|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Author, year**  **Quality** | **Sub-category** | **Study design** | **Country/ population/ setting** | **Inclusion/exclusion criteria** |
| **Mastectomy** |  |  |  |  |
| ***Current Review*** |  |  |  |  |
| Alamouti et al., 2015185  Poor | Surgical complications | Retrospective cohort, one-arm | U.K.  All patients undergoing RRM with immediate reconstruction from 2007 to 2012 by a single surgeon | Inclusion: women with BRCA mutations  Exclusion: known diagnosis of metastatic breast and/or ovarian cancer or significant comorbidities |
| Arver et al., 2011186  Fair | Surgical complications | Retrospective cohort, one-arm | Sweden  All Swedish women with BPM performed between 1995 and 2005, with increased risk but no personal history of breast cancer | Inclusion: Women with increased hereditary risk of breast cancer undergoing BPM between 1995 and 2005; previous ovarian cancer allowed  Exclusion: Previous breast malignancy |
| Gopie et al., 2013196  NA | Surgical complications | Before and after | The Netherlands  Academic and regional hospitals | Inclusion: Healthy, unaffected women at significantly increased risk of breast cancer due to a BRCA mutation or relevant family history who had opted for BPM with immediate breast reconstruction  Exclusion: Suspicion of breast cancer in the planning towards BPM and a detection of breast cancer in the followup, and not being able to understand and speak the Dutch language sufficiently |

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Author, year**  **Quality** | **Risk level definition** | **N** | **Demographics** | **Duration/followup** |
| **Mastectomy** |  |  |  |  |
| ***Current Review*** |  |  |  |  |
| Alamouti et al., 2015185  Poor | BRCA mutation | Enrolled: 91  RRM: 66  Therapeutic: 25 | Mean age, years: 42.9 | Surgery from July 2007 to July 2012, retrospective study (patients invited to participate after surgery) |
| Arver et al., 2011186  Fair | Included women divided into 6 risk categories: *BRCA1* carriers; *BRCA2* carriers; women with ≥ 3 relatives with breast or ovarian cancer, unknown mutation; women from an HBOC family without a proven *BRCA* mutation ("50% risk carriers"); women with < 3 affected relatives and Claus ≥ 30% risk; and women with <3 affected relatives and Claus < 30% risk. | Enrolled: 223  Analyzed for complications: 223  *BRCA1:* 43.9% (98/223)  *BRCA2:* 13.9% (31/223) | Median age at BPM, years: 40.0 (range 25 to 67) | Surgery 1995 to 2005, followup through 2008  Mean 6.6 years (range 2.1 to 14.0)  1468 person-years |
| Gopie et al., 2013196  NA | Unclear, had to either have *BRCA 1/2* mutation or relevant family history | Eligible: 73  Enrolled: 50  Analyzed: 50 | Mean age at time of BPM, years: 37.1 (SD 10.2)  PBSO: 22.9% (11/50) | Surgery December 2007 to May 2010  Mean followup, months: 21.7 (range 12 to 35) |

|  |  |  |  |
| --- | --- | --- | --- |
| **Author, year Quality** | **Surgical procedure** | **Results** | **Funding source** |
| **Mastectomy** |  |  |  |
| ***Current Review*** |  |  |  |
| Alamouti et al., 2015185  Poor | Risk-reducing mastectomy with immediate reconstruction performed in one operative episode | Complications of autologous reconstruction: 7.7% (4/52) complete or partial flap failure  Complications of implant-based reconstruction: 5.1% (2/39) red breast syndrome (erythema along inferior pole of breast) | NR |
| Arver et al., 2011186  Fair | A) Bilateral prophylactic mastectomy (all)  B) BPM with implant reconstruction: 93.3% (208/223)  C) BPM with flap (autologous tissue) reconstruction: 5.4% (12/223)  D) BPM with no reconstruction: 1.3% (3/223) | A) Early complications (≤ 30 days): 51.6% (115/223)  Partial skin necrosis or epidermolysis: 29.9% (63/211), patients with flap reconstruction excluded  Wound infection: 17.0% (38/223)  Other complications, occurring in < 10% of patients: hematoma, seroma, wound rupture, blood loss with transfusion, deep venous thrombosis, pneumothorax, pneumonia, fall trauma, and urinary tract infection  Late wound infection (>30 days): 9.9% (22/223)  B) Implant complications: 29.8% (62/208)  Capsular contracture requiring surgery: 13.9% (29/208)  Implant loss due to infection/necrosis: 10.1% (21/208)  Other complications, occurring in <10% of patients: implant rupture, expander port leakage  C) Flap-related complications: 58.3% (7/12)  Partial or complete flap failure: 41.7% (5/12)  Reoperation due to anastomotic failure: 33.3% (4/12)  Donor site infection/necrosis: 25.0% (3/12) | Stockholm County Council, Karolinska Institutet *[sic]* , Cancer Society in Stockholm, and the Johan & Jakob Söderberg Foundation |
| Gopie et al., 2013196  NA | RRM with reconstruction | 24% (12/50) reported severe postoperative complications leading to an unfinished result or removal of the primary breast mound reconstruction. | Dutch Cancer Society (UL 2007- 3726) |

