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Interventions for bacterial folliculitis and boils (furuncles and carbuncles) (Protocol)

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[Intervention Protocol]

Interventions for bacterial folliculitis and boils (furuncles and carbuncles)

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ABSTRACT

This is a protocol for a Cochrane Review (Intervention). The objectives are as follows:

To assess the effects of interventions (such as topical antibiotics, topical antiseptic agents, systemic antibiotics, phototherapy, and incision and drainage) for people with bacterial folliculitis and boils.

BACKGROUND

Description of the condition

Please see Table 1 for explanations of specific terms used in this review.

Folliculitis is inflammation of the hair follicle caused by infection, chemical stimulation, or physical injury (Pasternack 2015). The aetiology of folliculitis is diverse, including occlusion folliculitis resulting from blockages caused by exposure to topical products that block the opening of the hair follicle, leading to inflammation, and Malassezia folliculitis, which is caused by *Malassezia furfur* (also known as *Pityrosporum ovale*) and presents as itching red papules over the chest, shoulders, or back (Gunatheesan 2018).

The interest of this Review is bacterial folliculitis, which is a bacterial infection within the hair follicle that typically presents as a red swelling with or without a pustule over the follicular opening (Craft 2012). Without treatment, bacterial folliculitis may resolve in seven to 10 days or may progress to boils; for some cases of folliculitis, especially those caused by *Staphylococcus aureus*, a course of oral antibiotics may be administered over seven to 10 days (Laureano 2014).

A boil, also known as a furuncle, is a bacterial infection involving the perifollicular tissue that usually originates from pre-existing folliculitis (Lopez 2006). A boil appears as a painful red swelling around the follicular opening and may progress to form an abscess (Craft 2012). Some boils may be treated with moist heat application; others with surrounding cellulitis or fever may require treat-

ment with systemic antibiotics (Pasternack 2015). Systemic antibiotics should be continued until the lesion resolves (Pasternack 2015). Carbuncles are large painful swellings with multiple pus-discharging openings and constitutional symptoms including fever and malaise (Craft 2012). They affect the deeper layers of soft tissue and can lead to scarring. Without control, boils may occasionally be complicated by severe skin infections such as cellulitis or lymphadenitis combined with constitutional symptoms such as fever, fatigue, and chills.

Bacterial folliculitis and boils are prone to occur in areas of the skin subject to rubbing, occlusion, and sweating, such as neck, face, axillae, and buttocks (Craft 2012). Clinicians usually diagnose bacterial folliculitis and boils based on physical examination findings (Craft 2012).

Bacterial folliculitis and boils are bacterial infections with a worldwide prevalence, but their exact prevalence and incidence are unclear. One study reported a prevalence of around 1.3% in school children (Al-Saeed 2006). Another study found that 27% of immunosuppressed organ transplant recipients presented with persistent folliculitis (Lally 2011). In 2010, at least 280,000 boil episodes were reported, and hospital admissions for abscesses, carbuncles, boils, and cellulitis almost doubled in the UK - from 123 admissions per 100,000 in 1998/1999 to 236 admissions per 100,000 in 2010/2011 (Shallcross 2015). This rise might have occurred because staphylococcal strains have become more severe or difficult to treat and may cause recurrent infection, as seen with the increased virulence of community-onset methicillin-resistant *S aureus* (MRSA) produced by toxins such as Panton-Valentine leukocidin (PVL) (Dufour 2002).

Staphylococcus aureus is the most common pathogen of folliculitis and boils. However, gram-negative pathogens including *Klebsiella*, *Enterobacter*, and *Proteus* species may replace the gram-positive flora on facial skin, nasal mucous membranes, and neighbouring areas, causing gram-negative folliculitis and boils (Böni 2003). 'Hot tub' folliculitis is caused by *Pseudomonas aeruginosa* contamination of undertreated water in saunas or whirlpools (Zacherle 1982).

Certain people are affected by recurrent furunculosis (i.e. furuncles that have a propensity to recur and may spread among family members) (Ibler 2014). Recurrent boils are a bothersome disorder that may affect patients' quality of life (Ibler 2014). Colonisation of *S aureus* in the anterior nares plays an important role in the origin of chronic or recurrent furunculosis (Ibler 2014).

Description of the intervention

Various interventions have been suggested for treating folliculitis (Craft 2012; O'Dell 1998), including local application of moist heat, phototherapy, antiseptic agents, antibiotics alone, or combination therapy. Treatment of fluctuating boils often requires drainage of the lesion, and for severe infections systemic antibiotics should be given until the signs of inflammation have regressed.

Local moist heat around 38°C to 40°C applied for 15 to 20 minutes may increase local blood flow, may establish drainage, and has proved helpful in treatment of newly emerged folliculitis or boils (Pasternack 2015). No adverse effects of local moist heat are known (Petrofsky 2009).

Topical antibiotics may be used in treating folliculitis and boils when the number of lesions is limited, or they may be used in combination with other interventions, for example, incision and drainage (Laureano 2014). Available preparations include fusidic acid 2% cream twice daily (Frosini 2017; Koning 2002), clindamycin 2% gel twice daily, and mupirocin 2% ointment applied two to three times daily (Micromedex 2018). These drugs are topically applied over the lesion. Topical antibiotics may cause contact dermatitis, dryness, or pruritus over the applied area. However, these adverse events are usually minor (Tran 2017). No major drug-drug interactions between these topical antibiotics and other medications are known (Micromedex 2018).

Topical antiseptic agents may be manufactured as gel (such as benzoyl peroxide 2% to 10% twice daily), cream, soap, or solution (e.g. hypochlorite 3% to 5% solution) (Micromedex 2018). These antiseptics may be used alone or in combination with antibiotics for treating folliculitis and boils, especially in recurrent furunculosis (Davido 2013). No specific restrictions apply to the use of topical antiseptics (Pasternack 2015). The adverse events of benzoyl peroxide are usually mild and mainly include skin irritation over the application site (Kawashima 2017). No drug interactions of topical antiseptics are known (Micromedex 2018).

