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Management of Chemotherapy-Induced Alopecia: A Systematic Review and Meta-Analysis

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ABSTRACT

Introduction: Chemotherapy-induced alopecia (CIA) is a common and distressing side effect that can lead to treatment refusal or discontinuation.

Objectives: This systematic review and meta-analysis evaluated the effectiveness, safety, and patient-reported outcomes of interventions for CIA.

Methodology: Following PRISMA guidelines, we searched PubMed, EBSCO, Medline, Google Scholar, Wiley, and Web of Science for relevant randomized and quasi-experimental trials.

Results: Thirteen studies comprising over 1,200 patients were included. Scalp cooling reduced moderate-to-severe CIA by more than half. Acceptable hair preservation rates ranged from 75–95% with cooling versus 8–49% in controls. In a meta-analysis of three trials, cooling increased the odds of maintaining cosmetically acceptable hair over fourteen-fold (OR 14.42; 95% CI 2.79–74.63; P = 0.001; I^2 = 62%). A separate meta-analysis of four trials (N = 262) showed a 90% reduction in the odds of moderate-to-severe alopecia (OR 0.10; 95% CI 0.02–0.54; P = 0.007; I^2 = 70%). Patient-reported need for wigs fell from 45–84% in controls to 5–33% with cooling. Adverse events were

mild (headaches in up to 25%, chills, cold sensation) and led to discontinuation in fewer than 30% of cooled patients.

Conclusion: Scalp cooling is a safe, well-tolerated intervention that substantially mitigates hair loss, achieves high patient satisfaction, and reduces the psychosocial burden of CIA. It should be considered standard supportive care for patients receiving hair-toxic chemotherapy.

Introduction

Around the world, 18.1 million people received a cancer diagnosis in 2020 (not including non-melanoma skin cancers), and by 2040, that figure is expected to increase to 26 million. The number of patients who need first-line chemotherapy annually is expected to rise by around 50% to 15.0 million by 2040 [1]. An estimated 65% of chemotherapy patients are predicted to experience chemotherapy-induced alopecia (CIA) and potential alterations in the color, texture, quantity, and growth of their hair [2,3]. The National Cancer Database (NCDB) classifies several immunotherapies and numerous popular targeted treatments such as chemotherapy [4]. Depending on the chemotherapy protocol, the prevalence of CIA varies; severe hair loss is especially linked to anthracyclines, taxanes, and alkylating agents [5]. Although research indicates that 65–100% of patients, depending on the medication and dosage, have some degree of alopecia [6], the issue is frequently neglected in clinical practice, giving patients few alternatives for care or prevention [7].

Direct toxicity from chemotherapeutic drugs to rapidly dividing hair follicle cells, especially during the anagen (growth) phase of the hair cycle, is a pathophysiological aspect of CIA [8]. Regrowth is frequently delayed, and changes in texture and color occur due to this disruption, which can cause hair shaft breakage, thinning, or total loss [9]. The necessity for effective therapy is highlighted by the psychological impact and duration of hair loss, even though it is usually reversible, especially when using certain regimens such as taxane-based therapies [10]. Furthermore, the significance of treating CIA as a vital part of comprehensive cancer care is underscored by individual and cultural variations in how hair loss is seen [11]. Patient results can be further complicated by the emotional toll of CIA, which has an impact on quality of life and can result in anxiety, depression, and decreased treatment adherence, which may additionally influence choices about the advantages and disadvantages of treatment [12].

Scalp cooling methods, medication, and supportive care approaches are just a few of the treatments and preventive measures that have been employed to reduce CIA [13]. Depending on the chemotherapy regimen and cooling technology employed, scalp cooling, one of the most researched preventive techniques, reduces scalp temperature to decrease the transport of drugs to hair follicles. Success rates have been reported to range from 10% to 90% [14]. The potential of pharmacological treatments, such as minoxidil, to encourage hair regrowth has been investigated; however, the data remain conflicting [15]. The goal of emerging therapies such as topical medications and innovative biologics is to preserve hair follicles or promote healing; however, additional research is necessary to confirm their effectiveness and safety [4]. Treating the psychosocial effects of CIA also requires non-pharmacological treatments such as counseling and cosmetics like wigs or scalp coverage [16].

Despite these developments, numerous unanswered questions remain about the most effective ways to prevent and treat CIA in the literature. It has been challenging to draw firm conclusions regarding the effectiveness of current therapies due to study design variability, small sample sizes, and a lack of standardized outcome measures [17]. Additionally, there is a lack of knowledge about the long-term effects of preventive strategies such as cooling the scalp, hair regeneration, and scalp health [18]. The necessity for a thorough synthesis of the available data to direct clinical treatment and guide future research is highlighted by the lack of consensus guidelines for managing CIA [19].

Study Objectives

By investigating the clinical and psychological aspects of CIA, this study aimed to fill significant knowledge gaps and identify opportunities to provide innovative patient care. By integrating data on the efficacy, safety, and impact on patient outcomes of CIA, this systematic review aimed to identify best practices for managing and preventing CIA while also investigating the barriers to its use in various healthcare settings. This will provide a solid foundation for evidence-based recommendations.

Methodology

This systematic review was performed following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses

(PRISMA) guidelines [20]. It was registered in PROSPERO with ID: CRD420251082500.

Literature Search Strategy

To identify relevant studies, a comprehensive literature search was performed across multiple electronic databases: PubMed, EBSCO, Medline, Google Scholar, Wiley, and Web of Science. The search utilized the following keywords: ("chemotherapy-induced alopecia" OR "chemotherapy hair loss") AND (treatment OR prevention OR intervention) AND (scalp cooling OR minoxidil OR PRP).

Selection of Articles and Data Extraction

Following the initial database search, two reviewers independently screened the titles and abstracts of retrieved articles to identify potentially relevant studies based on predefined inclusion criteria. The full texts of these selected articles were then obtained and assessed for final eligibility, again by two independent reviewers. Any disagreement regarding study inclusion were resolved through discussion and consensus or by consultation with a third reviewer, if necessary. Data from the included studies were extracted by two reviewers using a standardized data extraction form designed for this review. The information collected included study characteristics (first author, publication year, study design, country), patient demographics (number of patients, mean age, sex, cancer type, chemotherapy used, type and severity of alopecia), intervention details (treatment used, duration, frequency, comparator specifics), efficacy outcomes (alopecia reduction, patient satisfaction), and safety outcomes (number and percentage of patients with treatment-emergent adverse events, common and serious adverse events).

