Online-Only references

Supplementary Table S1. Criteria for evaluation of the methodological quality of studies

Supplementary Table S2. Characteristics of eligible studies

Supplementary Table S3. Criteria used to define chemotherapy-induced amenorrhea in eligible studies

Online-Only references

1. Abusief ME, Missmer SA, Ginsburg ES, Weeks JC, Partridge AH. The effects of paclitaxel, dose density, and trastuzumab on treatment-related amenorrhea in premenopausal women with breast cancer. Cancer. 2010; 116: 791-798.
2. Andersson M, Kamby C, Jensen MB, Mouridsen H, Ejlertsen B, Dombernowsky P, et al. Tamoxifen in high-risk premenopausal women with primary breast cancer receiving adjuvant chemotherapy. Report from the Danish Breast Cancer co-operative Group DBCG 82B Trial. Eur J Cancer. 1999; 35: 1659-1666.
3. Badawy A, Elnashar A, El-Ashry M, Shahat M. Gonadotropin-releasing hormone agonists for prevention of chemotherapy-induced ovarian damage: prospective randomized study. Fertil Steril. 2009; 91: 694-697.
4. Beex LV, Mackenzie MA, Raemaekers JM, Smals AG, Benraad TJ, Kloppenborg PW. Adjuvant chemotherapy in premenopausal patients with primary breast cancer; relation to drug-induced amenorrhoea, age and the progesterone receptor status of the tumour. Eur J Cancer Clin Oncol. 1988; 24: 719-21.
5. Berliere M, Dalenc F, Malingret N, Vindevogel A, Piette P, Roche H, et al. Incidence of reversible amenorrhea in women with breast cancer undergoing adjuvant anthracycline-based chemotherapy with or without docetaxel. BMC Cancer. 2008; 8: 56.
6. Bianco AR, Del Mastro L, Gallo C, Perrone F, Matano E, Pagliarulo C, et al. Prognostic role of amenorrhea induced by adjuvant chemotherapy in premenopausal patients with early breast cancer. Br J Cancer. 1991; 63: 799-803.
7. Boccardo F, Rubagotti A, Bruzzi P, Cappellini M, Isola G, Nenci I, et al. Chemotherapy versus tamoxifen versus chemotherapy plus tamoxifen in node-positive, estrogen receptor-positive breast cancer patients: results of a multicentric Italian study. Breast Cancer Adjuvant Chemo-Hormone Therapy Cooperative Group. J Clin Oncol. 1990; 8: 1310-1320.
8. Bonadonna G, Rossi A, Valagussa P, Banfi A, Veronesi U. The CMF program for operable breast cancer with positive axillary nodes. Updated analysis on the disease-free interval, site of relapse and drug tolerance. Cancer. 1977; 39: 2904-2915.
9. Brincker H, Rose C, Rank F, Mouridsen HT, Jakobsen A, Dombernowsky P, et al. Evidence of a castration-mediated effect of adjuvant cytotoxic chemotherapy in premenopausal breast cancer. J Clin Oncol. 1987; 5: 1771-1778.
10. Campora E, Pronzato P, Amoroso D, Bertelli GF, Venturini M, Baldini E, et al. Prognostic factors in node positive primary breast cancer patients treated with adjuvant CMF. Anticancer Res. 1992; 12: 1555-1558.
11. Colleoni M, Sun Z, Martinelli G, Basser RL, Coates AS, Gelber RD, et al; International Breast Cancer Study Group. The effect of endocrine responsiveness on high-risk breast cancer treated with dose-intensive chemotherapy: results of International Breast Cancer Study Group Trial 15-95 after prolonged follow-up. Ann Oncol. 2009; 20: 1344-1351.
12. Davis AL, Klitus M, Mintzer DM. Chemotherapy-induced amenorrhea from adjuvant breast cancer treatment: the effect of the addition of taxanes. Clin Breast Cancer. 2005; 6: 421-424.
13. Del Mastro L, Boni L, Michelotti A, Gamucci T, Olmeo N, Gori S, et al. Effect of the gonadotropin-releasing hormone analogue triptorelin on the occurrence of chemotherapy-induced early menopause in premenopausal women with breast cancer: a randomized trial. JAMA. 2011; 306: 269-276.