Systemic antibiotics may be used for treating folliculitis and boils, especially when systemic symptoms such as fever, lymphadenitis, or cellulitis appear (Pereira 1996). We have listed regimens and common drug-drug interactions of systemic antibiotics in Table 2. First-line oral antibiotics including dicloxacillin (250 mg four times daily) and cephalosporins (such as cefadroxil 500 mg twice daily) are commonly used. For antibiotic-resistant *S aureus* that has emerged in the community, clindamycin, tetracyclines, trimethoprim-sulphamethoxazole, linezolid, or glycopeptide, for example, parenteral vancomycin, may be used (Laureano 2014; Nagaraju 2004). Oral or parenteral ciprofloxacin 400 to 500 mg twice daily with antipseudomonal activity may be administered for gram-negative folliculitis such as 'hot tub' folliculitis (Craft 2012). Potential adverse events of systemic antibiotics include allergic reactions, neurological or psychiatric disturbances, and diarrhoea (Shehab 2008). Systemic antibiotics may be used in combination with topical antiseptics for treating folliculitis and boils (Pasternack 2015).

Surgical interventions, such as incision and drainage, are likely to be adequate for simple fluctuant folliculitis or boils (Ibler 2014). Incision may cause scarring at the incised site (Ahmad 2017). Combination with topical or systemic antibiotics is often employed, especially with lack of response to incision and drainage alone, or when the lesion is in an area that is difficult to completely drain (e.g. face, hands, genitalia) (Ibler 2014).

Phototherapy by monochromatic excimer light (308 nm) with 0.5

to 2 minimal erythema dose (MED) has been used as treatment for superficial folliculitis. Nisticò 2009 reported only mild adverse events such as local erythema.

How the intervention might work

As mentioned above, bacterial folliculitis and boils occur as inflammation of the follicle and perifollicular tissue caused by bacterial infection. Therefore, antibacterial, antiseptic, and anti-inflammatory interventions may be used for treatment.

Topical antibiotics, for example, clindamycin, aminoglycosides, and fusidic acid, directly kill or inhibit pathogenic bacteria within the follicle, avoiding further tissue damage by these pathogens (Frosini 2017).

Therapeutic effects of antiseptic agents are attributed to the killing of bacteria that cause folliculitis and boils, for example, *S aureus* (Fisher 2008). Benzoyl peroxide is an antiseptic that confers not only antibacterial effects but also keratolytic effects, which cause the skin to dry and peel (Kawashima 2017).

Systemic antibiotics can directly inhibit or kill the pathogenic bacteria causing folliculitis and boils. When bacterial cultures are available, systemic antibiotics can be administered according to the pathogen identified (Ibler 2014).

Ultraviolet-B radiation, primarily affecting the epidermis and the superficial dermis, is absorbed by endogenous chromophobes, such as nuclear DNA, which initiates a cascade of immunomodulatory effects (Bulat 2011). For its anti-inflammatory effects, phototherapy has been proposed as a treatment option for folliculitis (Nisticò 2009).

Given that pus or even an abscess may be present with fluctuant folliculitis and boils, incision and drainage may be used to remove toxic purulent material, decompress the tissues, and support better blood perfusion, which increases drug concentration in an affected area and improves local immune response and tissue repair (Ibler 2014).

Why it is important to do this review

The Cochrane Skin Review Group undertook an extensive prioritisation exercise alongside the Global Burden of Disease and the World Health Organization to identify a core portfolio of the most clinically important titles. Consequently, our title was identified as a clinically important priority by the expert panel for development, maintenance, and investment of resources by the editorial base. As aforementioned, folliculitis and boils are worldwide prevalent diseases that cause a great burden on the quality of life of individuals, with an estimation of 1,944,776 DALYs (disability-adjusted life years) worldwide in 2016 (range, 1,249,848 to 2,603,083) (GBD 2018).

To the best of our knowledge, no systematic reviews to date have examined interventions for folliculitis and boils. We wish to conduct a systematic review to find and evaluate the best evidence on effects of available interventions for folliculitis and boils.

OBJECTIVES

To assess the effects of interventions (such as topical antibiotics, topical antiseptic agents, systemic antibiotics, phototherapy, and incision and drainage) for people with bacterial folliculitis and boils.

METHODS

Criteria for considering studies for this review

Types of studies

We will include only randomised controlled trials (RCTs), including parallel, cluster, cross-over, and split-body within-participant RCTs.

Types of participants

Participants will include people with bacterial folliculitis or boils diagnosed by a healthcare professional or a trained researcher based on clinical presentation or bacterial culture (e.g. via a sensitivity test). We will exclude those with non-bacterial folliculitis, for example, *Pityrosporum* folliculitis and mite folliculitis. We will include RCTs conducted in any setting and will include participants with no restrictions on demographic factors such as age and sex.

When a study includes participants with various superficial bacterial infections of the skin, we will include the study only if study authors report separate data for those with bacterial folliculitis or boils. When the publication does not provide separate data, we will contact study authors and will request separate data for bacterial folliculitis and boils.

Types of interventions

Interventions will include systemic antibiotics, topical antibiotics, topical antiseptics such as topical benzoyl peroxide, phototherapy, and surgical interventions (e.g. incision and drainage). Participants may receive a single intervention or a combination of interventions.

Comparators will include another active intervention, placebo, or no treatment.

Types of outcome measures

We will consider outcome data measured at ≤ 1 month and > 1 month as short-term and long-term outcomes, respectively. For studies with multiple time points, we will consider data from longest follow-up only.