Quality Assessment

The Cochrane risk-of-bias tool for randomized trials (RoB2) was employed to evaluate the risk of bias in the studies. It focuses on five crucial areas: the process of randomization, any deviations from the planned interventions, the handling of missing data, the accuracy of outcome measurements, and the selection of outcomes that were reported. Each area is categorized as having low risk, some concerns, or high risk of bias, and the overall bias risk for each study is established based on these evaluations [21]. Studies with a high risk of bias were excluded from the meta-analysis.

Statistical Analysis

We used RevMan 5.4.1 [22]. Dichotomous data were analyzed as proportions and a 95% confidence interval (CI). Statistical heterogeneity among the studies was assessed using I-squared (I^2) and chi-squared (Chi^2) statistics. I^2 values of 50% were indicative of high heterogeneity.

Results

PRISMA Diagram

A total of 1,375 papers were extracted from six databases: PubMed, EBSCO, Medline, Google Scholar, Wiley, and Web of Science. Out of these, 923 were removed as duplicates. Of the remaining 452 articles, only 76 were initially included in the review. Ultimately, 13 articles were deemed suitable for analysis as they were RCTs. Thus, thirteen articles were included in the systematic review (Figure 1).

This review of 13 randomized and quasi-experimental studies conducted from the 1980s to 2022 demonstrated that scalp cooling, usually achieved using electrically chilled caps (such as Paxman systems), significantly reduces chemotherapy-induced hair loss across various cancers, including breast, ovarian, endometrial, lung, prostate, and gastrointestinal cancers. These studies involved groups of 25–142 patients, with most comparing extended post-infusion cooling times (ranging from 45 to 150 minutes) to shorter durations (20 to 90 minutes) or to no cooling at all. The results showed that scalp cooling lowered median alopecia scores. For example, in a 2019 study by Komen, the rates of grade 2–3 alopecia dropped from 49% to 33%. Similarly, in Nangia's 2017 study, control patients experienced 100% grade 2 alopecia, whereas those using scalp cooling had a 49.5% success rate (grades 0–1). Moreover, scalp cooling was more effective than non-cooling comparators and alternative interventions, such as reflexology massage, topical lotions, placebo sprays, or minoxidil. Across these diverse settings and chemotherapy regimens, longer and customized cooling protocols provided the most significant hair preservation benefits while maintaining an acceptable safety profile, as indicated in Table 1.

Numerous clinical trials have shown that scalp cooling, which is administered before, during, and after chemotherapy, significantly reduces the incidence of moderate-to-severe hair loss by at least 50%. In fact, 70–95% of patients can retain cosmetically acceptable hair and often do not need to use wigs or head coverings. The high level of patient satisfaction reflects the positive impact on self-image and quality of life. Although some mild side effects have been reported, such as headaches, chills, cold sensations, and scalp tenderness, these generally lead to dropout rates of less than 30%. In comparison, alternative methods like topical lotions, reflexology, or placebo sprays have shown only modest benefits. Overall, scalp cooling is recognized as a safe, well-tolerated, and highly effective approach to reducing hair loss caused by chemotherapy, as detailed in Table 2.

Figure 2 presents the quality assessment of thirteen RCT studies, evaluated using the ROB-2 quality assessment tool. Most of them had some concerns.

In a meta-analysis of three randomized trials, scalp cooling significantly increased the likelihood of maintaining

