

Supplementary file

Table S1. Search Strategies (run on 19 September 2024).

Databases	Search strategy	Results
MEDLINE (Pubmed)	#1 “Impetigo”[Mesh] OR Impetigo OR Impetigos OR (Impetigo Contagiosa) OR (Contagiosa, Impetigo) OR (Contagiosas, Impetigo) OR (Impetigo Contagiosas) #2 (randomized controlled trial[Publication Type] OR (randomized[Title/Abstract] AND controlled[Title/Abstract] AND trial[Title/Abstract]))	77
Embase	#1 ‘impetigo’/exp OR Impetigo OR Impetigos OR ‘Impetigo Contagiosa’ OR ‘Contagiosa, Impetigo’ OR ‘Contagiosas, Impetigo’ OR ‘Impetigo Contagiosas’ #2 ‘randomized controlled trial’ OR ‘controlled clinical trial’ OR ‘pragmatic clinical trial’ OR ‘equivalence trial’ OR ‘clinical trial, phase iii’ #3 ‘randomized controlled trial’/exp #4 ‘randomized controlled trials as topic’/exp OR ‘randomized controlled trial (topic)’ #5 ‘controlled clinical trial’/exp OR ‘controlled clinical trial’ #6 ‘controlled clinical trial (topic)’/exp OR ‘controlled clinical trial (topic)’ #7 ‘randomization’/exp OR randomization #8 ‘random allocation’/exp OR ‘random allocation’ #9 ‘double blind procedure’/exp OR ‘double blind procedure’ #10 ‘double-blind method’/exp OR ‘double-blind method’ #11 ‘double-blind studies’/exp OR ‘double-blind studies’ #12 ‘single-blind method’/exp OR ‘single-blind method’ #13 ‘single blind procedure’/exp OR ‘single blind procedure’ #14 ‘single-blind studies’/exp OR ‘single-blind studies’ #15 ‘placebo’/exp OR placebo OR placebos #16 ‘control group’/exp OR ‘control group’ OR ‘control groups’ #17 random* OR sham OR placebo* #18 (singl* OR doubl*) NEAR/2 (blind* OR dumm* OR mask*) #19 (tripl* OR trebl*) NEAR/2 (blind* OR dumm* OR mask*) #20 control* NEAR/3 (study OR studies OR trial* OR group*) #21 (nonrandom* OR non) AND random* OR ‘non random*’ OR ‘quasi random*’ OR quasirandom* #22 allocated OR allocate* #23 (equivalence OR superiority OR ‘non inferiority’ OR noninferiority) NEAR/3 (study OR studies OR trial*) #24 ‘pragmatic study’ OR ‘pragmatic studies’ #25 (pragmatic OR practical) NEAR/3 trial* #26 (quasiexperimental OR ‘quasi experimental’) NEAR/3 (study OR studies OR trial*) #27 phase NEAR/3 (iii OR ‘3’) NEAR/3 (study OR studies OR trial*) #28 #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 #29 #28 AND #1 AND [embase]/lim NOT ([embase]/lim AND [medline]/lim)	335

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Table S1. Search Strategies (run on 19 September 2024). (continued)

Databases	Search strategy	Results
CENTRAL	#1 MeSH descriptor: [Impetigo] explode all trees #2 Impetigo OR Impetigos OR (Impetigo Contagiosa) OR (Contagiosa, Impetigo) OR (Contagiosas, Impetigo) OR (Impetigo Contagiosas) #3 #1 OR #2 (In Trials)	307
Biblioteca Virtual em Saúde (BVS)	#1 MH:Impetigo OR Impétigo OR Impetigo OR (Impetigo Contagioso) OR Impetigo OR Impetigos OR (Impetigo Contagiosa) OR (Contagiosa, Impetigo) OR (Contagiosas, Impetigo) OR (Impetigo Contagiosas) OR C01.150.252.410.868.951.360 OR C01.150.252.410.890.587 OR C01.150.252.819.770.360 OR C01.800.720.770.360 OR C17.800.838.765.770.360 AND (db:(“LILACS” OR “BDENF” OR “LIPECS” OR “SES-SP” OR “BINACIS” OR “CUMED” OR “HANSENIASE” OR “BBO” OR “MINSAPERU” OR “MTYCI” OR “coleccionaSUS”))	188

Table S2. Risk of Bias Judgments for Each Included RCT.