Primary outcomes

1. Clinical cure: clearance of all visible lesions of folliculitis or boils (i.e. disappearance of all papular or pustular lesions of folliculitis or boils at the end of treatment)
2. Severe adverse events leading to withdrawal of treatment

Secondary outcomes

1. Quality of life: as measured by validated tools, including Dermatology Life Quality Index (DLQI), Short Form-36 (SF-36), Skindex 29, Skindex 17, or Dermatology Quality of Life Scale (DQOLS)

    i) We will consider a DLQI score change of at least 5 as a minimally important difference (Khilji 2002)

2. Recurrence of folliculitis or boil following completion of treatment
3. Minor adverse events not leading to withdrawal of treatment

Search methods for identification of studies

We aim to identify all relevant RCTs regardless of publication language or status (published, unpublished, in press, or in progress).

Electronic searches

The Cochrane Skin Information Specialist will search the following databases for relevant trials with no restriction by date.

1. Cochrane Skin Specialised Register.
2. Cochrane Central Register of Controlled Trials (CENTRAL), in the Cochrane Library.
3. MEDLINE via Ovid (from 1946 onwards).
4. Embase via Ovid (from 1974 onwards).

The Information Specialist has devised a draft search strategy for RCTs for MEDLINE (Ovid), which we have displayed in Appendix 1. We will use this as the basis for search strategies for the other databases listed.

Trials registers

We will search the following trials registers using the terms 'boil/s', 'furuncle/s', 'furunculosis', 'folliculitis', 'carbuncle', 'sycosis', and 'sycoses'.

1. International Standard Randomized Controlled Trials Number (ISRCTN) register (www.isrctn.com).
2. US National Institutes of Health Ongoing Trials Register (www.clinicaltrials.gov).
3. Australian New Zealand Clinical Trials Registry (www.anzctr.org.au).
4. World Health Organization International Clinical Trials Registry Platform (ICTRP) (apps.who.int/trialsearch/).
5. EU Clinical Trials Register (www.clinicaltrialsregister.eu).

Searching other resources

Searching reference lists

We will check the bibliographies of included RCTs and any relevant systematic reviews identified for further references to relevant trials.

Unpublished literature

We will contact the authors of reports of relevant RCTs published within the last three years to ask if they are aware of any relevant unpublished data.

Adverse effects

We will not perform a separate search for adverse effects of interventions used for treatment of folliculitis and boils. We will consider only adverse events described in included RCTs.

Data collection and analysis

Some parts of this section use text that was originally published in another Cochrane protocol or in the *Cochrane Handbook for Systematic Reviews of Interventions* (Chi 2015; Higgins 2011, respectively).

Selection of studies

Two review authors (HL and PL) will independently check titles and abstracts derived from the searches. We will not be blinded to the names of trials or their institutions. If we can judge from the title and abstract that a study does not relate to an RCT on interventions for treating folliculitis and boils, we will exclude it straight away. The same two review authors will independently examine the full text of each remaining study and will judge whether it meets our inclusion criteria. If the two review authors disagree on whether they should include a study, they will achieve unanimity through discussion with a third review author (CC). We will list the studies that we exclude after examining the full text and will provide reasons for exclusion in the 'Characteristics of excluded studies' tables. We will use Covidence for selection of studies (Covidence 2017).

Data extraction and management

Two review authors (HL and PL) will independently extract data from the included RCTs using a data extraction form to collect the following information: study methods, participants, interventions, outcomes, country, setting, and funding source (see Appendix 2). We have already pilot-tested the data extraction form. We will use WebPlotDigitizer to extract data from figures and graphs (WebPlotDigitizer 2017). We will use extracted data to create the 'Characteristics of included studies' tables. If we encounter disagreement about some data, the two review authors will consult with a third review author (CC) to achieve unanimity. One review author (PL) will enter the data into Review Manager 5 (RevMan 2014), and another review author (HL) will recheck the entered data.

Assessment of risk of bias in included studies

We will use Cochrane's tool for assessing risk of bias in RCTs by evaluating the following domains (Higgins 2011).

1. Random sequence generation (selection bias): adequacy of the method of random sequence generation to produce comparable groups in every aspect except for the intervention.
2. Allocation concealment (selection bias): adequacy of the method used to conceal the allocation sequence to prevent anyone from foreseeing the allocation sequence in advance of, or during, enrolment.
3. Blinding of participants and personnel (performance bias): adequacy of blinding participants and investigators from knowledge of which intervention a participant receives.
4. Blinding of outcome assessment (detection bias): adequacy of blinding outcome assessors from knowledge of which intervention a participant receives.
5. Incomplete outcome data (attrition bias): completeness of outcome data for each main outcome, including attrition and exclusions from analysis, whether attrition and exclusions are reported, the numbers in each intervention group (compared with total randomised participants), reasons for attrition or exclusions when reported, and any re-inclusions in our analyses.
6. Selective reporting (reporting bias): when the trial protocol is available, we will determine whether all pre-specified outcomes are reported. When the study protocol is unavailable, we will identify whether published reports include all expected outcomes, including those that are pre-specified.
7. Other bias: any important concerns about bias not addressed in the other domains, for example, design-specific risks of bias and baseline imbalance.

We will determine the overall risk of bias for each outcome (across domains) within studies as follows (Higgins 2011).

1. Low risk of bias when all domains are assessed as being at low risk (plausible bias unlikely to seriously alter the results).
2. Unclear risk of bias when at least one domain is classified as being at unclear risk (plausible bias that raises some doubt about the results).
3. High risk of bias when at least one domain is judged as being at high risk (plausible bias that seriously weakens confidence in the results).

We will determine the overall risk of bias for each outcome (across domains) across studies as follows (Higgins 2011).

1. Most information is obtained from studies at low risk of bias (plausible bias unlikely to seriously alter the results).
2. Most information is obtained from studies at low or unclear risk of bias (plausible bias that raises some doubt about the results).
3. The proportion of information from studies at high risk of bias is sufficient to affect the interpretation of results (plausible bias that seriously weakens confidence in the results).

Two review authors (HL and PL) will independently assess the risk of bias of included RCTs. We will discuss with a third review author (CC) to resolve disagreements in assessment.

