

# Topical Antimicrobial Agents for the Prevention of Burn-Wound Infection. What Do International Guidelines Recommend? A Systematic Review

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**Received:** 19 Oct 2022

**Accepted:** 19 Sep 2022

## ABSTRACT

**Background:** Choosing adequate topical antimicrobial agents in burn patients still represents a challenge. Therefore, this systematic review was conducted to compile and evaluate current recommendations in international clinical practice guidelines (CPGs) to develop more consistent clinical guidance.

**Methods:** A systematic search for CPGs was conducted independently by two reviewers using PubMed, EMBASE, Google Scholar, and external citations. The quality of the selected CPGs was evaluated separately using the AGREE II instrument, and intraclass correlation coefficients were calculated. Statistical analysis was performed using R V 1.4.1 statistical software.

**Results:** Eleven CPGs were included in the study. Most guidelines tend to recommend silver-containing dressings over antiseptics or antibiotics, regardless of the depth of the burn. Silver sulfadiazine is the most recommended topical antimicrobial in low-resource settings. An overall mean appraisal AGREE II score of 68.2% was obtained. The global intraclass correlation coefficient was 0.62 (95% confidence intervals 0.54-0.69), which corresponds to a substantial global concordance between both appraisers.

**Conclusions:** Great heterogeneity was found between recommendations and CPGs. The three determining factors considered to issue a recommendation were the clinical scenario, burn-wound depth, and burn severity. There is consensus among the guidelines to use topical antimicrobials as a tool to prevent infection, and most of these recommend the use of silver-containing dressings for most scenarios. However, there is currently no ideal topical antimicrobial agent that can be recommended for all clinical scenarios. The development of more consistent recommendations is warranted to standardize clinical practice.

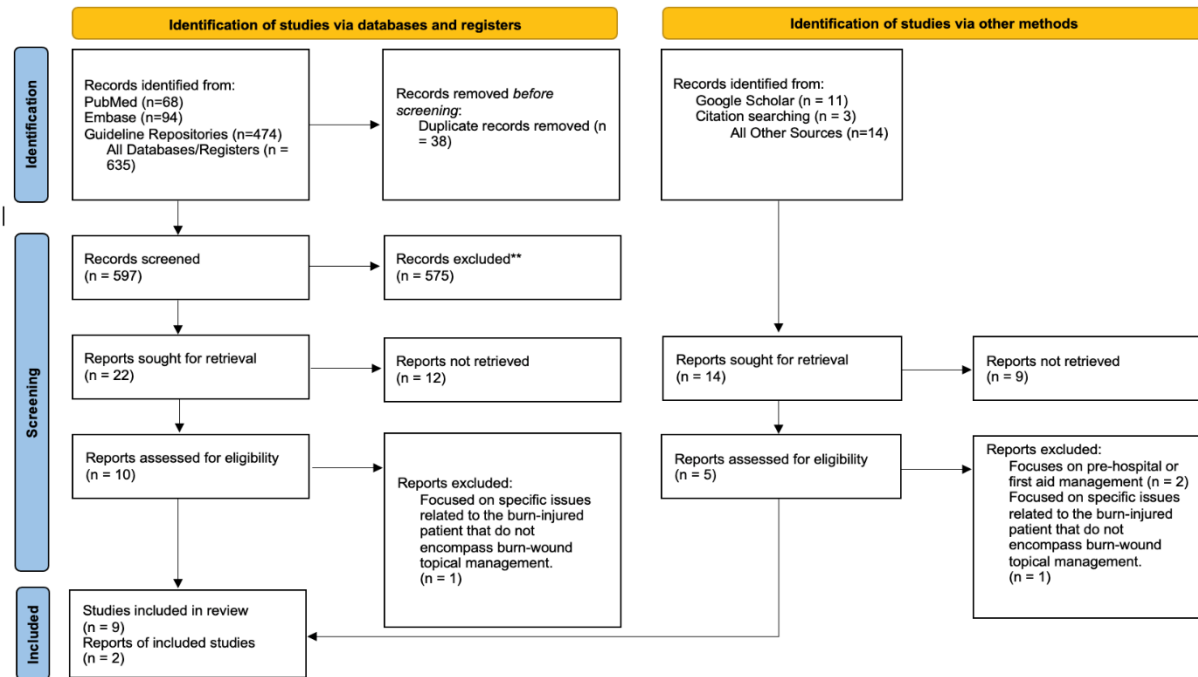
**Keywords:** Burn; Infection; Prevention; Antimicrobials; Topical