Study/Year	Randomization	Allocation concealment	Blinding participants/personnel (subjective outcomes)	Blinding outcome assessors (subjective outcomes)	Incomplete outcome	Selective reporting	Other bias
Anusharani 2019	UNCLEAR Quote: "Patients were randomly allocated to two treatment groups" Comment: No sufficient information on random sequence generation.	UNCLEAR No sufficient information to judge.	HIGH Quote: "open-label study".	HIGH Quote: "open-label study".	LOW Comment: No losses during the follow-up.	UNCLEAR No study protocol registry available.	LOW No other sources of bias were identified.
Barton 1988	UNCLEAR Quote: "Patients were randomly assigned in a double-blind manner by the hospital pharmacists to receive 10 days of either erythromycin or dicloxacillin." Comment: No sufficient information on random sequence generation.	UNCLEAR No sufficient information to judge.	LOW Quote: "Patients were randomly assigned in a double-blind manner by the hospital pharmacists to receive 10 days of either erythromycin or dicloxacillin." Comment: No sufficient information on random sequence generation.	HIGH Comment: The blinding of outcome assessors was not confirmed, and this lack of blinding can indeed influence the results.	LOW Comment: lost less than 20% (12%), with reasons.	UNCLEAR No study protocol registry available.	LOW No other sources of bias were identified.
Ciftci 2002	UNCLEAR Quote: "the patients were randomized into two groups." Comment: No sufficient information on random sequence generation.	UNCLEAR No sufficient information to judge.	HIGH Comment: Insufficient information is available to make a judgment. Nonetheless, the absence of blinding among participants and personnel can significantly impact the outcomes.	HIGH Comment: The blinding of outcome assessors was not confirmed, and this lack of blinding can indeed influence the results.	HIGH Comment: lost more than 20% (22%).	UNCLEAR No study protocol registry available.	LOW No other sources of bias were identified.

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Table S2. Risk of Bias Judgments for Each Included RCT. (continued)

Study/Year	Randomization		Allocation concealment		Blinding participants/personnel (subjective outcomes)		Blinding outcome assessors (subjective outcomes)		Incomplete outcome	Selective reporting	Other bias			
Dagani 1992	LOW	Quote: "The randomized code was prepared by Beecham Pharmaceuticals and was not known to the investigators until after the raw data were tabulated."	LOW	Quote: "The randomized code was prepared by Beecham Pharmaceuticals and was not known to the investigators until after the raw data were tabulated."	LOW	Quote: "prospective double-blind controlled study comparing topical mupirocin with oral erythromycin in the treatment of impetigo to determine; the erythromycin group, which received a placebo ointment (ointment containing polyethylene glycol only)"	HIGH	Comment: The blinding of outcome assessors was not confirmed, and this lack of blinding can indeed influence the results.	LOW	Comment: lost less than 20% (11.7%), with reasons.	UNCLEAR	No study protocol registry available.	LOW	No other sources of bias were identified.
Dash 2023	UNCLEAR	Quote: "the subjects were randomly allotted to treatment groups." Comment: No sufficient information on random sequence generation.	UNCLEAR	No sufficient information to judge.	HIGH	Quote: "in a single-centre, open-label, random allocation study" Comment: lack of blinding of participants and personnel probably influences the results (subjective outcomes).	LOW	Quote: "Evaluation of clinical and bacteriologic efficacy was determined by a blinded observer, a consultant from our department, not involved in this study." Comment: blinding of outcome assessors was adequately performed.	LOW	Comment: no losses during the follow up.	UNCLEAR	No study protocol registry available.	LOW	No other sources of bias were identified.
Demidovich 1990	UNCLEAR	Quote: "The pharmacist randomly assigned them to one of three treatment regimens" Comment: No sufficient information on random sequence generation.	UNCLEAR	No sufficient information to judge.	HIGH	Comment: Insufficient information is available to make a judgment. Nonetheless, the absence of blinding among participants and personnel can significantly impact the outcomes.	LOW	Quote: "Patients were reevaluated 3 to 5 and 8 to 10 days after beginning therapy by one of the authors (CD, or M.R.), both of whom were blinded to the treatment each child was receiving."	LOW	Comment: lost less than 20% (2.6%), with reasons.	UNCLEAR	No study protocol registry available.	LOW	No other sources of bias were identified.