Measures of treatment effect

Dichotomous data

We will express dichotomous data as risk ratios (RRs) with 95% confidence intervals (CIs). When the RR is statistically significant, we will also present the number needed to treat for an additional beneficial outcome (NNTB) and the number needed to treat for an additional harmful outcome (NNTH) with 95% CIs.

Continuous data

We will express continuous data as mean differences (MDs) with 95% CIs. When different outcome scales are pooled, we will express continuous data as standardised mean differences (SMDs) with 95% CIs.

Time-to-event data

We will express time-to-event data as hazard ratios (HRs) with 95% CIs. We will extract HRs as presented in the included study report. When HRs were not reported, we will use the methods described in Tierney 2007 to estimate the HRs if sufficient data are provided.

Unit of analysis issues

We will analyse separately studies of the following types of design using appropriate techniques as described in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011).

Cluster-randomised trials

For cluster-randomised trials that have not adjusted for clusters in their analysis, we will employ the Rao methods described in Chapter 16.3.4 in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011; Rao 1992), and we will estimate the intervention effect assuming an intracluster correlation coefficient (ICC) of 0.05 .

Cross-over trials

For cross-over trials, we will include only data from the first period for analysis. If these data are not available, we will employ the statistical methods described in Section 16.4.6 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011), undertaking paired analyses by imputing missing standard deviations.

Studies with multiple treatment groups

For studies with multiple intervention groups, we will make separate pairwise comparisons of one intervention versus another. For example, if an RCT includes three interventions groups - Group A (placebo or the most frequently used intervention), Group B, and Group C - we will make separate pairwise comparisons of B versus A and C versus A.

Split-body trials

For split-body trials, we will conduct paired analyses using data from one side of the body versus the other side of the body. We will analyse continuous and dichotomous data by using the paired *t*-test and McNemar's test, respectively.

Dealing with missing data

We will contact the authors of studies less than 10 years old to ask for missing data. When missing data are not available, we will conduct an intention-to-treat (ITT) analysis to recalculate the intervention effect estimates, that is, we will include all randomised participants in the analysis and will assume that those with missing dichotomous outcome data experienced treatment failure. For missing continuous outcome data, we will attempt to adopt the last observation carried forward (LOCF) approach in analysis if the trials provide relevant original data, that is, we will replace a missing value with the participant's last observed value. Furthermore, we will conduct a sensitivity analysis by assuming that those with missing dichotomous outcome data experienced treatment success.

Assessment of heterogeneity

We will calculate the I^2 statistic to assess statistical heterogeneity across the included trials. The importance of the observed value of the I^2 statistic depends on (1) magnitude and direction of effects and (2) strength of evidence for heterogeneity (e.g. P value from Chi^2 test, CI for I^2 statistic) (Higgins 2011). For the confidence interval for an I^2 statistic, the rule of thumbs is as follows.

1. 0% to 40%: might not be important.
2. 30% to 60%: may represent moderate heterogeneity.
3. 50% to 90%: may represent substantial heterogeneity.
4. 75% to 100%: may show considerable heterogeneity.

We will also assess statistical heterogeneity via forest plot inspection, as in some analyses, a high I^2 might not be a serious issue, especially if the estimates are all on the same side of the forest plot. However, we will examine whether statistical heterogeneity suggests a dose-response relationship or the presence of minimum therapeutic dose by conducting a subgroup analysis based on different dosages of the intervention.

Assessment of reporting biases

When at least 10 trials are included in a meta-analysis on primary outcomes for an intervention, we will prepare a funnel plot to assess for publication bias (Higgins 2011).

Data synthesis

We will provide a narrative description of all outcomes when data are available. We will pool only trials that are sufficiently similar in terms of participants, interventions, and outcomes. We will perform a meta-analysis employing the random-effects model to obtain a pooled intervention effect. When a meta-analysis is not feasible, we will summarise the data narratively instead.

When results are estimated for individual studies with low numbers of outcomes (fewer than 10 in total), or when the total sample size is less than 30 participants and a RR is used, we will report the proportion of outcomes in each group together with a P value based on Fisher's exact test.

The comparisons of interest that we expect for this review include topical antibiotics versus topical antiseptics, topical antibiotics versus systemic antibiotics, and phototherapy versus sham light.

Subgroup analysis and investigation of heterogeneity

We will conduct the following subgroup analyses when relevant data are available.

1. Paediatric versus adult participants (further divided into bacterial culture-proven or clinical diagnosis only).
2. Immunocompetent versus immunosuppressed participants (further divided into bacterial culture-proven or clinical diagnosis).

3. Methicillin-sensitive *S aureus (*MSSA) versus MRSA (including PVL gene type).
4. Different dosages of an intervention.

To test for subgroup differences, we will employ random-effects model analysis and will use the methods developed by Borenstein 2008 , which have been implemented in Review Manager software (RevMan 2014).

Sensitivity analysis

If possible, we will conduct a sensitivity analysis to examine intervention effects after excluding trials with high risk of bias for one or more domains for the associated outcome. We will also conduct a sensitivity analysis by assuming that those with missing dichotomous outcome data experienced treatment success.

'Summary of findings' tables and GRADE assessments

We will present at least one 'Summary of findings' table in our review to summarise data on our primary outcomes including clinical cure, severe adverse events leading to withdrawal of treatment, and secondary outcomes including quality of life, recurrence, and minor adverse events not leading to withdrawal of treatment for the most important comparisons: topical antibiotics versus topical antiseptics, topical antibiotics versus systemic antibiotics, and phototherapy versus sham light (see Types of outcome measures). When several major comparisons are reported, or when outcomes need to be summarised for different populations, we will produce additional 'Summary of findings' tables.