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Author, year**  **Quality** | **Sub-category** | **Study design** | **Country/ population/ setting** | **Inclusion/exclusion criteria** |
| **Mastectomy** |  |  |  |  |
| ***Current Review*** |  |  |  |  |
| Heemskerk- Gerritsen et al., 2007197  Fair | Surgical complications | Retrospective and prospective cohort, one- arm | The Netherlands  Women with increased familial or genetic predisposition to breast cancer undergoing prophylactic mastectomy between 1994 and 2004 and/or followup at one site | Inclusion: All women at increased risk of hereditary BC who underwent prophylactic bilateral or contralateral mastectomy ± PBSO between January 1, 1994 and December 31, 2004  Exclusion: Women from families with specific BRCA mutations who did not carry those mutations |
| Nurudeen et al., 2017207  Fair | Surgical complications | Retrospective cohort | U.S.  BRCA carriers undergoing mastectomy from 1997 to 2013 in a single healthcare system in Boston | Inclusion: BRCA mutation undergoing mastectomy with reconstruction (risk-reducing or therapeutic, reported separately),  Exclusion: patients receiving postmastectomy radiation, or reconstruction not considered implant and/or autologous |

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Author, year**  **Quality** | **Risk level definition** | **N** | **Demographics** | **Duration/followup** |
| **Mastectomy** |  |  |  |  |
| ***Current Review*** |  |  |  |  |
| Heemskerk- Gerritsen et al., 2007197  Fair | Women with either a proven *BRCA1/2* mutation or a genetic susceptibility (50% risk carriers from an HBOC family). | Enrolled with no history of breast cancer: 177  *BRCA1/2* : 145  HBOC: 32 | Median age at PM, years  *BRCA1/2:* 36.0 (range 22 to 65)  HBOC: 38.5 (range 28 to 55) | Surgery 1994 to 2004  Median followup, years  *BRCA1/2:* 4.4  HBOC: 4.7 |
| Nurudeen et al., 2017207  Fair | BRCA mutation | RRM: 104  *BRCA1*: 59  *BRCA2*: 45 | Median age at RRM, years: 41.1 (range 21 to 64.6) | Surgery 1997 to 2013 (retrospective) |

| **Author, year**  **Quality** | **Surgical procedure** | **Results** | **Funding source** |
| --- | --- | --- | --- |
| **Mastectomy** |  |  |  |
| ***Current Review*** |  |  |  |
| Heemskerk- Gerritsen et al., 2007197  Fair | Prophylactic bilateral mastectomy: 177 unaffected women  PM with breast reconstruction: 166  With PBSO before, at, or after PM: 83  Without PBSO: 62 | Women with complications after breast reconstruction: 49% (82/166)  Total number of complications: 127  Early complications (<6 weeks after reconstruction): 33% (42/127)  Surgery due to early complications: 36% (15/42)  Infection: 19% (8/42)  Necrosis: 26% (11/42)  Bleeding: 48% (20/42)  Other complications, occurring in < 10% of patients: prosthesis luxation, poor arterial inflow, pneumothorax  Late complications (>6 weeks after reconstruction): 67% (85/127)  Surgery due to late complications: 87% (74/85)  Capsular formation: 36% (31/85)  Poor cosmetic result: 36% (31/85)  Dog ear: 19% (16/85)  Other complications, occurring in <10% of patients: infection, necrosis, prosthesis luxation | Not reported |
| Nurudeen et al., 2017207  Fair | Bilateral prophylactic mastectomy, or contralateral prophylactic mastectomy in patients with previous unilateral therapeutic mastectomy | Any complication: 69.3% (n’s NR)  Complications requiring surgery (some patients may have had more than one complication): 26.0% (27/104)  Skin necrosis: 10.6% (11/104)  Other complications, rate <10% of patients: infection, seroma, hematoma, implant removal  Unexpected revisions: 56.7% (59/104); 59 patients had one or more unplanned surgical procedures to complete reconstruction beyond expected stages of reconstruction | Reported as none |