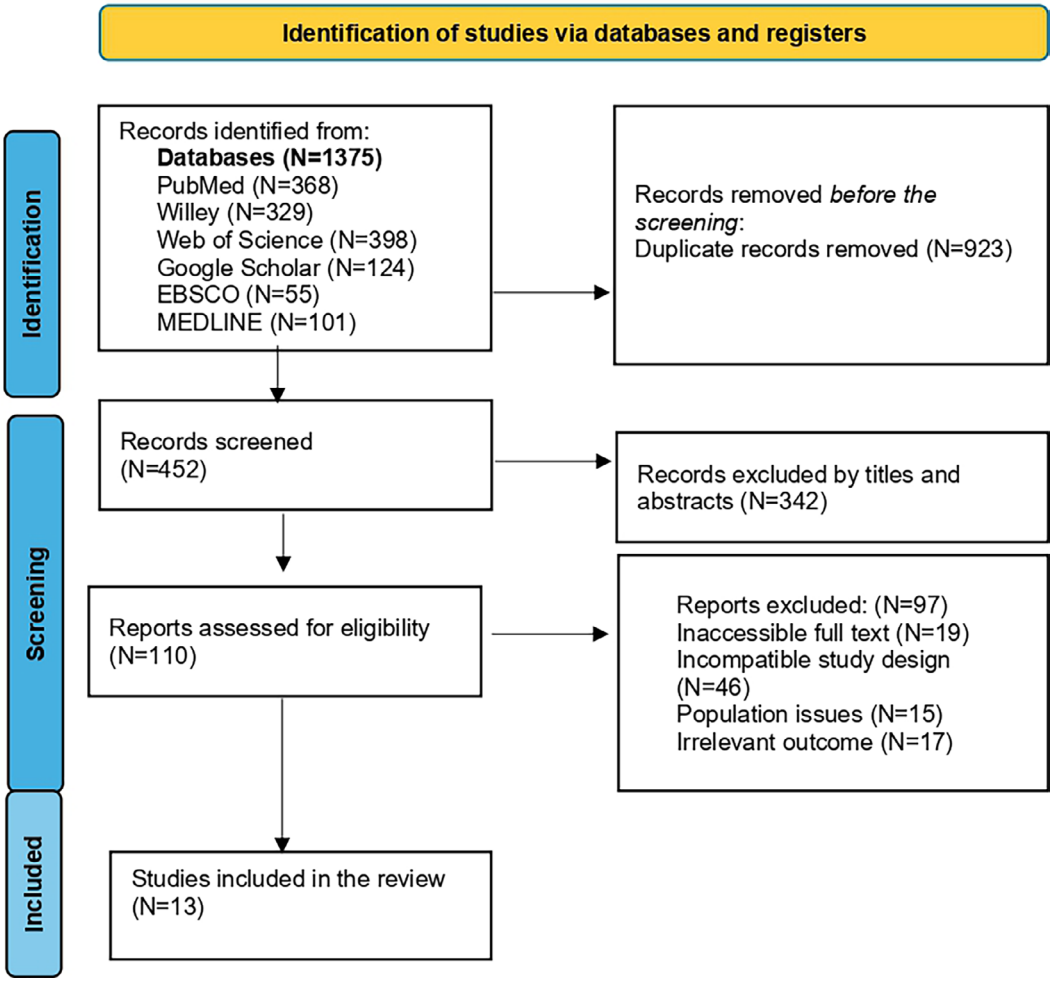

Figure 1. Schematic representation of the criteria for selecting studies in the systematic review.

cosmetically acceptable hair by more than 14 times compared to no cooling (pooled OR=14.42; 95% CI: 2.79–74.63; *P*=0.001), with moderate heterogeneity (I^2=62%), as illustrated in Figure 3.

In a meta-analysis of four randomized trials including 262 patients (156 with scalp cooling, 106 without), scalp cooling reduced the odds of moderate-to-severe chemotherapy-induced alopecia by 90% compared to no cooling (pooled OR=0.10; 95% CI: 0.02–0.54; *P*=0.007). Between-study heterogeneity was substantial (I^2=70%), as shown in Figure 4.

In a meta-analysis of three RCTs, adverse events occurred in 62/150 versus 0/95. Scalp cooling markedly increased the odds of any adverse event (pooled OR, 86.63; 95% CI, 3.72–2018.61; p = 0.005). Between-study heterogeneity was moderate (I^2 = 65%), as shown in Figure 5.

Discussion

The effectiveness of scalp cooling in treating CIA has been well documented in various studies. However, many of these studies lacked control, had small sample sizes, and lacked robust data [35 grevelman]. In 1990, the US FDA prohibited the sale of scalp cooling devices due to insufficient evidence regarding their safety and effectiveness [26 alley]. The cumulative evidence from 13 clinical trials conducted between 1984 and 2022 across Asia, Europe, Africa, and North America confirmed that scalp cooling is the most effective strategy for reducing CIA. Early studies using scalp hypothermia caps demonstrated a significant reduction in severe hair loss. For instance, Satterwhite and Zimm (1984) reported that 75% of patients who underwent cooling experienced acceptable hair preservation, compared to only 8% of those in the control group. Additionally, only 25% of the cooled patients faced severe hair loss, whereas this figure rose to 92% in the no-cooling group [34]. Another study by Rodriguez et al. (1994) found no benefit from using topical minoxidil, further emphasizing that mechanical cooling is more effective than pharmacological methods for preventing hair loss during chemotherapy [33].

Subsequent trials focused on refining the timing and duration of cooling regimens. Ron et al. (1997) demonstrated that a cooling protocol involving a 30-minute pre-infusion period, a 60-minute infusion, and a 60-minute post-infusion cooling phase significantly improved hair preservation.

Table 1. Study characteristics for the comparison between treatment lines and preventive measures of chemotherapy-induced alopecia.

First author, year	Study design and setting	Number of patients and sex M/F (n)	The mean (SD) age (years)	Type and stage of cancer	Chemotherapy used	Type and severity of alopecia	Intervention, treatment duration, and frequency
Lugtenberg et al., 2022 [23]	Prospective, open-label, randomized multi-center trial in the Netherlands	**Total:91** **I:** 46 (20-min PICT) **C:**45 (45-min PICT). **F:**95% (86/91)	**I:**57 ±11.1 years. **C:**58 ±13.7 years	Breast, ovarian, endometrial, lung, other.	Paclitaxel (70–90 mg/m²), monotherapy or combined with other chemotherapy/ monoclonal antibodies.	Scalp alopecia. **Severity of alopecia:** -Median total score at 45 min PICT: 5.0 (0–23). -Median total score at 20 min PICT: 4.0 (0–20).	Scalp cooling (Paxman PSC-1 machine). **Duration:** - Pre-cooling: 30 min before infusion. - Post-infusion cooling time: 20 or 45 min **Comparator:** 20 or 45 min (vs. historical 90 min)
Ghavami et al., 2020 [24]	Randomized controlled trial in Iran	**Total:**60 **I:**30, **C:**30 All patients were females.	**I:**39.50 ± 6.57 years, **C:**40.30 ± 7.05 years	Breast cancer. **Stage:** I–III	Adriamyci, cyclophosphamide, taxanes	Full scalp alopecia	Reflexology massage. **Duration:** 15 min, 3 times daily (per 8 h), for 3 months. **Comparator:** Routine health care.
Obuseng et al., 2021 [25]	Randomized controlled pilot trial in South Africa	**Total:** 37 **I:**17(45.9%) **C:**20 (54.1%). All patients were females.	**I:**47.76 ± 10.28 years **C:**49.35 ± 7.56 years	Breast cancer.	Adriamycin or epirubicin and cyclophosphamide followed by paclitaxel.	Scalp alopecia	Scalp cooling (Paxman Hair Loss Prevention System). **Duration:** pre-cooling for 30 min before chemotherapy, continued during and for 90 min after. **Comparator:** No scalp cooling.
Kang et al., 2019 [26]	Pilot randomized double-blind controlled clinical trial in South Korea.	**Total:**35 **I:**18 **C:**17 All patients were females.	**I:**52.1 ± 6.8 years **C:**41.6 ± 7.8 years	Breast cancer. **Cancer Stage:** **-Stage 1:** 6 (17.1%) **-Stage 2:** 13 (37.1%) **-Stage 3:** 14 (40%)	Anthracycline-based (e.g., AC, FAC, TAC) or taxane-based (e.g., TC, AC + T).	Scalp alopecia. Permanent chemotherapy-induced alopecia (PCIA).	CG428 topical lotion. **Duration:** 80-mL spray dispenser; applied twice daily for 6 months. **Comparator:** Placebo lotion