Two review authors (HL and PL) will assess the quality of the body of evidence using the five Grading of Recommendations Assessment, Development and Evaluation (GRADE) considerations: study limitations, consistency of effect, imprecision, indirectness, and publication bias (Schünemann 2013). The certainty (or quality) of evidence can be downgraded from high to moderate, low, or very low based on the five considerations stated above. We will resolve disagreements by discussion with a third review author (CC). We will use GRADEpro GDT (GRADEpro GDT 2015) to prepare 'Summary of findings' tables and to assess the certainty of evidence.

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REFERENCES

Additional references

Ahmad 2017
Ahmad H, Siddiqui SS. An unusually large carbuncle of the temporofacial region demonstrating remarkable post-debridement wound healing process: a case report. *Wounds* 2017;**29**(4):92–5. [PUBMED: 28448262]

Al-Saeed 2006
Al-Saeed WY, Al-Dawood KM, Bukhari IA, Bahnassy AA. Prevalence and pattern of skin disorders among female school children in Eastern Saudi Arabia. *Saudi Medical Journal* 2006;**27**(2):227–34. [PUBMED: 16501682]

Borenstein 2008
Borenstein M, Hedges LV, Higgins JPT, Rothstein HR. *Introduction to Meta-analysis*. Chichester: John Wiley & Sons, 2008.

Bulat 2011
Bulat V, Situm M, Dediol I, Ljubicić I, Bradić L. The mechanisms of action of phototherapy in the treatment of the most common dermatoses. *Collegium Antropologicum* 2011;**35**(Suppl 2):147–51. [PUBMED: 22220423]

Böni 2003
Böni R, Nehrhoff B. Treatment of gram-negative folliculitis in patients with acne. *American Journal of Clinical Dermatology* 2003;**4**(4):273–6. [PUBMED: 12680804]

Chi 2015
Chi CC, Ko SH, Yeh ML, Wang SH, Tsai YS, Hsu MY. Lifestyle changes for treating psoriasis. *Cochrane Database of Systematic Reviews* 2015, Issue 11. DOI: 10.1002/14651858.CD011972

Covidence 2017 [Computer program]
Veritas Health Innovation. Covidence systematic review software. Melbourne, Australia: Veritas Health Innovation, 2017.

Craft 2012
Craft N. Chapter 176. Superficial cutaneous infections and pyodermas. In: Goldsmith LA, Katz SI, Gilchrest BA, Paller AS, Leffell DJ, Wolff K editor(s). *Fitzpatrick's Dermatology in General Medicine*. Eighth. New York: The McGraw-Hill Companies, Inc, 2012:2134–2136. [ISBN: 978–0–07–171755–7]

Davido 2013
Davido B, Dinh A, Salomon J, Roux AL, Gosset-Woimant M, Pierre I, et al. Recurrent furunculosis: efficacy of the CMC regimen - skin disinfection (chlorhexidine), local nasal antibiotic (mupirocin), and

systemic antibiotic (clindamycin). *Scandinavian Journal of Infectious Diseases* 2013;**45**(11):837–41. DOI: 10.3109/00365548.2013.810815

Dufour 2002
Dufour P, Gillet Y, Bes M, Lina G, Vandenesch F, Floret D, et al. Community-acquired methicillin-resistant Staphylococcus aureus infections in France: emergence of a single clone that produces Panton-Valentine leukocidin. *Clinical Infectious Diseases* 2002;**35**(7):819–24. DOI: 10.1086/342576

Fisher 2008
Fisher RG, Chain RL, Hair PS, et al. Hypochlorite killing of community-acquired methicillin-resistant Staphyloccus aureus. *Pediatric Infectious Disease Journal* 2008;**27**(10):934–5. DOI: 10.1097/INF.0b013e318175d871

Frosini 2017
Frosini SM, Bond R, Loeffler A, Larner J. Opportunities for topical antimicrobial therapy: permeation of canine skin by fusidic acid. *BMC Veterinary Research* 2017;**13**(1):345. DOI: 10.1186/s12917-017-1270-6; PUBMED: 29162115

GBD 2018
Institute for Health Metrics and Evaluation. Global Burden of Disease (GBD). vizhub.healthdata.org/gbd-compare/ (accessed 18 March 2018).

Gilbert 2018
Gilbert DN, Chambers HF, Eliopoulos GM, Saag MS, Pavia AT, editor(s). *Sanford Guide to Antimicrobial Therapy*. 8th Edition. Sperryville, VA: Antimicrobial Therapy, Inc., 2018.

GRADEpro GDT 2015 [Computer program]
McMaster University (developed by Evidence Prime). GRADEpro GDT: GRADEpro Guideline Development Tool. Hamilton (ON): McMaster University (developed by Evidence Prime), 2015.

Gunatheesan 2018
Gunatheesan S. Folliculitis. www.dermcoll.edu.au/atoz/folliculitis/ (accessed 13 June 2018).

Higgins 2011
Higgins JPT, Green S (editors). *Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 (updated March 2011)*. The Cochrane Collaboration, 2011. Available from www.cochrane-handbook.org.

Ibler 2014
Ibler KS, Kromann CB. Recurrent furunculosis - challenges and management: a review. *Clinical, Cosmetic and Investigational Dermatology* 2014;**2014**(7):59–64. DOI: https://doi.org/10.2147/CCID.S35302

Kawashima 2017
Kawashima M, Nagare T, Doi M. Clinical efficacy and safety of benzoyl peroxide for acne vulgaris: comparison between Japanese and Western patients. *Journal of Dermatology* 2017;**44**(11):1212–8. DOI: 10.1111/1346-8138.13996; PUBMED: 28791735

Khilji 2002
Khilji FA, Gonzalez M, Finlay AY. Clinical meaning of change in Dermatology Life Quality Index scores. *British Journal of Dermatology* 2001;**147**(Suppl 62):50. DOI: 10.1046/j.1365-2133.147.s62.16.x