Eells 1986	LOW	Quote: "Patients were randomized between the two treatment groups by a computer-generated set of random numbers in blocks of five per group."	UNCLEAR	No sufficient information to judge.	HIGH	Comment: Insufficient information is available to make a judgment. Nonetheless, the absence of blinding among participants and personnel can significantly impact the outcomes.	HIGH	Comment: The blinding of outcome assessors was not confirmed, and this lack of blinding can indeed influence the results.	HIGH	Quote: "Of the 52 patients enrolled, 38 were evaluable." Comment: Loss of more than 20% of the sample. (27%)	UNCLEAR	No study protocol registry available.	LOW	No other sources of bias were identified.
Goldfarb 1988	UNCLEAR	Quote "Enrolled children were randomly assigned to groups that received either mupirocin topical therapy in a 2% polyethylene glycol ointment or oral erythromycin ethylsuccinate." Comment: No sufficient information on random sequence generation.	UNCLEAR	No sufficient information to judge.	HIGH	Quote: "Parents or legal guardians of the children in the mupirocin group were instructed to apply the 2% mupirocin ointment three times per day, using the cotton swabs provided. Parents or legal guardians of children in the erythromycin group were given instructions and medication to administer erythromycin ethylsuccinate at 40 mg/kg of body weight per day in four doses." Comment: Different forms of interventions (oral and topical) prevent masking.	HIGH	Comment: The blinding of outcome assessors was not confirmed, and this lack of blinding can indeed influence the results.	LOW	Comment: lost less than 20% (14%), with reasons.	UNCLEAR	No study protocol registry available.	LOW	No other sources of bias were identified.

Table S2 continues

Table S2. Risk of Bias Judgments for Each Included RCT. (continued)

Study/Year	Randomization	Allocation concealment	Blinding participants/personnel (subjective outcomes)	Blinding outcome assessors (subjective outcomes)	Incomplete outcome	Selective reporting	Other bias
Gropper 2014	<p>LOW</p> <p>Quote: "Patients were allocated unique identification numbers and randomization was performed by an independent statistician using an interactive web response system and they were stratified into age subsets, thus ensuring a 1:1:1 distribution in each age group without selection bias."</p>	<p>LOW</p> <p>Quote: "Patients were allocated unique identification numbers and randomization was performed by an independent statistician using an interactive web response system and they were stratified into age subsets, thus ensuring a 1:1:1 distribution in each age group without selection bias."</p>	<p>LOW</p> <p>Quote: "Double-blind for ozenoxacin versus placebo comparison (ozenoxacin and placebo did not differ in color, smell or consistency and they were presented in identical aluminum tubes) and investigator-blinded for retapamulin versus placebo because of the different formulation appearances (since retapamulin is formulated as an ointment, it could not be included in the double-blind design, but was administered in investigator-blinded fashion)"</p> <p>Comment: blinding of participants and personnel was adequately done.</p>	<p>LOW</p> <p>Quote: "Double-blind for ozenoxacin versus placebo comparison (ozenoxacin and placebo did not differ in color, smell or consistency and they were presented in identical aluminum tubes) and investigator-blinded for retapamulin versus placebo comparison because of the different formulation appearances (since retapamulin is formulated as an ointment, it could not be included in the double-blind design, but was administered in investigator-blinded fashion)"</p> <p>Comment: blinding of outcome assessors was adequately performed.</p>	<p>LOW</p> <p>Comment: lost less than 20% (2%), with reasons.</p>	<p>UNCLEAR</p> <p>No study protocol registry available.</p>	<p>LOW</p> <p>No other sources of bias were identified.</p>
Iovino 2011	<p>UNCLEAR</p> <p>Quote: "children aged 2-12 years with micro-biologically documented primary non-bullous impetigo were enrolled and randomized into a dose-ranging parallel group study testing 3 different doses"</p> <p>Comment: No sufficient information on random sequence generation.</p>	<p>UNCLEAR</p> <p>No sufficient information to judge.</p>	<p>HIGH</p> <p>Comment: Insufficient information is available to make a judgment. Nonetheless, the absence of blinding among participants and personnel can significantly impact the outcomes.</p>	<p>HIGH</p> <p>Comment: The blinding of outcome assessors was not confirmed, and this lack of blinding can indeed influence the results.</p>	<p>LOW</p> <p>Quote: "A total of 120 subjects (96%) completed all 7 days of treatment and were assessed at end of treatment."</p>	<p>UNCLEAR</p> <p>No study protocol registry available.</p>	<p>LOW</p> <p>No other sources of bias were identified.</p>