Table 1 (*Continued*)

Table 1. Study characteristics for the comparison between treatment lines and preventive measures of chemotherapy-induced alopecia. *(continued)*

First author, year	Study design and setting	Number of patients and sex M/F (n)	The mean (SD) age (years)	Type and stage of cancer	Chemotherapy used	Type and severity of alopecia	Intervention, treatment duration, and frequency
Komen et al., 2019 [27]	Prospective multi-center randomized trial in the Netherlands	**Total:** 102 **I:**51 (150-min post-infusion cooling) **C:**51 (90-min post-infusion cooling). All patients were females.	**Mean age:**52 years. **Age Range:** 30–72 years	Breast cancer. Early stage.	Fluorouracil, epirubicin, and cyclophosphamide.	Scalp Alopecia. **WHO grades 2–3 (moderate-complete alopecia):** **I:**17/51 (33%) **C:**25/51 (49%)	Paxman Scalp Cooling System, epirubicin 90 or 100 mg/m²; FEC ± docetaxel. **Duration:** 30 min pre-infusion, 60 min during infusion, then 90 min or 150 min post-infusion cooling. **Comparator:** 90-min post-infusion cooling (control) vs. 150-min (intervention).
Nangia et al., 2017 [14]	Multicenter randomized clinical trial in the United States.	**Total:** 142 **I:**119 **C:**63 All patients were females.	52.6 ± 10.1 years	Breast cancer. Early Stage I and II	Anthracycline-based 51 patients (36%) and taxane-based 91 patients (64%).	Scalp Alopecia. **Severity Graded using CTCAE v4.0:** **-Success (grade 0–1): I:**50.5% **C:**0% **-Failure (grade 2):** **I:** 49.5% **C:**100% **Onset of alopecia:** Assessed at the end of 4 cycles.	Scalp cooling (Orbis Paxman Hair Loss Prevention System). **Duration:** -Pre-cooling: 30 min. -During infusion: Continuous. -Post-infusion: 90 min. **Comparator:** No scalp cooling
Komen et al., 2016 [28]	Prospective, multi-center, randomized controlled trial in the Netherlands	**Total: 134** **I:**64 (20 min PICT), **M:**36 (56 %) **F:**28 (44 %). **C:**70 (45 min PICT), **M:**46 (66 %) **F:**24 (34 %).	**Age range:** 25-83 years	Prostate, breast, lung, gastrointestinal, and other	Docetaxel monotherapy (75–100 mg/m², 3-weekly) or combined with other agents.	Scalp alopecia. **Severity of Alopecia:** **WHO scale:** Grade 0 (no hair loss) in 45–46%, Grade 1 (minimal) in 34–37%, Grade 2 (moderate) in 15%, Grade 3 (patchy) in 2–6%	Scalp cooling. **Duration:** -Pre-cooling: 30 min before infusion. -Post-infusion cooling: 20 or 45 min. **Comparator:** 45-min vs. 20-min post-infusion cooling

Mohammed et al., 2016 [29]	Quasi-experimental research study in Egypt	**Total:**60 **I:**30 **C:**30 All patients were females.	**Age Range:** 18–60 years	NA.	Taxol-carpolinate FAC (floruracil-adriamycincyclophosphamide [endoxan]) Foulox	Scalp Alopecia. **WHO scale:** **Grade 0 (no hair loss):** **I:**(1/30) 3.3% **C:**0% **Grade 4 (total alopecia):** **I:** (1/30) 3.3% **C:** (14/30) 43.3%	Scalp cooling group (SCG). **Duration:** 30 min before chemotherapy, during infusion, 60 min after Six cycles of adjuvant chemotherapy **Comparator:** Routine hospital care
Ekwall et al., 2013 [30]	Randomized controlled trial in Sweden	**Total:43** **I:**20 (3° C group) **C:**23 (8° C group). All patients were females.	**The mean Age:** 64.3 years, **Age Range:** 38–84 years.	Ovarian cancer, endometrial cancer, cervical cancer, tubal cancer, and peritoneal cancer.	Paclitaxel (175 mg/m²) + carboplatin (AUC 5–6).	Scalp alopecia.	Scalp cooling, Coolant medium (water/glycol) at pre-set temperatures of 3°C or 8°C. **Duration**: Cooling initiated 30 min before chemotherapy, continued for 5 hours (during paclitaxel + carboplatin infusion). **Comparator**: 3°C vs. 8°C coolant temperatures.
van den Hurk et al., 2012 [31]	Observational study followed by a randomized controlled trial in the Netherlands	**Total:**76 **I:**38 (45 min PCIT), **M:**19(50%) **F:**19(50%) **C:**38 (90 min PCIT) **M:**17(45%) **F:**21(55%)	**Mean age**: 61 years	Breast, prostate, lung, ovarian, gastrointestinal/ colorectal.	Docetaxel monotherapy or combined with carboplatin, doxorubicin, or capecitabine.	Scalp alopecia.	Scalp cooling (Docetaxel: 75 mg/m² or 100 mg/m²) **Duration:** Pre-cooling: 30 min before infusion. Post-infusion cooling (PICT): 45 min or 90 min **Comparato**r: 45-min vs. 90-min PICT.

Table 1 (*Continued*)

Table 1. Study characteristics for the comparison between treatment lines and preventive measures of chemotherapy-induced alopecia. *(continued)*

First author, year	Study design and setting	Number of patients and sex M/F (n)	The mean (SD) age (years)	Type and stage of cancer	Chemotherapy used	Type and severity of alopecia	Intervention, treatment duration, and frequency
Ron et al., 1997 [32]	Randomized controlled trial in Israel	**Total:**35 **I:**19 **C:**16 All patients were females	NA	Breast cancer	CMF (cyclophosphamide 600 mg/m², methotrexate 40 mg/m², 5-FU 600 mg/m², days 1 and 8 of a 28-day cycle).	Scalp alopecia **Onset of alopecia:** Most patients experienced hair loss after 1–2 cycles Severity of alopecia: graded by WHO criteria: Grade 0: No loss (53% cooling vs. 19% control). Grade 1: Mild loss (32% vs. 44%). Grades 2–3: Moderate/severe loss (16% vs. 38%).	Scalp cooling (electrically cooled cap, SCS II). **Duration:** 30 minutes before, during, and for one hour after treatment. **Comparator:** Ambient temperature (no cooling).