**Please cite this paper as:**

Garcia Garcia JA, Gonzalez Chavez AM, Orozco Grados JDJ. Topical Antimicrobial Agents for the Prevention of Burn-Wound Infection. What Do International Guidelines Recommend? A Systematic Review. World J Plast Surg. 2022;11(3):-0.

doi: 10.29252/wjps.11.3.\*\*\*

SUPPLEMENTARY MATERIAL



Supplementary Figure 1: PRISMA flow diagram of searches and study selection.

**Supplementary Table 1: Search methods.**

|  |   |  |   |
|--|---|--|---|
| <b>Searches</b>  | <b>PUBMED<br/>(MeSH terms)</b>                  | <p><b>ALGORITHM:</b></p> <p>((("Burns"[MeSH Major Topic] OR "Adult"[MeSH Major Topic]) AND ("Practice Guidelines as Topic"[MeSH Major Topic] OR "Practice Guideline"[Publication Type]) AND ("anti infective agents, local/therapeutic use"[MeSH Terms] OR "anti infective agents/prevention and control"[MeSH Terms] OR "anti infective agents/therapeutic use"[MeSH Terms] OR "burns/therapy"[MeSH Terms] OR "wounds and injuries/therapeutic use"[MeSH Terms] OR "infections/therapy"[MeSH Terms] OR "wounds and injuries/therapeutic use"[MeSH Terms] OR "wounds and injuries/therapy"[MeSH Terms] OR "infections/prevention and control"[MeSH Terms])) AND (2010:2021[mdat]))</p> <p><b>Filters:</b> 2010-2021</p>  | <p><b>Eligible results:</b> 6</p> <p><b>After duplicate removal:</b> 3</p>  |
|  | <b>EMBASE</b>                                   | <p><b>ALGORITHM:</b></p> <p>(practice guideline*:ti OR guideline*:ti) AND burn*:ti AND [2010-2021]/py</p> <p><b>Filters:</b><br/>2010-2021</p>   | <p><b>Eligible results:</b> 12</p> <p><b>After duplicate removal:</b> 3</p> |
|  | <b>GOOGLE Scholar</b>                           | <p><b>ALGORITHM:</b></p> <p>(allintitle: burn guidelines)</p> <p><b>Filters:</b><br/>Range 2010-2021, Do not include citations</p>   | <p><b>Eligible results:</b> 11</p> <p><b>After duplicate removal:</b> 3</p> |
|  | <b>Burn associations and journals websites:</b> | <ul style="list-style-type: none"> <li>• European Burn association</li> <li>• American Burn Association</li> <li>• Journal of Burn Care &amp; Research: Practice Guideline Collection</li> <li>• Deutschen Gesellschaft für Verbrennungsmedizin</li> <li>• British Burn Association</li> <li>• Asia-Pacific Burn Association</li> </ul>  | <p><b>Eligible results:</b> 4</p> <p><b>After duplicate removal:</b> 2</p>  |
|  | <b>Guideline repositories:</b>                  | <p><b>Search:</b> "Management of burns" and "Burns"</p> <p><b>Date filter:</b> 2010-2021</p> <ul style="list-style-type: none"> <li>• <b>Canadian Medical Association – Infobase: Clinical Practice Guidelines:</b><br/><a href="https://ioulecoma.ca/cpg/homepage">https://ioulecoma.ca/cpg/homepage</a><br/><b>Filters:</b> Does not apply.</li> <li>• <b>New Zealand Ministry of Health - Guidelines:</b><br/><a href="https://www.health.govt.nz/publications?f%5B0%5D=im_field_publication_type%3A26">https://www.health.govt.nz/publications?f%5B0%5D=im_field_publication_type%3A26</a><br/><b>Filters:</b> Does not apply.</li> <li>• <b>NICE Clinical Guidelines (UK) – Evidence search:</b><br/><a href="https://www.evidence.nhs.uk">https://www.evidence.nhs.uk</a><br/><b>Filters:</b> Guidance, 2010-2021</li> <li>• <b>Guidelines International Network (GIN):</b><br/><a href="https://guidelines.ebmportal.com">https://guidelines.ebmportal.com</a><br/><b>Filters:</b> Guideline publication status: Published</li> <li>• <b>Australian Clinical Practice Guidelines</b><br/><a href="https://www.clinicalguidelines.gov.au">https://www.clinicalguidelines.gov.au</a><br/><b>Filters:</b> Does not apply.</li> </ul> | <p><b>Eligible results:</b> 4</p> <p><b>After duplicate removal:</b> 3</p>  |
| Guidelines referenced in the database search results' title or abstract (Evaluations, editorials or implementation reports of specific guidelines) were also included. |   | <p><b>Eligible results:</b> 1</p>  |   |