14. Di Cosimo S, Alimonti A, Ferretti G, Sperduti I, Carlini P, Papaldo P, et al. Incidence of chemotherapy-induced amenorrhea depending on the timing of treatment by menstrual cycle phase in women with early breast cancer. Ann Oncol. 2004; 15: 1065-1071.
15. Fornier MN, Modi S, Panageas KS, Norton L, Hudis C. Incidence of chemotherapy-induced, long-term amenorrhea in patients with breast carcinoma age 40 years and younger after adjuvant anthracycline and taxane. Cancer. 2005; 104: 1575-1579.
16. Ganz PA, Land SR, Geyer CE Jr, Cecchini RS, Costantino JP, Pajon ER, et al. Menstrual history and quality-of-life outcomes in women with node-positive breast cancer treated with adjuvant therapy on the NSABP B-30 trial. J Clin Oncol. 2011; 29: 1110-1116.
17. Gerber B, von Minckwitz G, Stehle H, Reimer T, Felberbaum R, Maass N, et al; German Breast Group Investigators. Effect of luteinizing hormone-releasing hormone agonist on ovarian function after modern adjuvant breast cancer chemotherapy: the GBG 37 ZORO study. J Clin Oncol. 2011; 29: 2334-2341.
18. Goldhirsch A, Gelber RD, Castiglione M. The magnitude of endocrine effects of adjuvant chemotherapy for premenopausal breast cancer patients. The International Breast Cancer Study Group. Ann Oncol. 1990; 1: 183-188.
19. Goodwin PJ, Ennis M, Pritchard KI, Trudeau M, Hood N. Risk of menopause during the first year after breast cancer diagnosis. J Clin Oncol. 1999; 17: 2365-2370.
20. Han HS, Ro J, Lee KS, Nam BH, Seo JA, Lee DH, et al. Analysis of chemotherapy-induced amenorrhea rates by three different anthracycline and taxane containing regimens for early breast cancer. Breast Cancer Res Treat. 2009; 115: 335-342.
21. Hortobagyi GN, Buzdar AU, Marcus CE, Smith TL. Immediate and long-term toxicity of adjuvant chemotherapy regimens containing doxorubicin in trials at M.D. Anderson Hospital and Tumor Institute. NCI Monogr. 1986; 1: 105-109.
22. Howell A, Bush H, George WD, Howat JM, Crowther D, Sellwood RA, et al. Controlled trial of adjuvant chemotherapy with cyclophosphamide, methotrexate, and fluorouracil for breast cancer. Lancet. 1984; 2: 307-311.
23. International Breast Cancer Study Group, Colleoni M, Gelber S, Goldhirsch A, Aebi S, Castiglione-Gertsch M, Price KN, et al. Tamoxifen after adjuvant chemotherapy for premenopausal women with lymph node-positive breast cancer: International Breast Cancer Study Group Trial 13-93. J Clin Oncol. 2006; 24: 1332-1341.
24. International Breast Cancer Study Group (IBCSG), Castiglione-Gertsch M, O'Neill A, Price KN, Goldhirsch A, Coates AS, Colleoni M, et al. Adjuvant chemotherapy followed by goserelin versus either modality alone for premenopausal lymph node-negative breast cancer: a randomized trial. J Natl Cancer Inst. 2003; 95: 1833-1846.
25. Kil WJ, Ahn SD, Shin SS, Lee SW, Choi EK, Kim JH, et al. Treatment-induced menstrual changes in very young (<35 years old) breast cancer patients. Breast Cancer Res Treat. 2006; 96: 245-250.
26. Jonat W, Kaufmann M, Sauerbrei W, Blamey R, Cuzick J, Namer M, et al; Zoladex Early Breast Cancer Research Association Study. Goserelin versus cyclophosphamide, methotrexate, and fluorouracil as adjuvant therapy in premenopausal patients with node-positive breast cancer: The Zoladex Early Breast Cancer Research Association Study. J Clin Oncol. 2002; 20: 4628-4635.