Koning 2002
Koning S, van Suijlekom-Smit LW, Nouwen JL, Verduin CM, Bernsen RM, Oranje AP, et al. Fusidic acid cream in the treatment of impetigo in general practice: double blind randomised placebo controlled trial. *BMJ* 2002;**324**(7331):203–6. [PUBMED: PMC64791]

Lally 2011
Lally A, Casabonne D, Imko-Walczuk B, Newton R, Wojnarowska F. Prevalence of benign cutaneous disease among Oxford renal transplant recipients. *Journal of the European Academy of Dermatology and Venereology* 2011;**25**(4):462–70. DOI: 10.1111/j.1468-3083.2010.03814.x

Laureano 2014
Laureano AC, Schwartz RA, Cohen PJ. Facial bacterial infections: folliculitis. *Clinics in Dermatology* 2014;**2**(6):711–4. DOI: 10.1016/j.clindermatol.2014.02.009

Lopez 2006
Lopez FA, Lartchenko S. Skin and soft tissue infections. *Infectious Disease Clinics of North America* 2006;**20**(4):759–72. DOI: 10.1016/j.idc.2006.09.006

Micromedex 2018
DRUGDEX®. IBM Micromedex® (electronic version). www.micromedexsolutions.com/. Greenwood Village: Truven Health Analytics, (accessed 13 June 2018).

Nagaraju 2004
Nagaraju U, Bhat G, Kuruvila M, Pai GS, Jayalakshmi, Babu RP. Methicillin-resistant Staphylococcus aureus in community-acquired pyoderma. *International Journal of Dermatology* 2004;**43**(6):412–4. DOI: 10.1111/j.1365-4632.2004.02138.x; PUBMED: 15186220

Nisticò 2009
Nisticò SP, Saraceno R, Carboni I, Chimenti S. Treatment of folliculitis with monochromatic excimer light (308 nm). *Dermatology* 2009;**218**(1):33–6. DOI: 10.1159/000165627; PUBMED: 18946200

O'Dell 1998
O'Dell ML. Skin and wound infections: an overview. *American Family Physician* 1998;**57**(10):2424–32. [PUBMED: 9614412]

Pasternack 2015
Pasternack MS, Swartz MN. Cellulitis, necrotizing fasciitis, and subcutaneous tissue infections. *Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases*. Eighth. Vol. **95**, St. Louis, MO: Elsevier, 2015:1194–215.

Pereira 1996
Pereira LC. Comparative clinical study between roxithromycin and cephalexin in the treatment of folliculitis, furunculosis and erysipelas/cellulitis. *Revista Brasileira de Medicina* 1996;**53**(1):81–6.

Petrofsky 2009
Petrofsky JS, Bains G, Raju C, Lohman E, Berk L, Prowse M, et al. The effect of the moisture content of a local heat

source on the blood flow response of the skin. *Archives of Dermatology Research* 2009;**301**(8):581–5. DOI: 10.1007/s00403-009-0957-3

Rao 1992
Rao JNK, Scott AJ. A simple method for the analysis of clustered binary data. *Biometrics* 1992;**48**(2):577–85. DOI: 10.2307/2532311

RevMan 2014 [Computer program]
The Nordic Cochrane Centre, The Cochrane Collaboration. Review Manager (RevMan) 5.3. Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014.

Schünemann 2013
Schünemann H, Broż ek J, Guyatt G, Oxman A, editors. *GRADE Handbook for Grading Quality of Evidence and Strength of Recommendations*. The GRADE Working Group, 2013.

Shallcross 2015
Shallcross LJ, Hayward AC, Johnson AM, Petersen I. Evidence for increasing severity of community-onset boils and abscesses in UK general practice. *Epidemiology and Infection* 2015;**143**(11):2426–9. DOI: 10.1017/S0950268814003458; PUBMED: 25530161

Shehab 2008
Shehab N, Patel PR, Srinivasan A, Budnitz DS. Emergency department visits for antibiotic-associated adverse events. *Clinical Infectious Diseases* 2008;**47**(6):735–43. DOI: 10.1086/591126; PUBMED: 18694344

Tierney 2007
Tierney JF, Stewart LA, Ghersi D, Burdett S, Sydes MR. Practical methods for incorporating summary time-to-event data into meta-analysis. *Trials* 2007;**8**:16. DOI: 10.1186/1745-6215-8-16; PUBMED: 17555582

Tran 2017
Tran K, Wright MD. Topical antibiotics for infected dermatitis: a review of the clinical effectiveness and guidelines (CADTH rapid response report: summary with critical appraisal). www.cadth.ca/topical-antibiotics-infected-dermatitis-review-clinical-effectiveness-and-guidelines. Canadian Agency for Drugs and Technologies in Health, (accessed 18 March 2018). [PUBMED: 29528606]

WebPlotDigitizer 2017 [Computer program]
Ankit Rohatgi. WebPlotDigitizer. Austin, Texas, USA: Ankit Rohatgi, October 2017.

Zacherle 1982
Zacherle BJ, Silver DS. Hot tub folliculitis: a clinical syndrome. *Western Journal of Medicine* 1982;**137**(3):191–4. [PUBMED: 7147933]

* *Indicates the major publication for the study*

ADDITIONAL TABLES

Table 1. Glossary

Clinical term	Explanation
Anterior nares	External portion of the nostrils, which opens anteriorly into the nasal cavity and allows air inhalation and exhalation
Antipseudomonal	Agents used as drugs to destroy bacteria of the genus *Pseudomonas*
Axilla (pl. axillae)	Also known as the armpit, underarm, or oxter; the area directly under the joint where the human arm connects to the shoulder
Cellulitis	Term commonly used to indicate non-necrotising inflammation of the skin and subcutaneous tissues, a process usually related to acute infection that does not involve the fascia or muscles
Endogenous chromophobes	A chemical group (such as an azo group) that absorbs light at a specific frequency and so imparts colour to a molecule that originates from within an organism, tissue, or cell
Epidermis	One or more layers of cells forming the outermost portion of the skin or integument
Fluctuant	Being movable or compressible; often used to describe a tumour or abscess