Rodriguez et al., 1994 [33]	Double-blind randomized controlled trial in Argentina.	**Total:** 48 **I:**21 **C:**22 All patients were females.	**Age Range:** 26–75 years (median: 51 years)	Breast carcinoma (41 patients), Soft-tissue sarcomas (5 patients), Endometrial carcinoma (2 patients).	**Doxorubicin-based:** Single agent (2 patients), With DTIC (5 patients), with 5-fluorouracil + cyclophosphamide (41 patients).	Scalp alopecia **Severity of alopecia:** In Grade 3, severe alopecia necessitating a wig was observed in 88% of the intervention group and 92% of the control group. **Onset of alopecia:** By the end of the second cycle (90–91% of patients)	5 mL of 2% solution (100 mg/mL minoxidil) **Duration:** Twice daily, starting 24 hours before chemotherapy, until hair loss. **Comparator:** Placebo (vehicle solution).
Satterwhite et al.,1984 [34]	Randomized clinical trial in the USA	**Total:**25 **I:**12 **C:**13 **M:** 7/25 (28%) **F:** 18/25 (72%)	**Age Range:** 20–81 years (median: 52 years)	Breast (9 patients), stomach (4), lung (3), non-Hodgkin's lymphoma (2), liver (2), endometrium (1), ovary (1), Hodgkin's disease (1), fibrosarcoma (1), and urethra (1). Cancer stage was NR.	5FU/mitomycin C, cyclophosphamide, vincristine	Scalp alopecia.	Scalp hypothermia (Chemo Cap with cryogel + tourniquet). **Duration:** Applied 15 minutes pre-infusion and maintained for 60 minutes post-infusion. **Comparator:** No scalp cooling.

Table 2. Efficacy and safety characteristics of treatment lines and preventive measures for chemotherapy-induced alopecia.

First author, year	Alopecia reduction	Patient satisfaction	Adverse events	Conclusion
Lugtenberg et al., 2022 [23]	• **The mean Dean scale:** **For 20 min:** 1.31 ±1.01 **For 45 min:**1.77 ±1.07 • **Median total score** for severity of CIA after six cycles: **For 20 min:** 12 (2–25). **For 45 min:** 4.0 (0–14). • **The mean NCI CTCAE v4.03 grade of alopecia:** **For 20 min:** 1.00 ±0.63. **For 45 min:** 1.15 ±0.61.	**Self-determined need to wear a wig/head covering:** **20-min PICT:** 31/38 (81.6%) (no head covering) **45-min PICT:** 27/36(75%). **90-min PICT:** 611/723(84.5%)	**AE**: Headache (most common). **Severity**: mild.	By lowering the post-infusion cooling time (PICT) to 20 minutes, this study demonstrates that it can prevent paclitaxel-induced alopecia as effectively as 45 or 90 minutes, with success rates of 82%, 75%, and 85%, respectively. Significant advantages of the shorter PICT include shorter hospital stays for patients and increased logistical effectiveness without sacrificing efficacy or tolerability.
Ghavami et al., 2020 [24]	**The Mean hair regrowth rate:** **I:** 1.85±0.52, 12.45±1.72, and 22.28±2.39%. **C:** 1.32±0.46, 11.44±1.46, and 21.53±2.14%.	Hair regrowth significantly improved in the intervention group Compared to the control group.	NA	When compared to routine treatment alone, this randomized clinical trial shows that reflexology massage dramatically improves hair regrowth in females with chemotherapy-induced alopecia (CIA). The technique was safe, non-invasive, and economical. It entailed specifically massaging the nail beds three times a day for three months.
Obuseng et al., 2021 [25]	**The mean change in alopecia severity:** **I:**37.29 ± 20.52 % **C:**58.15 ± 28.46 % **Hair preservation:** **I: 13/17** **C: 8/20**	NA	Six patients (35.29%) cited headaches, two patients (11.76%) withdrew because of feeling cold, and one patient (5.88%) withdrew because of scalp tenderness. I: 7/24 C: 4/24	The results of this study indicate that scalp cooling works, since patients who received scalp cooling experienced a statistically significant decrease in the overall mean CIA severity when compared to the control group. Since there was no discernible overall decrease in CIA between patients with straight and curly hair, hair curvature does not appear to influence the efficacy of this intervention.

Kang et al., 2019 [26]	**At Baseline:** **-Mean hair density:** **I:** 97.6 ± 6.4 hairs/cm². **C:** 126.8 ±30.3 hairs/cm² **-hair thickness:** **I:** 49.9 ±12.7 µm **C:** 48.1 ± 8.4 µm **After 6 months:** **-Change in Hair Density:** **I:** 34.7 (29.6) % **C:** 24.9 (28.9) % **-Change in Hair Thickness** **I:** 19.8 (39.0) % **C:** 35.6 (26.6) %	The intervention group reported higher improvements (e.g., 4.1 vs. 2.7 for overall volume).	One patient in the placebo group had grade 1 scalp Cellulitism.	In this pilot RCT, 35 breast cancer survivors were treated for permanent chemotherapy-induced alopecia (PCIA) using CG428, a botanical topical lotion. For six months, CG428 demonstrated a non-significant trend toward increasing hair thickness. Results reported by patients showed only slight subjective improvements.
Komen et al., 2019 [27]	**Patients without head coverings:** **I:**16/48 (33%) **C:**21/46 (45%).	37/94 of patients (40%) did not need to wear a wig or other head covering.	Headaches were reported as mild, moderate, or severe in 66 (20%), 20 (6%), and 3 (1%) sessions, respectively.	In patients with breast cancer undergoing adjuvant FEC chemotherapy, this randomized research shows that prolonging post-infusion scalp cooling from 90 to 150 minutes was well tolerated but did not substantially lessen the requirement for head covers.
Nangia et al., 2017 [14]	More than 50% hair loss does not require a wig. **Severe hair loss** I:47/95 C:47/47	No significant difference in emotional or social functioning after four cycles of chemotherapy.	Chills, dizziness, headache, nausea, paresthesia, pruritus, sinus pain, skin and subcutaneous tissue disorders, and skin ulceration. **Severity**: All adverse events were grade 1 (N=46) or grade 2 (N=8). I:28/101 C:0/49	In females with stage I–II breast cancer receiving chemotherapy based on taxanes or anthracyclines, scalp cooling dramatically decreased chemotherapy-induced alopecia, according to the SCALP Randomized Clinical Trial. After four chemotherapy cycles, women in the scalp cooling group had a considerably higher chance of keeping at least 50% of their hair than those in the control group.