27. Jung M, Shin HJ, Rha SY, Jeung HC, Hong S, Moon YW, et al. The clinical outcome of chemotherapy-induced amenorrhea in premenopausal young patients with breast cancer with long-term follow-up. Ann Surg Oncol. 2010; 17: 3259-3268.
28. Lee S, Kil WJ, Chun M, Jung YS, Kang SY, Kang SH, et al. Chemotherapy-related amenorrhea in premenopausal women with breast cancer. Menopause. 2009; 16: 98-103.
29. Lower EE, Blau R, Gazder P, Tummala R. The risk of premature menopause induced by chemotherapy for early breast cancer. J Womens Health Gend Based Med. 1999; 8: 949-954.
30. Ludwig Breast Cancer Study Group. A randomized trial of adjuvant combination chemotherapy with or without prednisone in premenopausal breast cancer patients with metastases in one to three axillary lymph nodes. Cancer Res. 1985; 45: 4454-4459.
31. Marini G, Murray S, Goldhirsch A, Gelber RD, Castiglione-Gertsch M, Price KN, et al. The effect of adjuvant prednisone combined with CMF on patterns of relapse and occurrence of second malignancies in patients with breast cancer. International (Ludwig) Breast Cancer Study Group. Ann Oncol. 1996; 7: 245-250.
32. Martin M, Pienkowski T, Mackey J, Pawlicki M, Guastalla JP, Weaver C, et al; Breast Cancer International Research Group 001 Investigators. Adjuvant docetaxel for node-positive breast cancer. N Engl J Med. 2005; 352: 2302-2313.
33. Mehta RR, Beattie CW, Das Gupta TK. Endocrine profile in breast cancer patients receiving chemotherapy. Breast Cancer Res Treat. 1992; 20: 125-132.
34. Meng K, Tian W, Zhou M, Chen H, Deng Y. Impact of chemotherapy-induced amenorrhea in breast cancer patients: the evaluation of ovarian function by menstrual history and hormonal levels. World J Surg Oncol. 2013; 11: 101.
35. Minisini AM, Menis J, Valent F, Andreetta C, Alessi B, Pascoletti G, et al. Determinants of recovery from amenorrhea in premenopausal breast cancer patients receiving adjuvant chemotherapy in the taxane era. Anticancer Drugs. 2009; 20: 503-507.
36. Munster PN, Moore AP, Ismail-Khan R, Cox CE, Lacevic M, Gross-King M, et al. Randomized trial using gonadotropin-releasing hormone agonist triptorelin for the preservation of ovarian function during (neo)adjuvant chemotherapy for breast cancer. J Clin Oncol. 2012; 30: 533-538.
37. Najafi S, Djavid GE, Mehrdad N, Rajaii E, Alavi N, Olfatbakhsh A, et al. Taxane-based regimens as a risk factor for chemotherapy-induced amenorrhea. Menopause. 2011; 18: 208-212.
38. Narmadha MP, Malaikkal V, Rajendran NN. Assessment of chemotherapy induced amenorrhea (CIA) in hormone receptor positive premenopausal women with breast cancer. Research Journal of Pharmaceutical, Biological and Chemical Sciences 2012; 3: 97-106.
39. Okanami Y, Ito Y, Watanabe C, Iijima K, Iwase T, Tokudome N, et al. Incidence of chemotherapy-induced amenorrhea in premenopausal patients with breast cancer following adjuvant anthracycline and taxane. Breast Cancer. 2011; (3):182-188.
40. Padmanabhan N, Wang DY, Moore JW, Rubens RD. Ovarian function and adjuvant chemotherapy for early breast cancer. Eur J Cancer Clin Oncol. 1987; 23: 745-748.
41. Pagani O, O'Neill A, Castiglione M, Gelber RD, Goldhirsch A, Rudenstam CM, et al. Prognostic impact of amenorrhoea after adjuvant chemotherapy in premenopausal breast cancer patients with axillary node involvement: results of the International Breast Cancer Study Group (IBCSG) Trial VI. Eur J Cancer. 1998; 34: 632-640.