Table 1. Glossary (*Continued*)

Gram-negative bacteria	Bacteria that contain an additional outer membrane composed of phospholipids and lipopolysaccharides that do not retain the crystal violet dye in the Gram stain protocol
Immunomodulatory	Substance that affects the functioning of the immune system
Keratolytic	Causing the horny outer layer of skin to soften and shed
Lymphadenitis	Associated with the lymph nodes, which are responsible for fighting off infections of the body; refers to the condition by which lymph nodes become inflamed, swell, and become tender during an infection
Monochromatic	Existing in only one colour or particular wavelength
Perifollicular tissue	Tissue surrounding a hair follicle; usually used to describe the histopathological appearance of the infiltrate surrounding a hair follicle
Pathogen	Any small organism, such as a virus or a bacterium, that can cause disease
Pseudomonal	Of or related to the *Pseudomonas* species, which is a ubiquitous strictly aerobic gram-negative bacterium with a predilection to moist environments and is a clinically significant opportunistic pathogen, often causing nosocomial infections
Purulent	Full of pus or like pus
Superficial dermis	Middle layer of skin, deep to the epidermis and superficial to the subcutaneous layer

Table 2. Regimens and drug-drug interactions of systemic antibiotics

Drug	**Dose/Regimen**	**Drug-Drug interaction** (Gilbert 2018; Micromedex 2018)
Cefadroxil	• Adult: 1 g orally daily in a single dose or in divided doses twice a day • Pediatric: 30 mg/kg orally once daily or in equally divided doses every 12 hours	• Concurrent use of cefadroxil and warfarin may result in increased risk of bleeding • Concurrent use of cefadroxil and contraceptives (combination) may result in decreased contraceptive effectiveness
Ciprofloxacin	• Adult: 500 mg orally every 12 hours for 7 to 14 days; 400 mg IV every 12 hours for 7 to 14 days	• Concurrent use of ciprofloxacin and insulin and oral hypoglycaemics may result in increased or decreased blood sugar • Concurrent use of ciprofloxacin and caffeine may result in increased caffeine plasma concentrations • Concurrent use of ciprofloxacin and cimetidine may result in increased blood level of ciprofloxacin

Table 2. Regimens and drug-drug interactions of systemic antibiotics (*Continued*)

		• Concurrent use of ciprofloxacin and cyclosporine may result in an increased cyclosporine plasma concentration • Concurrent use of ciprofloxacin and didanosine may result in a decreased ciprofloxacin plasma concentration • Concurrent use of ciprofloxacin and cations (e.g. Al^{3+}, Ca^{2+}, Fe^{2+}, Mg^{2+}, Zn^{2+}) (cireate/citric acid) may result in a decreased plasma concentration of ciprofloxacin • Concurrent use of ciprofloxacin and methadone may result in an increased plasma concentration of methadone • Concurrent use of ciprofloxacin and NSAIDs may result in increased risk CNS stimulation/seizure • Concurrent use of ciprofloxacin and phenytoin may result in an increased or decreased plasma concentration of phenytoin • Concurrent use of ciprofloxacin and probenecid may result in a decreased plasma concentration of ciprofloxacin • Concurrent use of ciprofloxacin and rasagiline may result in an increased plasma concentration of rasagiline • Concurrent use of ciprofloxacin and sucralfate may result in decreased absorption of ciprofloxacin • Concurrent use of ciprofloxacin and theophylline may result in an increased plasma concentration of theophylline • Concurrent use of ciprofloxacin and thyroid hormone may result in a decreased plasma concentration of thyroid hormone • Concurrent use of ciprofloxacin and tizanidine may result in an increased plasma concentration of tizanidine • Concurrent use of ciprofloxacin and warfarin may result in increased prothrombin time
Clindamycin	• Adult: 150 to 300 mg orally every 6 hours, 600 to 1200 mg/d IV or IM divided every 6 to 12 hours • Pediatric: 8 to 16 mg/kg/d ORALLY divided every 6 to 8 hours; 15 to 20 mg/kg/d IV or IM divided every 6 to 8 hours	• Concurrent use of clindamycin and kaolin may result in decreased absorption of kaolin • Concurrent use of clindamycin and muscle relaxants (e.g. atracurium, baclofen, diazepam) may result in increased frequency and duration of respiratory paralysis • Concurrent use of clindamycin and St

Table 2. Regimens and drug-drug interactions of systemic antibiotics (*Continued*)

		John's wort may result in a decreased level of clindamycin
Tetracyclines	• Adult: 500 mg orally twice daily or 250 mg orally 4 times per day • Pediatric: (older than 8 years) 25 to 50 mg/kg orally in 4 equally divided doses	• Concurrent use of tetracycline and atovaquone may result in decreased atovaquone levels • Concurrent use of tetracycline and digoxin may result in increased toxicity of digoxin • Concurrent use of tetracycline and methoxyflurane may result in increased toxicity, polyuria, and renal failure • Concurrent use of tetracycline and sucralfate may result in decreased absorption of tetracycline • Concurrent use of tetracycline and aluminium, bismuth, iron, or Mg^{2+} may result in decreased absorption of tetracycline • Concurrent use of tetracycline and barbiturates or hydantoins may result in a decreased serum half-life of tetracycline • Concurrent use of tetracycline and carbamazepine may result in a decreased serum half-life of tetracycline • Concurrent use of tetracycline and digoxin may result in an increased serum level of digoxin • Concurrent use of tetracycline and warfarin may result in increased activity of warfarin
Trimethoprim-sulphamethoxazole	• Adult: sulfamethoxazole 800 mg/ trimethoprim 160 mg to sulfamethoxazole 1600 mg/trimethoprim 320 mg orally twice daily • Pediatric: (older than 1 month) based on trimethoprim component: 8 to 12 mg/kg/d orally in 2 divided doses	• Concurrent use of trimethoprim-sulphamethoxazole and angiotensin-converting enzyme inhibitors may result in an increased serum potassium concentration • Concurrent use of trimethoprim-sulphamethoxazole and amantadine may result in increased serum levels and toxicity of tetracycline • Concurrent use of trimethoprim-sulphamethoxazole and azathioprine may lead to side effects of leukopaenia • Concurrent use of trimethoprim-sulphamethoxazole and barbiturates or hydantoins may result in a decreased serum half-life of tetracycline • Concurrent use of trimethoprim-sulphamethoxazole and loperamide may result in an increased serum level of loperamide