**Supplementary Table 2: Inclusion and exclusion criteria.**

|   |                  |  |
|---|------------------|--|
| <b>Inclusion and exclusion criteria</b> | <b>Inclusion</b> | <ol style="list-style-type: none"> <li>1. The latest issue of clinical practice guidelines published by an international society or journal.</li> <li>2. Explicit recommendations on the topical management of partial and full-thickness thermal burn-wounds.</li> <li>3. Addresses topical burn-wound infection prevention.</li> <li>4. Adult patients.</li> <li>5. CPGs in English, Spanish, French, and German.</li> </ol>   |
|   | <b>Exclusion</b> | <ol style="list-style-type: none"> <li>1. Focuses on pre-hospital or first aid/emergency management.</li> <li>2. Focuses only on the management of established (No prevention) burn-wound infection, cellulitis, necrotizing fasciitis as defined by the American Burn Association Consensus Conference to Define Sepsis and Infection in Burns' Classification of Burn Wound Infections) (2)</li> <li>3. Guidelines focusing on specific issues related to the burn-injured patient that do not encompass burn-wound topical management.</li> <li>4. Clinical practice guidelines aimed specifically at nursing care.</li> <li>5. Guidelines focusing on injury other than thermal (chemical, electrical, radiation)</li> <li>6. Guidelines focusing only on the management of eye, inhalation/respiratory, or GI tract burn injuries.</li> <li>7. Guidelines focusing on populations with specific comorbidities (e.g., diabetes, vasculopathies, cardiopathies).</li> <li>8. Guidelines focusing on specific populations (e.g., children, pregnancy)</li> <li>9. Non-relevant search results</li> </ol> |