Jeffrey 1990	LOW	Quote: "Using a random numbers table, the hospital pharmacy randomly assigned each patient to one of two groups."	UNCLEAR	No sufficient information to judge.	LOW	Quote: "The child's group assignment was not known to parents or investigators." Comment: blinding of participants and personnel was adequately done.	LOW	Quote: "The child's group assignment was not known to parents or investigators." Comment: blinding of outcome assessors was adequately performed.	HIGH	Quote: "12 losses (22.2%), two were dropped when misdiagnosis was suspected and antifungal therapy begun, and one was removed from the study after the development of S. pyogenes pharyngitis, leading to treatment with intramuscular penicillin." Comment: Loss of more than 20% of the sample (22.2%)	UNCLEAR	No study protocol registry available.	LOW	No other sources of bias were identified.
Koning 2002	LOW	Quote: "An independent statistician provided a computer generated list of random set numbers in permuted blocks of six. The hospital pharmacist packed the study medication in identical blank tubes with a code number according to the randomisation list. We randomised the patients in blocks and stratified them for presence of pre-existing eczema at the site of the impetigo."	LOW	Quote: "The research nurse, who was unaware of the treatment allocation, allocated patients to the first available number of study cream in the corresponding block. The pharmacist kept the list of code numbers in a sealed envelope and was not involved in analysis of data or assessment of outcome."	LOW	Quote: "The placebo cream, prepared by the pharmacist, did not differ in colour, smell, or consistency from the fusidic acid cream. Unblinding took place after the primary statistical analysis had been done." Comment: blinding of participants and personnel was adequately done.	LOW	Quote: "The research nurse, who was unaware of the treatment allocation, allocated patients to the first available number of study cream in the corresponding block...as assessed by the research nurse." Comment: blinding of outcome assessors was adequately done.	LOW	Comment: lost less than 20% (3.7%), with reasons.	UNCLEAR	No study protocol registry available.	LOW	No other sources of bias were identified.

Table S2 continues

Table S2. Risk of Bias Judgments for Each Included RCT. (continued)

Study/Year	Randomization	Allocation concealment	Blinding participants/personnel (subjective outcomes)	Blinding outcome assessors (subjective outcomes)	Incomplete outcome	Selective reporting	Other bias
Koning 2008	<p>LOW</p> <p>Quote: "Randomization was centre based and performed using an automated telephone system."</p>	<p>LOW</p> <p>Quote: "Randomization was centre based and performed using an automated telephone system."</p>	<p>LOW</p> <p>Quote: "The packaging and labelling of study medication was identical for the active medication and its placebo counterpart. All efforts were made to make the study medication and placebo identical with respect to appearance and smell. Only in the case of an emergency, when knowledge of the investigational product was essential for the clinical management or welfare of the patient, could the investigator unblind a patient's treatment assignment."</p> <p>Comment: blinding of participants and personnel was adequately done.</p>	<p>LOW</p> <p>Quote: "The packaging and labelling of study medication was identical for the active medication and its placebo counterpart. All efforts were made to make the study medication and placebo identical with respect to appearance and smell. Only in the case of an emergency, when knowledge of the investigational product was essential for the clinical management or welfare of the patient, could the investigator unblind a patient's treatment assignment."</p> <p>Comment: blinding of outcome assessors was adequately performed.</p>	<p>HIGH</p> <p>Quote: "48 losses (22.5%), lack of efficacy, disease progression, decided to withdraw, adverse event, protocol violation, lost of follow-up"</p> <p>Comment: Loss of more than 20% of the sample. (22.5%)</p>	<p>LOW</p> <p>Study protocol registry available (NCT00133848). Comment: No differences were identified between the study and the protocol.</p>	<p>LOW</p> <p>No other sources of bias were identified.</p>
Kuniyuki 2005	<p>UNCLEAR</p> <p>Quote: "Forty-nine patients participated in a bacteriologically controlled, randomized, open-label, parallel group comparison"</p> <p>Comment: No sufficient information on random sequence generation.</p>	<p>UNCLEAR</p> <p>No sufficient information to judge.</p>	<p>HIGH</p> <p>Quote: "open-label study".</p>	<p>LOW</p> <p>Quote: "open-label study".</p>	<p>UNCLEAR</p> <p>Comment: no losses during the follow up.</p>	<p>LOW</p> <p>No study protocol registry available.</p>	<p>LOW</p> <p>No other sources of bias were identified.</p>