Table 2. Efficacy and safety characteristics of treatment lines and preventive measures for chemotherapy-induced alopecia *(continued)*

First author, year	Alopecia reduction	Patient satisfaction	Adverse events	Conclusion
Komen et al.,2016 [28]	**-The median pre-infusion cooling Time:** 33 min (IQR 15). **-The median follow-up for patients:** **20-min group:** 6.5 months **45-min group:**7.5 months. -A significant difference in the need to wear a head covering was seen when the dosages of docetaxel were 75 mg/m2 (5/65) (8%) compared to 100 mg/m2 (14/25) (57%). **-Tolerance (mean VAS score:** 8.3/10).	**The percentage for wig/head covering is needed:** **For 20-minute group:** 73%, 33/45 **For 45-minute group:** 79%, 41/52. No significant difference in the need to wear a head covering in the 20-minute group compared to the 45-min group. **Higher success in males 59 (95%) vs. females 15 (43%).**	**AE:** Headache (most common). **Severity:** Mild (11%), moderate (3%), severe (0.4%).	The results of this study highlight treatment efficiency and patient convenience by supporting the standardization of a 20-minute post-infusion cooling time for patients undergoing 3-weekly docetaxel chemotherapy.
Mohammed et al.,2016 [29]	**Hair preservation (WHO scale): (Grades 0–2)** **I:**86.6% (26/30) of patients **C:**16.7 % (5/30) of patients **Moderate-to-severe hair loss:** **I:**9/30 **C:** 17/30 **Alopecia:** **I: 1/30** **C: 14/30**	NA	**AE:** Cold sensation (100%), headache (100%), boredom (100%), need of blanket (70%). I:30/30 C:0/30	With 86.6% of patients in the scalp cooling group (SCG) having successful hair preservation compared to just 16.7% in the control group, this study showed that scalp cooling is quite efficient in avoiding chemotherapy-induced alopecia. The effectiveness of the intervention varied based on the chemotherapy regimen and was especially helpful for younger patients. Even with adverse effects like headaches and cold feelings, scalp cooling was well tolerated.
Ekwall et al.,2013 [30]	No significant difference was observed in hair preservation between patients treated with 3° C and those treated with 8° C.	49% of patients subjectively experienced >50% hair loss, and 38% reported the need for a wig.	**AE:** headache and coldness. (a marginally higher mean score for headache in the 3° C compared with the 8° C group)	During paclitaxel/carboplatin treatment, this study found no statistically significant difference in hair preservation between the two temperatures, but there was a trend toward 3° C. Headache and coldness were among the more common adverse effects linked to lower temperatures. The results emphasize how difficult it is to standardize scalp cooling because each person's scalp temperature response is different. To balance effectiveness with patient comfort and enhance cooling procedures, further study is required.

van den Hurk et al., 2012 [31]	**Hair preservation (no wig/head covering):** **I:**95% (36/38) patients (45-min PICT) **C:**79% (30/38) patients (90-min PICT). **Tolerance** (mean VAS score: 79/100).	Patient-reported wig/head covering use.	**AE:** Headache (minimal to severe) and cold sensation.	This study demonstrated excellent outcomes and scalp cooling tolerance after 3-week chemotherapy regimens containing docetaxel. Patients benefited from a 45-minute PICT. Refusing scalp cooling was frequently due to spending more time in the hospital than is necessary when undergoing chemotherapy. Time commitment was usually cited as a justification for either not implementing scalp cooling in a hospital or simply providing it to a select group of patients.
Ron et al., 1997 [32]	**Hair preserved graded by WHO:** **Grade 0: No loss:** **I:** 53% (10/19) **C:**19% (3/16) **Grade 1: Mild loss:** **I:** 32% (6/19) **C:** 44% (7/16) **Acceptable preservation:** **I:** 84% (16/19) **C:** 63% (10/16) **Grades 2–3: Moderate/severe loss:** **I:** 16% (3/19) **C:** 38% (6/16) **Incidence of alopecia:** **I:** 47% (9/19 patients) **C:** 81% (13/16 patients)	Patient acceptability was assessed to drop out of the study (none).	Cap weight (3 patients), slight headache (1 patient) I: 4/19 C: 0/16	With 53% of cooled patients maintaining their hair, compared to just 19% in the control group, this study showed that scalp cooling dramatically decreased the incidence of chemotherapy-induced alopecia in breast cancer patients undergoing CMF treatment. During a median follow-up of 14 months, the intervention was well tolerated, had few side effects, and no scalp metastasis was found.
Rodriguez et al., 1994 [33]	No significant difference in severe alopecia.	NA	NA	In female patients undergoing doxorubicin-based regimens, this randomized, double-blind study showed that topical minoxidil (2%) was not beneficial in avoiding severe chemotherapy-induced alopecia. Although 88% of minoxidil-treated patients and 92% of controls had Grade 3 alopecia (needing a wig) after the second chemotherapy cycle, the study did not find a significant difference in hair loss between the minoxidil and placebo groups.
Satterwhite et al., 1984 [34]	**Acceptable hair preservation:** **I:**75% (9 /12) **C:**8% (1/13) **Severe hair loss:** **I:**25% (3 /12) **C:**92% (12/13)	NA	Headache, cold sensation, cap heaviness.	In this randomized clinical research, 75% of treated patients maintained satisfactory hair preservation (little to moderate hair loss), compared to just 8% in the control group, indicating that scalp hypothermia with a Chemo Cap dramatically reduces doxorubicin-induced alopecia. Better results were obtained with smaller dosages of doxorubicin, and the protective effect was dose-dependent.

