major complications	54 per 1.000	**159 per 1.000** (120 to 196)	**OR 3.33** (2.41 to 4.30)	3260 (2 non-randomised studies)	⊕⊕⊕◯ Moderate[a]	Mastectomy alone or no reconstruction likely reduces the incidence of major complications compared to any breast reconstruction.
Minor complications	436 per 1.000	**274 per 1.000** (213 to 344)	**OR 0.49** (0.35 to 0.68)	720 (1 non-randomised study)	⊕⊕◯◯ Low[a]	Any breast reconstruction may decrease the incidence of minor complications compared to no reconstruction (mastectomy alone).

Summary of findings:

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: confidence interval; **MD:** mean difference; **OR:** odds ratio

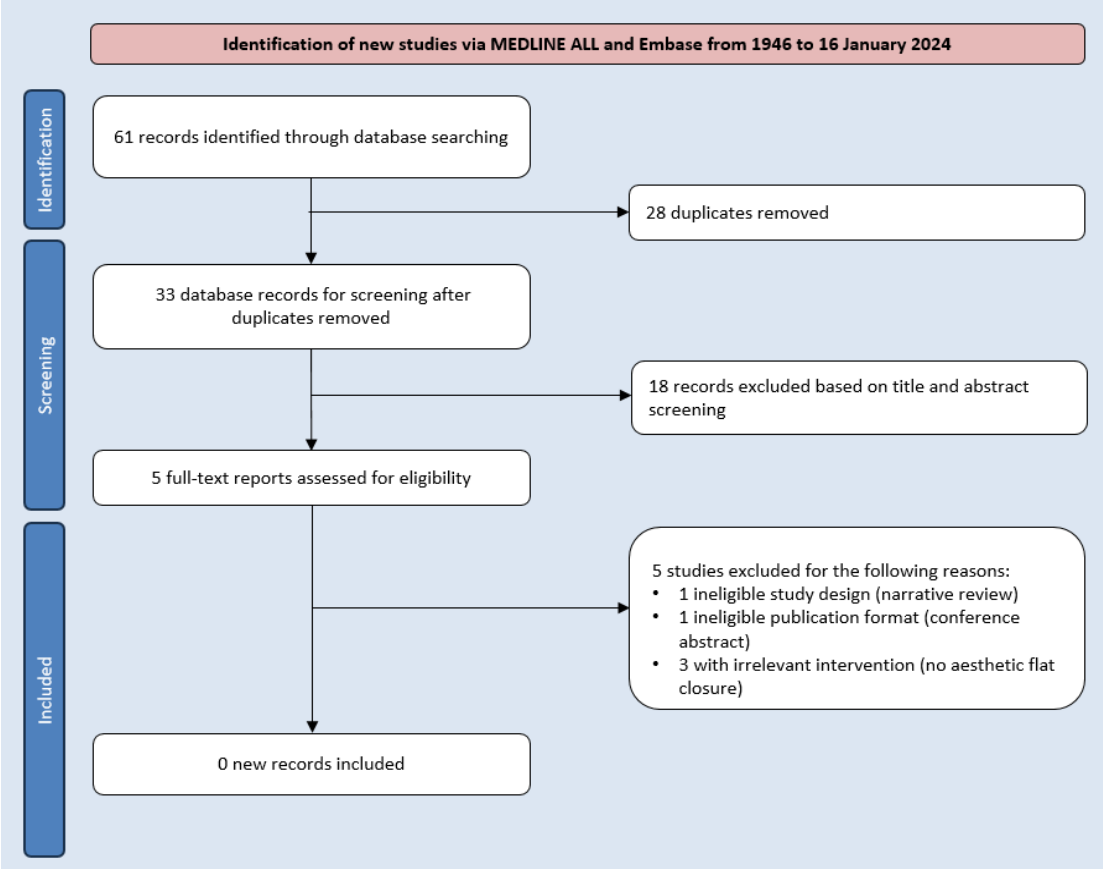
GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

Explanations

a. Downgraded by two levels due to very serious risk of bias: Included studies were observational only, and the majority did not adjust at all for relevant baseline characteristics. Results are thus prone to confounding.
b. Downgraded by one level due to serious inconsistency (above 70%): Outcome definitions varied between studies. In addition, heterogeneity is high.
c. Downgraded by one level due to serious imprecision; the 95% confidence interval includes both effects.
*Vohra et al. (2023) did not report standard deviations (SDs) and therefore was not included in the meta-analysis. Palmquist et al. (2023) only reported median BREAST-Q physical well-being score at 6 months, one year, and 2 years after reconstruction (immediate and delayed reconstruction reported separately). It was reported that median scores were higher in the reconstruction group compared to no reconstruction (or mastectomy alone). Due to potential non-normal distribution, we decided to not convert medians and IQRs to means and SDs, and therefore did not include this result in meta-analysis.

6.8 PICO 24

6.8.1 PRISMA Flowdiagramm



Hinweis: Da zu dieser PICO-Fragestellung keine geeignete Literatur identifiziert werden konnte, konnten weitere methodische Schritte nicht durchgeführt werden. Daher ist geplant, eine oder mehrere Empfehlungen auf Basis von Expertenkonsens zu formulieren

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