**Supplementary Table 3: AGREE II domain scores**

| Year                      | Guideline title   | 1. Scope and purpose (%) | 2. Stakeholder involvement (%) | 3. Rigor of development (%) | 4. Clarity of presentation (%) | 5. Applicability (%) | 6. Editorial independence (%) | Overall assessment (%) | Mean appraisal scores(%)                   |
|---------------------------|---|--------------------------|--------------------------------|-----------------------------|--------------------------------|----------------------|-------------------------------|------------------------|--|
| 2020                      | <i>Wound, pressure ulcer and burn guidelines – 6: Guidelines for the management of burns, second edition (40)</i>                                     | 86.11                    | 44.44                          | 72.91                       | 100                            | 56.25                | 87.5                          | 83.33                  | 75.79                                      |
| 2016                      | <i>Guidelines for Burn Care Under Austere Conditions- Surgical and Nonsurgical Wound Management (39)</i>  | 97.22                    | 69.44                          | 30.2                        | 61.11                          | 79.16                | 25                            | 58.33                  | 60.07                                      |
| 2017                      | <i>European Practice Guidelines for Burn Care (38)</i>  | 91.66                    | 61.11                          | 86.45                       | 80.55                          | 56.25                | 45.83                         | 75                     | 70.98                                      |
| 2021                      | <i>Behandlung thermischer Verletzungen des Erwachsenen (33)</i>   | 91.66                    | 61.11                          | 40.62                       | 77.77                          | 60.41                | 87.5                          | 66.66                  | 69.39                                      |
| 2018                      | <i>Best practice recommendations for the prevention and management of burns. In: Foundations of Best Practice for Skin and Wound Management. (32)</i> | 86.11                    | 58.33                          | 47.91                       | 63.88                          | 56.25                | 50                            | 66.66                  | 61.31                                      |
| 2019                      | <i>Prise en charge du brûlé grave à la phase aiguë chez l'adulte et l'enfant (36)</i>   | 100                      | 72.22                          | 67.7                        | 80.55                          | 66.66                | 95.83                         | 83.33                  | 80.90                                      |
| 2021                      | <i>Clinical Guidelines: Diagnosis and Treatment Manual, Chapter 10: Medical and Minor surgical procedures, Burns. (31)</i>                            | 38.88                    | 36.11                          | 4.16                        | 50                             | 16.66                | 20.83                         | 16.66                  | 26.19                                      |
| 2019                      | <i>Clinical Guidelines: Burn Patient Management (30)</i>  | 83.33                    | 58.33                          | 33.33                       | 83.33                          | 62.5                 | 41.66                         | 66.66                  | 61.31                                      |
| 2016                      | <i>ISBI Practice Guidelines for Burn Care. (37)</i>   | 100                      | 72.22                          | 91.66                       | 88.88                          | 97.91                | 87.5                          | 100                    | 91.17                                      |
| 2018                      | <i>ISBI Practice Guidelines for Burn Care, Part 2 (35)</i>  | 100                      | 72.22                          | 91.66                       | 88.88                          | 97.91                | 87.5                          | 100                    | 91.17                                      |
| 2015                      | <i>Guideline and treatment algorithm for burn injuries (34)</i>   | 72.22                    | 58.33                          | 26.04                       | 61.11                          | 47.91                | 50                            | 41.66                  | 51.04                                      |
| <b>Mean</b>               |   | 86.10                    | 60.35                          | 53.88                       | 76.01                          | 63.44                | 61.74                         | 68.94                  | <b>Overall appraisal mean score: 67.21</b> |
| <b>Median</b>             |   | 91.66                    | 61.11                          | 47.91                       | 80.55                          | 60.41                | 50.00                         | 66.66                  |  |
| <b>Standard deviation</b> |   | 17.88                    | 11.66                          | 29.85                       | 15.07                          | 22.87                | 27.88                         | 24.47                  |  |