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Author, year**  **Quality** | **Sub-category** | **Study design** | **Country/ population/ setting** | **Inclusion/exclusion criteria** |
| **Mastectomy** |  |  |  |  |
| ***2013 Review*** |  |  |  |  |
| Brandberg, et al., 2008190  Brandberg, et al., 2012189  NA | Sexual functioning  Psychological | Before and after | Sweden  Karolinska University Hospital | Inclusion: Women how had RRM including reconstruction.  Exclusion: Women with a breast cancer diagnosis. |
| Gahm et al., 2010195  NA | Pain | Cross-sectional | Sweden  Karolinska University Hospital | Inclusion: Women with increased risk for breast cancer, who had undergone RRM and immediate breast reconstruction  Exclusion: Personal history of breast cancer |

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Author, year**  **Quality** | **Risk level definition** | **N** | **Demographics** | **Duration/followup** |
| **Mastectomy** |  |  |  |  |
| ***2013 Review*** |  |  |  |  |
| Brandberg, et al., 2008190  Brandberg, et al., 2012189  NA | Lifetime risk definition not described  50% lifetime risk: 28.9% (26/90)  25% lifetime risk:8.9% (8/90) | Eligible: Not reported  Enrolled: 90  Analyzed: 65 | **Age, years**  20 to 29: 8% (7/90)  30 to 39: 37% (33/90)  40 to 49: 39% (35/90)  50 to 59: 14% (13/90)  60 to 69: 2% (2/90) | October 1997 to December 2005  1 year |
| Gahm et al., 2010195  NA | Not reported | Eligible: Not reported  Enrolled: 1784 (59 with RRM and 1725 included as reference sample) | Mean age, years: 40 (range 25 to 65) | 2004 to 2006  Mean followup, months: 29 (range 24 to 49) |

| **Author, year**  **Quality** | **Surgical procedure** | **Results** | **Funding source** |
| --- | --- | --- | --- |
| **Mastectomy** |  |  |  |
| ***2013 Review*** |  |  |  |
| Brandberg, et al., 2008190  Brandberg, et al., 2012189  NA | RRM with reconstruction | **Mean scales (SE), before RRM vs. 6 months after RRM vs. 1 year after RRM**  SAQ, discomfort subscale: 0.56 (0.15) vs. 0.53 (0.20) vs. 0.81 (0.19); p=NS  Bodily pain as reported by SF-36: 81.0 (2.98) vs. 80.7 (2.84) vs. 82.6 (3.29); p=NS | Swedish Cancer Society, the Swedish Association for Cancer and Traffic Victims, and the Stockholm County Council |
| Gahm et al., 2010195  NA | 1. RRM with reconstruction 2. Reference comparison group who did not undergo RRM | **Pain and discomfort questionnaire responses after RRM, A vs. B**  69% (38/55) pain in breasts  36% (20/55) pain affected sleep  22% (12/55) pain affected daily activities  71% (39/55) discomfort in breasts  87% (48/55) pain or discomfort in breasts  No association between pain and age (OR 0.99, p=0.771); pain and complication (OR 0.60, p=0.538); or pain and re-operation (OR 3.72, p=0.110)  Pain or discomfort not related with negative effects in sexual outcomes (p>0.05 for both)  **Post operative complications**  18.6% (11/59) had infections  5.1% (3/59) required implant extraction  6.8% (4/59) had hematoma  3.4% (2/59) required acute operative evacuation  3.4% (2/59) had revision of flap necrosis  59% (35/59) had corrective surgical procedures  41% (24/59) had procedure involving implant pockets | None |