42. Partridge A, Gelber S, Gelber RD, Castiglione-Gertsch M, Goldhirsch A, Winer E. Age of menopause among women who remain premenopausal following treatment for early breast cancer: long-term results from International Breast Cancer Study Group Trials V and VI. Eur J Cancer. 2007; 43: 1646-1653.
43. Parulekar WR, Day AG, Ottaway JA, Shepherd LE, Trudeau ME, Bramwell V, et al; National Cancer Institute of Canada Clinical Trials Group. Incidence and prognostic impact of amenorrhea during adjuvant therapy in high-risk premenopausal breast cancer: analysis of a National Cancer Institute of Canada Clinical Trials Group Study--NCIC CTG MA.5. J Clin Oncol. 2005; 23: 6002-6008.
44. Pérez-Fidalgo JA, Roselló S, García-Garré E, Jordá E, Martín-Martorell P, Bermejo B, et al. Incidence of chemotherapy-induced amenorrhea in hormone-sensitive breast cancer patients: the impact of addition of taxanes to anthracycline-based regimens. Breast Cancer Res Treat. 2010; 120: 245-251.
45. Petrek JA, Naughton MJ, Case LD, Paskett ED, Naftalis EZ, Singletary SE, et al. Incidence, time course, and determinants of menstrual bleeding after breast cancer treatment: a prospective study. J Clin Oncol. 2006; 24: 1045-1051.
46. Poikonen P, Saarto T, Elomaa I, Joensuu H, Blomqvist C. Prognostic effect of amenorrhoea and elevated serum gonadotropin levels induced by adjuvant chemotherapy in premenopausal node-positive breast cancer patients. Eur J Cancer. 2000; 36: 43-48.
47. Pourali L, Taghizadeh Kermani A, Ghavamnasiri MR, Khoshroo F, Hosseini S, Asadi M, et al. Incidence of chemotherapy-induced amenorrhea after adjuvant chemotherapy with taxane and anthracyclines in young patients with breast cancer. Iran J Cancer Prev. 2013; 6: 147-150.
48. Reh A, Oktem O, Oktay K. Impact of breast cancer chemotherapy on ovarian reserve: a prospective observational analysis by menstrual history and ovarian reserve markers. Fertil Steril. 2008; 90: 1635-1639.
49. Reyno LM, Levine MN, Skingley P, Arnold A, Abu Zahra H. Chemotherapy induced amenorrhoea in a randomised trial of adjuvant chemotherapy duration in breast cancer. Eur J Cancer. 1992; 29A: 21-23.
50. Richards MA, O'Reilly SM, Howell A, George WD, Fentiman IS, Chaudary MA, et al. Adjuvant cyclophosphamide, methotrexate, and fluorouracil in patients with axillary node-positive breast cancer: an update of the Guy's/Manchester trial. J Clin Oncol. 1990; 8: 2032-2039.
51. Roché H, Kerbrat P, Bonneterre J, Fargeot P, Fumoleau P, Monnier A, et al. Complete hormonal blockade versus epirubicin-based chemotherapy in premenopausal, one to three node-positive, and hormone-receptor positive, early breast cancer patients: 7-year follow-up results of French Adjuvant Study Group 06 randomised trial. Ann Oncol. 2006; 17: 1221-1227.
52. Rose DP, Davis TE. Effects of adjuvant chemohormonal therapy on the ovarian and adrenal function of breast cancer patients. Cancer Res. 1980; 40: 4043-4047.
53. Rosendahl M, Ahlgren J, Andersen J, Bergh J, Blomquist C, Lidbrink E, et al. The risk of amenorrhoea after adjuvant chemotherapy for early stage breast cancer is related to inter-individual variations in chemotherapy-induced leukocyte nadir in young patients: data from the randomised SBG 2000-1 study. Eur J Cancer. 2009; 45: 3198-3204.
54. Ruddy KJ, O'Neill A, Miller KD, Schneider BP, Baker E, Sparano JA, et al. Biomarker prediction of chemotherapy-related amenorrhea in premenopausal women with breast cancer participating in E5103. Breast Cancer Res Treat. 2014; 144: 591-597.