**Supplementary Table 4:** Intraclass correlation coefficients for each clinical practice guideline

| <b><i>Clinical Practice Guideline</i></b>   | <b><i>ICC (95% CI)</i></b> | <b><i>P value</i></b> |
|---|----------------------------|-----------------------|
| <i>Wound, pressure ulcer and burn guidelines – 6: Guidelines for the management of burns, second edition (40)</i>                                     | 0.59 (0.26 - 0.8)          | <0.001                |
| <i>Guidelines for Burn Care Under Austere Conditions- Surgical and Nonsurgical Wound Management (39)</i>  | 0.82 (0.64 - 0.92)         | <0.001                |
| <i>European Practice Guidelines for Burn Care (38)</i>  | 0.32 (-0.05 - 0.63)        | 0.045                 |
| <i>Behandlung thermischer Verletzungen des Erwachsenen (33)</i>   | 0.79 (0.57 - 0.9)          | <0.001                |
| <i>Best practice recommendations for the prevention and management of burns. In: Foundations of Best Practice for Skin and Wound Management. (32)</i> | 0.12 (-0.15 - 0.43)        | 0.214                 |
| <i>Prise en charge du brûlé grave à la phase aiguë chez l'adulte et l'enfant (36)</i>   | 0.50 (0.12 - 0.75)         | 0.007                 |
| <i>Clinical Guidelines: Diagnosis and Treatment Manual. Chapter 10: Medical and Minor surgical procedures, Burns. (31)</i>                            | 0.43 (0.06 - 0.7)          | 0.013                 |
| <i>Clinical Guidelines: Burn Patient Management (30)</i>  | 0.46 (0.1 - 0.72)          | 0.007                 |
| <i>ISBI Practice Guidelines for Burn Care. (37)</i>   | 0.34 (-0.07 - 0.65)        | 0.051                 |
| <i>ISBI Practice Guidelines for Burn Care, Part 2 (35)</i>  | 0.34 (-0.07 - 0.65)        | 0.051                 |
| <i>Guideline and treatment algorithm for burn injuries (34)</i>   | 0.27 (-0.11 - 0.59)        | 0.079                 |

**Supplementary Table 5:** Intraclass correlation coefficients corresponding to each AGREE Score domain.

| <b>AGREE SCORE DOMAIN</b>           | <b>ICC (95% CI)</b>   | <b>P VALUE</b> |
|-------------------------------------|-----------------------|----------------|
| <b>1. SCOPE AND PURPOSE</b>         | 0.61 ( 0.33 - 0.78 )  | <0.001         |
| <b>2. STAKEHOLDER INVOLVEMENT</b>   | 0.71 ( 0.49 - 0.84 )  | <0.001         |
| <b>3. RIGOUR OF DEVELOPMENT</b>     | 0.73 ( 0.62 - 0.82 )  | <0.001         |
| <b>4. CLARITY OF PRESENTATION</b>   | 0.27 ( -0.04 - 0.54 ) | 0.047          |
| <b>5. APPLICABILITY</b>             | 0.65 ( 0.29 - 0.82 )  | 0.001          |
| <b>6. EDITORIAL INDEPENDENCE</b>    | 0.21 ( -0.11 - 0.53 ) | 0.119          |
| <b>OVERALL GUIDELINE ASSESSMENT</b> | 0.86 ( 0.59 - 0.96 )  | <0.001         |

**Supplementary Table 6: Common topical antimicrobial agents in burn care (7)**

|   |             |   |  |   |
|---|-------------|---|--|---|
| Topical antimicrobial agents in burn care | Antiseptics | Agents that are nonselectively toxic to all cells, microorganisms hardly develop resistances to them, and are too toxic for systemic administration.            | Emulsifiers  | Chlorhexidine   |
|   |             |   | Oxidizers  | Dakin's solution (0.5% buffered hypochlorite), Povidone-iodine  |
|   |             |   | Acids  | Honey   |
|   |             |   | Heavy metals   | Silver compounds: Silver sulfadiazine (SSD) 1% cream, SSD + Cerium nitrate, silver nitrate 0.5%, silver-containing modern dressings (ionic, nanocrystalline, etc.). |
|   | Antibiotics | Agents that target a specific molecular mechanism in certain pathogens. These generate resistances (10) and sometimes need to be used in combination therapies. | <ul style="list-style-type: none"> <li>• Mafenide acetate 8.5% cream/ 5% solution (Topical synthetic sulfonamide)</li> <li>• Bacitracin ointment 500 units/gram</li> <li>• Combination (Bacitracin / Polymyxin B / Neomycin)</li> <li>• Mupirocin ointment 2%</li> </ul> |   |