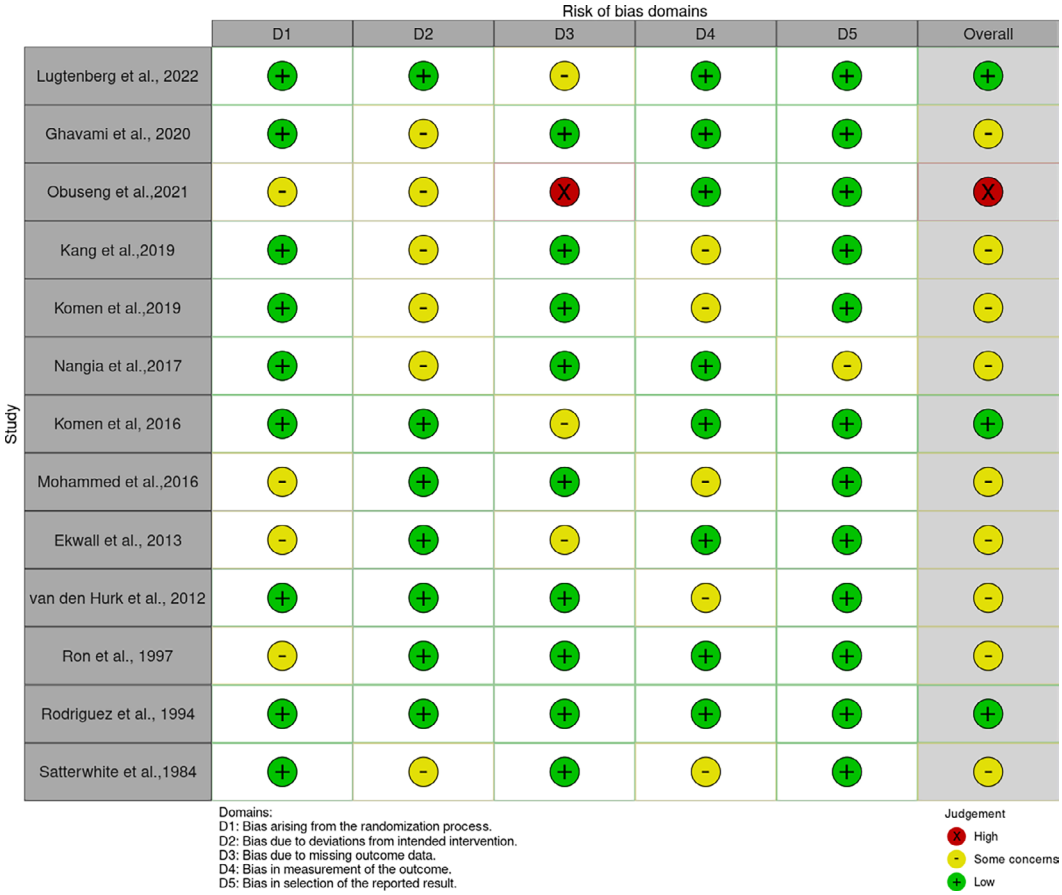

Figure 2. ROB quality assessment of thirteen RCT studies.

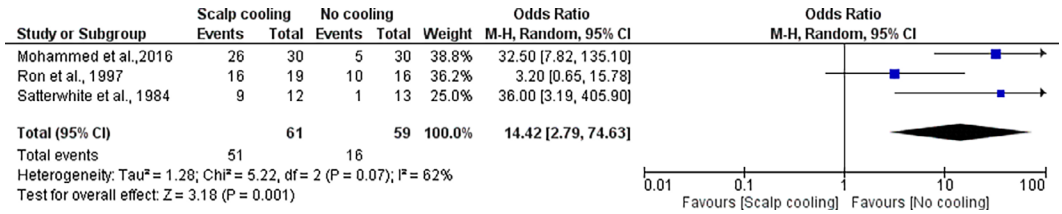

Figure 3. Forest Plot of the effectiveness of scalp cooling for acceptable hair preservation.

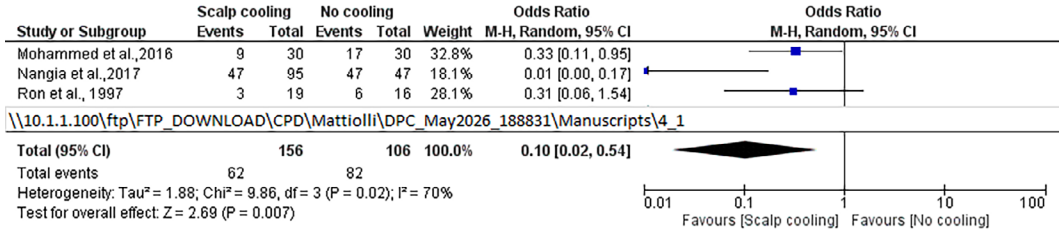

Figure 4. Forest plot of moderate-to-severe hair loss with scalp cooling vs no cooling.

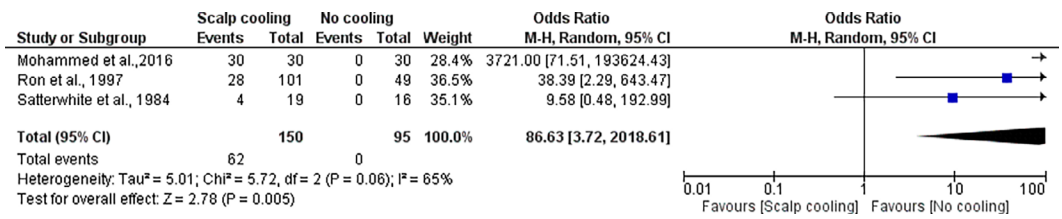

Figure 5. Forest plot of adverse events with scalp cooling vs no cooling.