McInn 1990	UNCLEAR	QUOTE: "Sixty patients participated in a bacteriologically controlled, randomized, open-label, parallel group comparison ..." Comment: No sufficient information on random sequence generation	UNCLEAR	No sufficient information to judge.	HIGH	Quote: "open-label study".	HIGH	Quote: "open-label study".	LOW	Comment: lost less than 20% (1.7%), with reasons.	UNCLEAR	No study protocol registry available.	LOW	No other sources of bias were identified.
Mertz 1989	LOW	Quote: "This was an investigator-blinded randomized study. Patients were randomized between the two treatment groups according to a computer-generated schedule having a block size of four."	LOW	Quote: "This was an investigator-blinded randomized study. Patients were randomized between the two treatment groups according to a computer-generated schedule having a block size of four."	HIGH	Quote: "Parents or guardians were instructed to either gently rub the mupirocin ointment into all the affected areas three times daily (morning, noon, and evening) for 8 ± 1 days (mean ± SD) or to give the patient 30 to 50 mg per kilogram (divided into two daily doses) of erythromycin ethylsuccinate suspension, chewable tablets, or capsules for 8 ± 1 days." Comment: Different forms of interventions (oral and topical) prevent masking.	LOW	Quote: "The randomization was predetermined by the sponsor (Beecham Laboratories, Bristol, Tenn) and the schedule for distribution of medications was entrusted to team member whose assignment was to dispense medication." "The identity of the patient assignment to each treatment was known to the support team but unknown to the physician evaluators."	HIGH	Comment: lost less than 20% (29%), with reasons.	UNCLEAR	No study protocol registry available.	LOW	No other sources of bias were identified.

Table S2 continues

Table S2. Risk of Bias Judgments for Each Included RCT. (continued)

Study/Year	Randomization	Allocation concealment	Blinding participants/personnel (subjective outcomes)	Blinding outcome assessors (subjective outcomes)	Incomplete outcome	Selective reporting	Other bias
Nolting 1988	<p>LOW</p> <p>Quote: "When patients enrolled in the trial, they were allocated, according to a computer-generated randomization code, to receive either sulconazole nitrate 1% cream or miconazole nitrate 2% cream."</p>	<p>LOW</p> <p>Quote: "When patients enrolled in the trial, they were allocated, according to a computer-generated randomization code, to receive either sulconazole nitrate 1% cream or miconazole nitrate 2% cream."</p>	<p>HIGH</p> <p>Comment: Insufficient information is available to make a judgment. Nonetheless, the absence of blinding among participants and personnel can significantly impact the outcomes.</p>	<p>HIGH</p> <p>Comment: The blinding of outcome assessors was not confirmed, and this lack of blinding can indeed influence the results.</p>	<p>LOW</p> <p>Quote: "All patients completed the 2-week study." Comment: no losses during the follow up.</p>	<p>UNCLEAR</p> <p>No study protocol registry available.</p>	<p>LOW</p> <p>No other sources of bias were identified.</p>
Oranje 2007	<p>LOW</p> <p>Quote: "Subjects were assigned randomly to retapamulin or sodium fusidate by means of a predetermined, center-based 2:1 schedule using the telephone-based, interactive, central Registration and Medication Ordering System. Randomization was also stratified according to the following age groups: 9 months to 5 years, 6-12 years and 6-13 years."</p>	<p>LOW</p> <p>Quote: "Subjects were assigned randomly to retapamulin or sodium fusidate by means of a predetermined, center-based 2:1 schedule using the telephone-based, interactive, central Registration and Medication Ordering System. Randomization was also stratified according to the following age groups: 9 months to 5 years, 6-12 years and 6-13 years."</p>	<p>LOW</p> <p>Quote: "observer-blinded" "In addition, subjects and, where appropriate, their parents/guardians were instructed not to discuss any details of the study medication with clinical assessors"</p> <p>Comment: no blinding of participants and personnel.</p>	<p>LOW</p> <p>Quote: "The blinded assessor was responsible for performing all clinical activities in assessing the subjects' lesion(s) following treatment. To maintain observer blinding, an unblinded person (other than the investigator) at the study site was responsible for dispensing the study medication, maintaining the patients' study treatment records and ensuring that the clinical assessor remained blinded to treatment assignments at all visits. In addition, subjects and, where appropriate, their parents/guardians were instructed not to discuss any details of the study medication with clinical assessors"</p>	<p>LOW</p> <p>Comment: lost less than 20% (7.9%)</p>	<p>Study protocol registry available (NCT00133874). Comment: No differences were identified between the study and the protocol.</p>	<p>LOW</p> <p>No other sources of bias were identified.</p>

