

Guidelines on the treatment of skin and oral HIV-associated conditions in children and adults

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1. Kaposi sarcoma

Kaposi sarcoma in children

Table 1.1 Should chemotherapy plus ART versus ART alone be used for Kaposi sarcoma for children with HIV infection?

| No. of studies | Design | Quality assessment | | | | | No. of patients | | Effect | | Quality | Importance |
|---|---------------------|-----------------------------|--------------------------|-------------------------|---------------------------|----------------------|-----------------|--------------|-------------------------|---|---------------|------------|
| | | Risk of bias | Inconsistency | Indirectness | Imprecision | Other considerations | Chemo + ART | ART | Relative (95% CI) | Absolute | | |
| Complete response to treatment | | | | | | | | | | | | |
| 1 | Observational study | Very serious ^{1,2} | No serious inconsistency | No serious indirectness | Very serious ³ | None | 17/26 (65.4%) | 2/13 (15.4%) | RR 4.25 (1.15 to 15.68) | 500 more per 1000 (from 23 more to 1000 more) | ⊕○○○ VERY LOW | CRITICAL |
| Complete/partial response to treatment | | | | | | | | | | | | |
| 1 | Observational study | Very serious ^{1,2} | No serious inconsistency | No serious indirectness | Very serious ³ | None | 23/26 (88.5%) | 2/13 (15.4%) | RR 5.75 (1.59 to 20.73) | 731 more per 1000 (from 91 more to 1000 more) | ⊕○○○ VERY LOW | CRITICAL |
| Complete among known outcome | | | | | | | | | | | | |
| 1 | Observational study | Very serious ¹ | No serious inconsistency | No serious indirectness | Very serious ³ | None | 17/24 (70.8%) | 2/2 (100%) | RR 0.84 (0.48 to 1.48) | 160 fewer per 1000 (from 520 fewer to 480 more) | ⊕○○○ VERY LOW | CRITICAL |
| Complete/partial among known outcome | | | | | | | | | | | | |
| 1 | Observational study | Very serious ¹ | No serious inconsistency | No serious indirectness | Very serious ³ | None | 23/24 (95.8%) | 2/2 (100%) | RR 1.13 (0.67 to 1.89) | 130 more per 1000 (from 330 fewer to 890 more) | ⊕○○○ VERY LOW | CRITICAL |
| Mean CD4% increase during chemotherapy (better indicated by higher values) | | | | | | | | | | | | |
| 1 | Observational study | Serious ¹ | No serious inconsistency | No serious indirectness | No serious imprecision | None | 24 | 24 | — | MD 13.2 higher (1.65 to 24.65 higher) | ⊕○○○ VERY LOW | CRITICAL |
| Mortality | | | | | | | | | | | | |
| 1 | Observational study | Very serious ¹ | No serious inconsistency | No serious indirectness | Very serious ³ | None | 13/36 (36.1%) | 7/14 (50%) | RR 0.72 (0.37 to 1.43) | 140 fewer per 1000 (from 315 fewer to 215 more) | ⊕○○○ VERY LOW | CRITICAL |

1 Unadjusted estimates.

2 Many patients had missing outcome data.

3 Very few cases (<50).

Table 1.2 Should chemotherapy plus ART versus ART alone be used for Kaposi sarcoma for children with HIV infection?

| No. of studies | Design | Quality assessment | | | | | No. of patients | | Effect | | Quality | Importance |
|---|-----------------------|-----------------------------|--------------------------|-------------------------|---------------------------|----------------------|----------------------------|----------------------------|------------------------|--|---------------|------------|
| | | Risk of bias | Inconsistency | Indirectness | Imprecision | Other considerations | Chemo + ART | ART | Relative (95% CI) | Absolute | | |
| Complete response to treatment | | | | | | | | | | | | |
| 1 | Observational study | Very serious ^{1,2} | No serious inconsistency | No serious indirectness | Very serious ³ | None | 17/26 (65.4%) | 1/10 (10%) | RR 6.54 (1 to 42.86) | 554 more per 1000 (from 0 more to 1000 more) | ⊕○○○ VERY LOW | CRITICAL |
| Complete/partial response to treatment | | | | | | | | | | | | |
| 1 | Observational study | Very serious ^{1,2} | No serious inconsistency | No serious indirectness | Very serious ³ | None | 23/26 (88.5%) | 6/10 (60%) | RR 1.47 (0.87 to 2.49) | 282 more per 1000 (from 78 fewer to 894 more) | ⊕○○○ VERY LOW | CRITICAL |
| Complete among known outcome | | | | | | | | | | | | |
| 1 | Observational study | Very serious ¹ | No serious inconsistency | No serious indirectness | Very serious ³ | None | 17/24 (70.8%) | 1/6 (16.7%) | RR 4.25 (0.7 to 25.91) | 542 more per 1000 (from 50 fewer to 1000 more) | ⊕○○○ VERY LOW | CRITICAL |
| Complete/partial among known outcome | | | | | | | | | | | | |
| 1 | Observational study | Very serious ¹ | No serious inconsistency | No serious indirectness | Very serious ³ | None | 23/24 (95.8%) | 6/6 (100%) | RR 1.01 (0.81 to 1.27) | 10 more per 1000 (from 190 fewer to 270 more) | ⊕○○○ VERY LOW | CRITICAL |
| Mortality | | | | | | | | | | | | |
| 2 | Observational studies | Very serious ¹ | No serious inconsistency | No serious indirectness | Very serious ³ | None | 25/66 (37.9%) ⁴ | 22/32 (68.8%) ⁴ | RR 0.46 (0.29 to 0.73) | 371 fewer per 1000 (from 186 fewer to 488 fewer) | ⊕○○○ VERY LOW | CRITICAL |