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Author, year**  **Quality** | **Sub-category** | **Study design** | **Country/ population/ setting** | **Inclusion/exclusion criteria** |
| **Mastectomy** |  |  |  |  |
| ***2013 Review*** |  |  |  |  |
| Metcalfe et al., 2004205  NA | Sexual functioning  Psychological | Case-series | Canada  Ontario hospitals in The Central East Health Information Partnership | Inclusion: Women who underwent a RRM at an Ontario hospital and returned the questionnaire  Exclusion: Prior or current diagnosis of invasive or in situ breast cancer |
| **Oophorectomy or salpingo-oophorectomy** | | | | |
| ***Current Review*** |  |  |  |  |
| Kenkhuis et al., 2010200  Good | Surgical complications | Retrospective cohort, one-arm (data from medical record) | The Netherlands  Women with increased familial or genetic predisposition to breast and/or ovarian cancer undergoing RRSO between 1995 and 2006 at one site | Inclusion: Women at increased risk of developing breast and/or ovarian cancer, either with a *BRCA1/2* mutation or from an HBOC family, who elected RRSO  Exclusion: Previous ovarian cancer diagnosis |
|  |  | | | |

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Author, year**  **Quality** | **Risk level definition** | | **N** | **Demographics** | **Duration/followup** |
| **Mastectomy** |  | |  |  |  |
| ***2013 Review*** |  | |  |  |  |
| Metcalfe et al., 2004205  NA | Strong family history: had either one 1st degree relative or two 2nd degree relatives with any of the following: 1) breast cancer diagnosed <50 years; 2) ovarian cancer; or 3) male breast cancer (55.0% of population, also did not have genetic testing done)  Limited family history: none of the above (23.3% of population, also did not have genetic testing done) | | Eligible: 122  Enrolled: 75  Analyzed: 60 | Mean age at time of surgery, years: 43.5 (SD 7.8)  Mean age at time of questionnaire , years: 47.8 (SD 8.6) | January 1991 to June 2000  Mean time between surgery and questionnaire, months: 52.2 (SD 32.3) |
| **Oophorectomy or salpingo-oophorectomy** | |  | |  |  |
| ***Current Review*** |  | |  |  |  |
| Kenkhuis et al., 2010200  Good | *BRCA1* or *BRCA2* mutation or at high risk from an HBOC family without detectable mutation | | Enrolled: 179  Analyzed: 159  *BRCA1:* 61% (97/159)  *BRCA2:* 20.1% (32/159)  HBOC: 18.9% (30/159) | Median age at RRSO, years: 43.8 (range 30.3 to 68.7) | Enrolled 1995 to 2006  Followup visit 6 weeks after surgery |
|  |  | | | | |

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Author, year**  **Quality** | **Surgical procedure** | **Results** | | **Funding source** |
| **Mastectomy** |  |  | |  |
| ***2013 Review*** |  |  | |  |
| Metcalfe et al., 2004205  NA | RRM  Total: 88.3% (53/60)  Subcutaneous: 11.7% (7/60) | **Post surgical symptoms**  38 (64.4%) of women reported post surgical symptoms: numbness(27), pain(7), tingling(7), infection (7), swelling(2), breast hardness(2), bleeding(1), organizing hematoma(1), failed reconstruction(1), breathing complications(1), thrombosis(1), pulmonary embolism(1)  18 women reported only 1 symptoms, 15 women reported having had 2 symptoms and 5 women reported having 3 symptoms as a result of surgery. No difference in reporting of post-surgical symptoms based on time elapsed since mastectomy. | | Not reported |
| **Oophorectomy or salpingo-oophorectomy** | | |  |  | |
| ***Current Review*** |  |  | |  |
| Kenkhuis et al., 2010200  Good | Risk-reducing salpingo-oophorectomy: 159 women with surgery at study site and medical records available  Primary laparoscopy: 96.9% (154/159)  Primary laparotomy: 3.1% (5/159)  Laparoscopy converted to laparotomy due to complication: 0.6% (1/159)  RRSO combined with breast surgery: 16.4% (26/159) | **Intraoperative complications:** 1.3% (2/159)  Broken needle (minor): 0.6% (1/159)  Bleeding (<500cm3) (major) 0.6% (1/159)  **Post-operative complications (within 6 weeks):** 3.1% (5/159)  Excessive pain (minor): 0.6% (1/159)  Wound infection (minor): 1.3% (2/159)  Hematoma (minor): 1.3% (2/159) | | Reported as none  Authors at the University of Groningen |

**Abbreviations:** BC=breast cancer; BPM=bilateral prophylactic mastectomy; BRCA=breast cancer susceptibility gene; cm=centimeter; HBOC=hereditary breast and ovarian cancer; NA=not applicable; NR=not reported; NS=not significant; OR=odds ratio; PBSO=prophylactic bilateral salpingo-oophorectomy; PM=prophylactic mastectomy; RRM=risk-reducing mastectomy; RRSO=risk-reducing salpingo-oophorectomy