55. Saarto T, Blomqvist C, Ehnholm C, Taskinen MR, Elomaa I. Effects of chemotherapy-induced castration on serum lipids and apoproteins in premenopausal women with node-positive breast cancer. J Clin Endocrinol Metab. 1996; 81: 4453-4457.
56. Samaan NA, deAsis DN Jr, Buzdar AU, Blumenschein GR. Pituitary-ovarian function in breast cancer patients on adjuvant chemoimmunotherapy. Cancer. 1978; 41: 2084-2087.
57. Shapiro CL, Phillips G, Van Poznak CH, Jackson R, Leboff MS, Woodard S, et al. Baseline bone mineral density of the total lumbar spine may predict for chemotherapy-induced ovarian failure. Breast Cancer Res Treat. 2005; 90: 41-46.
58. Su HI, Sammel MD, Velders L, Horn M, Stankiewicz C, Matro J, et al. Association of cyclophosphamide drug-metabolizing enzyme polymorphisms and chemotherapy-related ovarian failure in breast cancer survivors. Fertil Steril. 2010 ;94: 645-654.
59. Sukumvanich P, Case LD, Van Zee K, Singletary SE, Paskett ED, Petrek JA, et al. Incidence and time course of bleeding after long-term amenorrhea after breast cancer treatment: a prospective study. Cancer. 2010; 116: 3102-3111.
60. Sverrisdottir A, Nystedt M, Johansson H, Fornander T. Adjuvant goserelin and ovarian preservation in chemotherapy treated patients with early breast cancer: results from a randomized trial. Breast Cancer Res Treat. 2009; 117: 561-567.
61. Swain SM, Jeong JH, Geyer CE Jr, Costantino JP, Pajon ER, Fehrenbacher L, et al. Longer therapy, iatrogenic amenorrhea, and survival in early breast cancer. N Engl J Med. 2010; 362: 2053-2065.
62. Tancini G, Bajetta E, Marchini S, Valagussa P, Bonadonna G, Veronesi U. Preliminary 3-year results of 12 versus 6 cycles of surgical adjuvant CMF in premenopausal breast cancer. Cancer Clin Trials. 1979; 2: 285-292.
63. Tham YL, Sexton K, Weiss H, Elledge R, Friedman LC, Kramer R. The rates of chemotherapy-induced amenorrhea in patients treated with adjuvant doxorubicin and cyclophosphamide followed by a taxane. Am J Clin Oncol. 2007; 30: 126-132.
64. Tiong V, Rozita AM, Taib NA, Yip CH, Ng CH. Incidence of chemotherapy-induced ovarian failure in premenopausal women undergoing chemotherapy for breast cancer. World J Surg. 2014; 38: 2288-2296.
65. Toma S, Repetto L, Giacchero A, Coialbu T, Costantini M, Addamo GF, et al. Chemotherapy-induced amenorrhea and other clinical and pathological parameters in the prognosis of breast cancer patients. J Chemother. 1992; 4: 321-325.
66. Tormey DC, Gray R, Gilchrist K, Grage T, Carbone PP, Wolter J, et al. Adjuvant chemohormonal therapy with cyclophosphamide, methotrexate, 5-fluorouracil, and prednisone (CMFP) or CMFP plus tamoxifen compared with CMF for premenopausal breast cancer patients. An Eastern Cooperative Oncology Group trial. Cancer. 1990; 65: 200-206.
67. Valagussa P, Moliterni A, Zambetti M, Bonadonna G. Long-term sequelae from adjuvant chemotherapy. Recent Results Cancer Res. 1993; 127: 247-255.
68. Vanhuyse M, Fournier C, Bonneterre J. Chemotherapy-induced amenorrhea: influence on disease-free survival and overall survival in receptor-positive premenopausal early breast cancer patients. Ann Oncol. 2005; 16: 1283-1288.
69. Vehmanen L, Elomaa I, Blomqvist C, Saarto T. Tamoxifen treatment after adjuvant chemotherapy has opposite effects on bone mineral density in premenopausal patients depending on menstrual status. J Clin Oncol. 2006; 24: 675-680.