Table 2. Regimens and drug-drug interactions of systemic antibiotics (*Continued*)

		• Concurrent use of trimethoprim-sulphamethoxazole and methotrexate may result in enhanced marrow suppression • Concurrent use of trimethoprim-sulphamethoxazole and oral contraceptives, pimozide, and 6-mercaptopurine may result in decreased effects of oral contraceptives, pimozide, and 6-mercaptopurine • Concurrent use of trimethoprim-sulphamethoxazole and phenytoin may result in an increased serum level of phenytoin • Concurrent use of trimethoprim-sulphamethoxazole and rifampin may result in an increased serum level of phenytoin • Concurrent use of trimethoprim-sulphamethoxazole and spironolactone or sulfonylureas may result in an increased serum potassium level • Concurrent use of trimethoprim-sulphamethoxazole and warfarin may result in increased activity of warfarin
Linezolid	• Adult: 400 to 600 mg ORALLY every 12 hours for 10 to 14 days • Pediatric: (birth through 11 years) 10 mg/kg IV or ORALLY every 12 hours	• Concurrent use of linezolid and adrenergic agents may result in increased risk of hypertension • Concurrent use of linezolid and clarithromycin may result in an increased blood concentration of linezolid • Concurrent use of linezolid and meperidine may result in increased risk of serotonin syndrome • Concurrent use of linezolid and rasagiline may result in increased risk of serotonin syndrome • Concurrent use of linezolid and rifampin may result in a decreased serum level of linezolid • Concurrent use of linezolid and serotonergic drugs may result in increased risk of serotonin syndrome
Glycopeptide (as vancomycin)	Adult: 30 mg/kg/d IV in 2 divided doses or 40 mg/kg/d IV in 4 divided doses	• Concurrent use of vancomycin and aminoglycosides may result in increased frequency of nephrotoxicity

Al: aluminium; Ca: calcium; CNS: central nervous system; Fe: iron; Mg: magnesium; NSAIDs: non-steroidal anti-inflammatory drugs; Zn: zinc.

APPENDICES

Appendix 1. Draft MEDLINE (Ovid) search strategy

1. boil$1.ti,ab.
2. Furunculosis/
3. (furuncle$ or furunculos$).ti,ab.
4. Folliculitis/
5. folliculiti$.ti,ab.
6. CARBUNCLE/
7. carbuncle$.ti,ab.
8. (sycosis or sycoses).ti,ab.
9. (hair$1 adj3 follicle$ adj5 (infect$ or swell$ or pus$ or abscess or inflam$)).ti,ab.
10. or/1-9
11. randomized controlled trial.pt.
12. controlled clinical trial.pt.
13. randomized.ab.
14. placebo.ab.
15. clinical trials as topic.sh.
16. randomly.ab.
17. trial.ti.
18. 11 or 12 or 13 or 14 or 15 or 16 or 17
19. exp animals/ not humans.sh.
20. 18 not 19
21. 10 and 20

[Lines 10-19: Cochrane Highly Sensitive Search Strategy for identifying randomized trials in MEDLINE: sensitivity- and precision-maximizing version (2008 revision)]

Appendix 2. Data extraction form

Study characteristics	Data to be extracted	Instruction for data extraction
Study ID	(Surname of first author and publication year of first full report of study)	
Study information	Study title	Enter the title of the study.
Methods	Randomisation methods	How is the randomisation sequence generated?
	Blinding	Are participants, outcome assessors, or providers blinded to which treatment is given?
	Numbers of recruitment locations	At how many study sites are participants recruited for the trial?
Participants	Inclusion criteria	Enter the characteristics that the participants must have in this trial
	Exclusion criteria	Enter the characteristics that the participants cannot have if enrolled in this trial

(*Continued*)

	Numbers of participants randomised	How many participants were randomised in this trial?
	Mean age (years)	Enter the mean age ± SD of participants assigned to each group
	Sex (% male)	Enter the percentage of male participants assigned to each group
	Numbers of participants analysed	Data from how many participants are analysed in this trial?
	Numbers of dropouts	How many randomised participants are lost to follow-up during the study period?
	Dropout reasons	What are the reasons for participant dropouts?
Interventions	Types of interventions	Enter the types and methods of interventions, for example, topical antibiotics, antiseptic agents, systemic antibiotics, phototherapy, or surgical interventions
	Names of medications or methods	Enter the names of the interventions, such as the generic name of drugs
	Dosage	Enter the dose and frequency for drugs. Enter the duration and frequency for phototherapy. For surgical intervention, enter 'N/A'
	Duration	How long do participants receive therapy?
	Time point	When are the outcomes measured?
Outcomes	Primary outcomes	Enter data on primary outcomes.
	Secondary outcomes	Enter data on secondary outcomes.

CONTRIBUTIONS OF AUTHORS

CC was the contact person with the editorial base.

CC co-ordinated the contributions from co-authors and wrote the final draft of the protocol.

HL, PL, YT, and CC worked on the methods sections.

HL and CC drafted the clinical sections of the background and responded to clinical comments of the referees.

CC responded to methodology and statistics comments of the referees.

HL, PL, YT, SW, and CC contributed to writing of the protocol.

SW was the consumer co-author who checked the protocol for readability and clarity. She also ensured that the outcomes are relevant to consumers.

CC is the guarantor of the final review.

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