Specifically, the rate of grade 0–1 alopecia (no to minimal hair loss) increased from 19% in control patients to 53% in those who underwent cooling. Additionally, moderate-to-severe hair loss dropped from 38% to 16% in the cooled group [32]. Further studies by Van den Hurk et al. (2012) and Komen et al. (2016) compared short post-infusion cooling times (20 to 45 minutes) to standard durations (90 minutes) during docetaxel chemotherapy. They found comparable efficacy, with hair preservation rates between 80% and 95%, and reported high tolerability, as indicated by a visual analog scale (VAS) score of around 8 out of 10 [28,31]. Ekwall et al. (2013) also investigated the impact of coolant temperature on hair preservation, finding that cooler temperatures (3° C compared to 8° C) tended to yield better results. However, the differences did not reach statistical significance [30].

In larger multicenter randomized controlled trials (RCTs), Nangia et al. (2017) randomized 182 women receiving anthracycline- or taxane-based regimens. They found that using cooling methods led to a fivefold increase in successful outcomes (as defined by CTCAE grade 0–1 alopecia), with 50.5% success in the cooling group compared to 0% in the controls ($P < 0.001$). This established the effectiveness of cooling in treating early-stage breast cancer [14]. Moreover, a research study focusing on postmenopausal women undergoing chemotherapy for breast cancer revealed that a significant number of these women considered hair loss to be a more distressing experience than losing a breast [37]. This indicates that females may be more affected by changes in appearance than males are. Komen et al. (2019) extended the investigation by comparing post-infusion cooling durations of 90 minutes versus 150 minutes. They observed success rates of 33% and 49% for WHO grades 2–3 alopecia, respectively (P=0.11). This suggests that while longer cooling periods may offer modest improvements, they also come with increased logistical challenges [27]. Pilot studies and smaller trials have reinforced these findings in various settings. For instance, Mohammed et al. (2016) reported that 86.6% of Egyptian patients achieved WHO grades 0–2 alopecia with cooling, compared to only 16.7% in the control group, although 100% of participants in the cooling group reported experiencing headaches and cold sensations [29]. Meanwhile, Obuseng et al. (2021) conducted research in South Africa and found a significant reduction in the mean SALT score, from 58.2% to 37.3% (P=0.0167), with no difference observed based on hair texture, indicating the global applicability of the cooling method across different hair types [25]. Additionally, some studies examined alternative methods. Ghavami et al. (2020) studied reflexology massage, while Kang et al. (2020) studied a specific botanical lotion [24,26]. Both demonstrated modest benefits in hair regrowth but did not match the effectiveness of cooling, nor did they show superiority over it in direct comparisons. A previous meta-analysis indicated that scalp cooling, the leading method for prevention, notably lowered the likelihood of chemotherapy-induced alopecia (CIA), with a relative risk of 0.38 (95%CI: 0.32–0.45). In contrast, topical 2% minoxidil and other treatments did not significantly reduce the risk of CIA. Furthermore, no severe side effect associated with scalp cooling was reported. These findings imply that scalp cooling can effectively help prevent CIA in patients undergoing chemotherapy [26].

While scalp cooling is generally well accepted, it is not recommended for individuals with conditions such as cold sensitivity, cold agglutinin disease, cryoglobulinemia, and cryofibrinogenemia [35]. Additionally, certain studies have suggested a possible risk of scalp metastases associated with the use of scalp cooling [38]. Therefore, these cooling systems should be avoided in patients with circulating malignant cells, such as those with leukemia or lymphoma, who are undergoing chemotherapy aimed at curing the disease [35]. In the case of patients with solid tumors that have a high likelihood of skin metastasis, such as breast, lung, or gastric cancer, careful monitoring of the scalp for any sign of disease is essential [39]. The safety profiles across trials in our review were consistent, with mild headaches reported in up to 25% of patients, along with chills, cold intolerance, and occasional scalp tenderness being the primary adverse events. These side effects led to treatment discontinuation in fewer than 30% of cooled patients, with a mean rate of 12–18%. No trial reported serious complications or scalp metastases, aligning with systematic reviews that support scalp cooling as both safe and preferred by patients (Shin et al., 2015; Dunnill et al., 2018) [13,17]. Despite the strong evidence of efficacy, the field faces challenges due to the variability in cooling devices (e.g., Paxman, Orbis, and custom caps), temperature settings (ranging from 3 to 16°C), and timing protocols (with pre-infusion times of 15–30 minutes and post-infusion times of 20–150 minutes). These factors, along with different alopecia scales (including WHO, Dean, CTCAE, and SALT), make direct comparisons and meta-analyses difficult, resulting in an I^2 value of up to 81%.

Limitations

Several limitations should be recognized. First, the considerable variation in scalp-cooling protocols, such as differences in temperatures and durations, as well as chemotherapy regimens and alopecia assessment scales, makes direct comparisons difficult and contributes to statistical variability. Second, many trials were small and carried a moderate risk of bias due to incomplete blinding, inadequate allocation concealment, and missing outcome data. Additionally, only a few studies supported each pooled estimate, which reduces precision. Fourth, the follow-up periods were generally short, making it impossible to evaluate long-term or

permanent hair outcomes. Finally, potential biases related to publication and language, along with limited reporting on quality-of-life and cost data, hinder our understanding of the patient-centred and economic impacts.

Conclusion

Our review highlights that scalp cooling effectively reduces chemotherapy-induced hair loss, achieving hair preservation rates of 75–95%. Cooling should start 20–30 minutes before treatment, continue throughout the treatment, and last an additional 20–150 minutes afterward. Patients generally report high satisfaction, and side effects, such as mild headaches and chills, are rarely severe enough to stop treatment. Shorter post-infusion cooling times (20–45 minutes) are equally effective, allowing for improved workflow. These findings support the incorporation of scalp cooling into standard care for chemotherapy patients.

In conclusion, scalp cooling has proven to be the most effective, widely applicable, and well-tolerated method for preventing chemotherapy-induced alopecia (CIA). It outperforms alternative strategies such as topical treatments, manual techniques, and pharmacological interventions. Future research should focus on establishing standardized cooling protocols, unified outcome measures, and longer follow-up periods. This would help optimize patient selection, reduce resource utilization, and evaluate cost-effectiveness across different healthcare settings.

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