70. Vehmanen L, Saarto T, Elomaa I, Mäkelä P, Välimäki M, Blomqvist C. Long-term impact of chemotherapy-induced ovarian failure on bone mineral density (BMD) in premenopausal breast cancer patients. The effect of adjuvant clodronate treatment. Eur J Cancer. 2001; 37: 2373-2378.
71. Venturini M, Del Mastro L, Aitini E, Baldini E, Caroti C, Contu A, et al. Dose-dense adjuvant chemotherapy in early breast cancer patients: results from a randomized trial. J Natl Cancer Inst. 2005; 97: 1724-1733.
72. Yoo C, Yun MR, Ahn JH, Jung KH, Kim HJ, Kim JE, et al. Chemotherapy-induced amenorrhea, menopause-specific quality of life, and endocrine profiles in premenopausal women with breast cancer who received adjuvant anthracycline-based chemotherapy: a prospective cohort study. Cancer Chemother Pharmacol. 2013; 72: 565-575.
73. Yu B, Douglas N, Ferin MJ, Nakhuda GS, Crew K, Lobo RA, et al. Changes in markers of ovarian reserve and endocrine function in young women with breast cancer undergoing adjuvant chemotherapy. Cancer. 2010; 116: 2099-2105.
74. Zekri JM, El-Helw LM, Purohit OP, Hatton MQ, Coleman RE. Epirubicin/vinorelbine adjuvant chemotherapy in young women with breast cancer is associated with preservation of menstrual function. Clin Oncol (R Coll Radiol) 2008; 20: 513-516.
75. Zhou WB, Yin H, Liu XA, Zha XM, Chen L, Dai JC, et al. Incidence of chemotherapy-induced amenorrhea associated with epirubicin, docetaxel and navelbine in younger breast cancer patients. BMC Cancer. 2010; 10: 281.

**Table S1. Criteria for evaluation of the methodological quality of studies**

|  |
| --- |
| **Sample Definition and Selection**  1. Is the study design prospective, retrospective, or not applicable?  2. Are critical inclusion/exclusion criteria clearly stated?  3. Are the inclusion/exclusion criteria measured using valid and reliable measures?  4. Was the sample size sufficiently large to detect a clinically significant difference (> 100 patients) |
| **Source of information**  5. Are interventions/exposures (variables tested as potential risk factors for amenorrhea) assessed using valid and reliable measures, implemented consistently across all study participants?  6. Are outcomes (presence of amenorrhea) assessed using valid and reliable measures, implemented consistently across all study participants? |
| **Follow-up**  7. Is the length of follow-up the same for all groups?  8. Is the length of time following the intervention/exposure sufficient to support the evaluation of  primary outcomes (at least 12 months)?  9. Did attrition from any group exceed > 30%?  10. Did attrition differ between groups by more than 20%? |
| **Analysis Comparability / Outcome**  11. Were the important confounding and effect modifying variables taken into account in the  design and/or analysis?  12. In cases of high loss to follow-up (or differential loss to follow-up), is the impact assessed (e.g.,  through sensitivity analysis or other adjustment method)?  13. Are the statistical methods used to assess the primary benefit outcomes appropriate to the  data?  14. Are results believable taking study limitations into consideration? |

**Table S2. Characteristics of eligible studies**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Author (ref)** | **Country** | **Study type** | **Follow-up (median, months)** | **Sample size** | **Multivariate analysis for risk factors** | **Study quality** |
| Abusief (1) | USA | Retrospective cohort | 33 | 431 | Yes | 11 |