Rosen 2018	LOW	Quote: "Central randomization via an interactive web response system was used to allocate patients to treatment groups, stratified by age subset, to ensure a 1:1 distribution and avoid selection bias."	HIGH	There is insufficient information available to make a judgment. Nonetheless, the absence of blinding among participants and personnel can significantly impact the outcomes.	HIGH	Quote: "This randomized clinical trial was a multicenter, double-blind, vehicle-controlled, parallel group," Comment: The blinding of outcome assessors was not confirmed, and this lack of blinding can indeed influence the results.	LOW	Quote: "Overall, 13 patients in the placebo group discontinued the study owing to worsening of condition. Four patients withdrew owing to adverse events (1 in the ozenoxacin group and 3 in the placebo group), 4 were lost to follow-up (2 in each group), 3 withdrew consent (2 in the ozenoxacin group and 1 in the placebo group), and 2 discontinued for other reasons (1 in each group)." Comment: lost less than 20% (6.3%)	LOW	Study protocol registry available (NCT02090764). Comment: No differences were identified between the study and the protocol.	LOW	No other sources of bias were identified.
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Table S2 continues

Table S2. Risk of Bias Judgments for Each Included RCT. (continued)

Study/Year	Randomization	Allocation concealment	Blinding participants/personnel (subjective outcomes)	Blinding outcome assessors (subjective outcomes)	Incomplete outcome	Selective reporting	Other bias
Sudha 2017	UNCLEAR Quote: "They were randomly divided into two groups with 50 patients in each group." Comment: No sufficient information on random sequence generation	UNCLEAR No sufficient information to judge.	HIGH Quote: "This is a prospective, randomized, single blinded interventional study" Comment: The blinding of participants was not confirmed, and this lack of blinding can indeed influence the results.	HIGH Quote: "This is a prospective, randomized, single blinded interventional study" Comment: The blinding of outcome assessors was not confirmed, and this lack of blinding can indeed influence the results.	LOW Comment: no losses during the follow up.	UNCLEAR No study protocol registry available.	LOW No other sources of bias were identified.
Tong 2010	UNCLEAR Quote: "Participants were randomised to receive either a single dose of IM BPG (45 mg/kg up to 900 mg) or TMP-SMZ" Comment: No sufficient information on random sequence generation	LOW Quote: "Allocation was concealed by using sealed, sequentially marked, opaque envelopes."	HIGH There is insufficient information available to make a judgment. Nonetheless, the absence of blinding among participants and personnel can significantly impact the outcomes.	LOW Quote: "Assessment was by clinical examination and also by review of photographs by two investigators blinded to treatment allocation."	LOW Comment: no losses during the follow up.	LOW Study protocol registry available (ACTRN 12607000 592448). Comment: No differences were identified between the study and the protocol.	LOW No other sources of bias were identified.