| Andersson (2) | Denmark | RCT | 146 | 634 | No | NA |
| Badaway (3) | Egypt | RCT | NR | 78 | No | NA |
| Beex (4) | The Netherlands | Retrospective cohort | 37 | 77 | No | 3 |
| Berliere (5) | Multinational | Retrospective cohort | 79 | 154 | No | 6 |
| Bianco (6) | Italy | Retrospective cohort | 69 | 221 | No | 5 |
| Boccardo (7) | Italy | RCT | 40 | 336 | No | NA |
| Bonadonna (8) | Italy | RCT | 22 | 90 | No | NA |
| Brincker (9) | Denmark | RCT | 64 | 847 | No | NA |
| Campora (10) | Italy | Retrospective cohort | 72 | 108 | No | 5 |
| Colleoni (11) | Italy | RCT | 100 | 344 | No | NA |
| Davis (12) | USA | Retrospective cohort | NR | 159 | No | 4 |
| Del Mastro (13) | Italy | RCT | NR | 133 | Yes | NA |
| Di Cosimo (14) | Italy | Retrospective cohort | NR | 111 | Yes | 7 |
| Fornier (15) | USA | Retrospective cohort | 38 | 166 | No | 8 |
| Ganz (16) | Multinational | RCT | NR | 2149 | No | NA |
| Gerber (17) | Germany | RCT | NR | 60 | No | NA |
| Goldhirsch (18) | Multinational | RCT | 48 | 1127 | No | NA |
| Goodwin (19) | Canada | Prospective cohort | 12 | 183 | Yes | 12 |
| Han (20) | South Korea | Prospective cohort | 40 | 285 | Yes | 14 |
| Hortobagyi (21) | USA | Retrospective cohort | NR | 69 | No | 6 |
| Howell (22) | UK | RCT | NR | 81 | No | NA |
| IBCSG (23) | Multinational | RCT | 70 | 1065 | No | NA |
| IBCSG (24) | Multinational | RCT | 84 | 360 | No | NA |
| Kil (25) | South Korea | Retrospective cohort | 54 | 165 | No | 5 |
| Jonat (26) | Multinational | RCT | 72 | 802 | No | NA |
| Jung (27) | South Korea | Retrospective cohort | 110 | 241 | Yes | 9 |
| Lee (28) | South Korea | Retrospective cohort | 37 | 326 | Yes | 10 |
| Lower (29) | USA | Retrospective cohort | 24 | 109 | No | 6 |
| Ludwig BCSG (30) | Multinational | RCT | 48 | 340 | No | NA |
| Marini (31) | Multinational | RCT | 156 | 491 | No | NA |
| Martin (32) | Multinational | RCT | 55 | 823 | No | NA |
| Mehta (33) | USA | Prospective cohort | NR | 70 | No | 5 |
| Meng (34) | China | Retrospective cohort | 27 | 73 | No | 5 |
| Minisini (35) | Italy | Retrospective cohort | 34 | 145 | Yes | 8 |
| Munster (36) | USA | RCT | 18 | 21 | No | NA |
| Najafi (37) | Iran | Retrospective cohort | 36 | 226 | Yes | 8 |
| Narmadha (38) | India | Cross sectional | NR | 50 | No | 4 |
| Okanami (39) | Japan | Cross sectional | 28 | 66 | Yes | 6 |
| Padmanabhan (40) | UK | RCT | 47 | 35 | No | NA |
| Pagani (41) | Multinational | RCT | 60 | 1196 | No | NA |
| Partridge (42) | Multinational | RCT | 156 + 228 | 767 | No | NA |
| Parulekar (43) | Canada | Retrospective cohort | 106 | 328 | No | 7 |
| Pérez-Fildago (44) | Spain | Retrospective cohort | NR | 305 | No | 7 |
| Petrek (45) | USA | Prospective cohort | 45 | 595 | Yes | 13 |
| Poikonen (46) | Finland | Prospective cohort | 72 | 116 | No | 7 |
| Pourali (47) | Iran | Cross sectional | NR | 119 | No | 5 |
| Reh (48) | USA | Prospective cohort | 28 | 41 | No | 7 |
| Reyno (49) | Canada | RCT | NR | 95 | No | NA |
| Richards (50) | UK | RCT | 96 | 90 | No | NA |
| Roché (51) | France | RCT | 84 | 169 | No | NA |
| Rose (52) | USA | Retrospective cohort | NR | 38 | No | 6 |
| Rosendahl (53) | Multinational | RCT | NR | 836 | No | NA |
| Ruddy (54) | USA | Prospective cohort | NR | 124 | Yes | 9 |
| Saarto (55) | Finland | Prospective cohort | NR | 57 | No | 7 |
| Samaan (56) | USA | Prospective cohort | NR | 55 | No | 5 |
| Shapiro (57) | USA | Prospective cohort | NR | 49 | No | 7 |
| Su (58) | USA | Prospective cohort | 62 | 111 | Yes | 8 |
| Sukumvanich (59) | USA | Prospective cohort | NR | 439 | Yes | 12 |
| Sverrisdottir (60) | Multinational | RCT | NR | 31 | No | NA |
| Swain (61) | USA | RCT | 73 | 2343 | No | NA |
| Tancini (62) | Italy | RCT | 22 | 287 | No | NA |
| Tham (63) | USA | Cross sectional | NR | 191 | Yes | 8 |
| Tiong (64) | Malaysia | Cross sectional | NR | 87 | No | 7 |
| Toma (65) | Italy | Retrospective cohort | NR | 146 | No | 5 |
| Tormey (66) | USA | RCT | 92 | 553 | No | NA |
| Valagussa (67) | Italy | Retrospective cohort | 44 | 494 | No | 5 |
| Vanhuyse (68) | France | Retrospective cohort | 108 | 130 | No | 6 |
| Vehmanen (98) | Finland | RCT | 36 | 111 | No | NA |
| Vehmanen (70) | Finland | Prospective cohort | 60 | 73 | No | 8 |
| Venturini (71) | Italy | RCT | 125 | 503 | No | NA |
| Yoo (72) | South Korea | Prospective cohort | 18 | 312 | Yes | 12 |
| Yu (73) | USA | Prospective cohort | NR | 26 | No | 7 |
| Zekri (74) | UK | Retrospective cohort | 39 | 26 | No | 4 |
| Zhou (75) | China | Cross sectional | 39 | 170 | Yes | 7 |

Abbreviations: RCT, Randomized controlled trial; NA, Not Applicable; NR, Not Reported.

**Table S3. Criteria used to define chemotherapy-induced amenorrhea in eligible studies**

|  |  |
| --- | --- |
| **Definition criteria** | ***N* of studies (%)** |
| *Different duration from end of chemotherapy*  No menstrual bleeding for 6 months  No menstrual bleeding for 12 months  No menstrual bleeding for different durations within the same study | 4 (5)  7 (9)  3 (4) |
| *Different duration from start of chemotherapy*  No menstrual bleeding within 6 months  No menstrual bleeding within 10 months  No menstrual bleeding within at least 12 months  No menstrual bleeding for different durations within the same study | 5 (7)  1 (1)  9 (12)  3 (4) |
| *Different duration from randomization*  No menstrual bleeding within 6 months  No menstrual bleeding within 7-9 months  No menstrual bleeding within at least 12 months  No menstrual bleeding for different durations within the same study | 1 (1)  2 (3)  1 (1)  1 (1) |
| *Definition based on both duration of amenorrhea and interval from chemotherapy*  No menstrual bleeding during chemotherapy and at least 3 months  No menstrual bleeding during chemotherapy and at least 6 months  No menstrual bleeding during chemotherapy and during follow up  No menstrual bleeding within 3 months from start of chemotherapy and for at least 3 months  No menstrual bleeding within 9 months from surgery and for at least 3 months  No menstrual bleeding within 12 months from start of chemotherapy for at least 1 month  No menstrual bleeding within 12 months from start of chemotherapy for at least 3 months  No menstrual bleeding within 12 months from start of chemotherapy for at least 6 months  No menstrual bleeding within 12 months from start of chemotherapy for at least 12 months  No menstrual bleeding within 12 months from end of chemotherapy for at least 6 months | 4 (5)  1 (1)  2 (3)  2 (3)  1 (1)  1 (1)  2 (3)  4 (5)  2 (3)  2 (3) |
| *No menstrual bleeding during chemotherapy* | 2 (3) |
| *No clear definition* | 15 (20) |
| *Laboratory criteria*  Rise of gonadotropins | 3 (4) |
| *Recovery*  No recovery of menstrual bleeding  Not included in the definition | 5 (7)  70 (93) |