1 Unadjusted estimates.

2 Many patients had missing outcome data.

3 Very few cases (<50).

4 Imputed data from information in text for one study. Data not used in calculating RR.

Mild and moderate Kaposi sarcoma

Table 1.3 Should highly-active antiretroviral therapy (HAART) plus ABV versus HAART alone be used for mild and moderate treatment-naïve Kaposi sarcoma?

| No. of studies | Design | Quality assessment | | | | | No. of patients | | Effect | | Quality | Importance |
|--|------------------|-------------------------|---------------------------------------|----------------------|----------------------|----------------------|-----------------|-------------|-------------------------|--|----------|------------|
| | | Risk of bias | Inconsistency | Indirectness | Imprecision | Other considerations | HAART plus ABV | HAART alone | Relative (95% CI) | Absolute | | |
| Mortality (follow-up 12 months) | | | | | | | | | | | | |
| 1 | Randomized trial | No serious risk of bias | No serious inconsistency | Serious ¹ | Serious ² | None | 0/3 (0%) | 1/9 (11.1%) | RR 0.83 (0.04 to 16.46) | 19 fewer per 1000 (from 107 fewer to 1000 more) | ⊕⊕⊕⊕ LOW | CRITICAL |
| Complete response (follow-up 12 months) | | | | | | | | | | | | |
| 1 ³ | Randomized trial | No serious risk of bias | No serious inconsistency | Serious ¹ | Serious ² | None | 1/3 (33.3%) | 0/9 (0%) | RR 7.5 (0.38 to 148.13) | — | ⊕⊕⊕⊕ LOW | CRITICAL |
| Partial response (follow-up 12 months) | | | | | | | | | | | | |
| 1 ³ | Randomized trial | No serious risk of bias | No serious inconsistency | Serious ¹ | Serious ² | None | 2/3 (66.7%) | 5/9 (55.6%) | RR 1.2 (0.45 to 3.23) | 111 more per 1000 (from 306 fewer to 1000 more) | ⊕⊕⊕⊕ LOW | CRITICAL |
| Progression (at 12 months) | | | | | | | | | | | | |
| 1 ³ | Randomized trial | No serious risk of bias | No serious inconsistency | Serious ¹ | Serious ² | None | 0/3 (0%) | 1/9 (11.1%) | RR 0.83 (0.04 to 16.46) | 19 fewer per 1000 (from 107 fewer to 1000 more) | ⊕⊕⊕⊕ LOW | CRITICAL |
| Stable disease (follow-up 12 months) | | | | | | | | | | | | |
| 1 ³ | Randomized trial | No serious risk of bias | No serious inconsistency | Serious ¹ | Serious ² | None | 0/3 (0%) | 2/9 (22.2%) | RR 0.5 (0.03 to 8.27) | 111 fewer per 1000 (from 216 fewer to 1000 more) | ⊕⊕⊕⊕ LOW | IMPORTANT |
| KS IRIS | | | | | | | | | | | | |
| 1 | Randomized trial | No serious risk of bias | No serious inconsistency ¹ | Serious ¹ | Serious ² | None | 0/3 (0%) | 0/9 (0%) | Not pooled | Not pooled | ⊕⊕⊕⊕ LOW | IMPORTANT |
| Adverse events (Grade III-V) | | | | | | | | | | | | |
| 1 | Randomized trial | No serious risk of bias | No serious inconsistency | Serious ¹ | Serious ² | None | 0/3 (0%) | 0/9 (0%) | Not pooled | Not pooled | ⊕⊕⊕⊕ LOW | IMPORTANT |

1 Post-hoc analysis of study not specifically designed to evaluate patients with mild to moderate disease.

2 Single study, very small post-hoc analysis of only 12 patients with mild-moderate KS.

3 See [TABLE 1](#) in systematic review (Freeman et al., in press) for detailed definitions of outcomes. Mosam and colleagues (2012) modified these slightly, as below. Complete response (CR): resolution of any detectable disease for at least 4 weeks. Partial response (PR) is a 50% or > decrease in number and/or size of all existing lesions for at least 4 weeks, without the appearance of new lesions. A response may be assigned to a diminution in the diameter of all lesions, or to flattening of at least 50% of the lesions. The size of each lesion will be the product of the longest dimension and the maximum dimension perpendicular to it. Overall response: PR + CR. Stable disease: not meeting the criteria for progression, PR or CR. Progressive disease: at least a 25% increase in the size of any lesion or the appearance of any new lesions.

Table 1.4 Should HAART plus ABV versus HAART alone be used for mild and moderate treatment-naive Kaposi sarcoma (observational studies)?

| No. of studies | Design | Quality assessment | | | | | No. of patients | | Effect | | Quality | Importance |
|---|---------------------|-------------------------|--------------------------|-------------------------|---------------------------|----------------------|-----------------|-------------|------------------------|----------|------------------|------------|
| | | Risk of bias | Inconsistency | Indirectness | Imprecision | Other considerations | HAART plus ABV | HAART alone | Relative (95% CI) | Absolute | | |
| Overall response (complete + partial) (follow-up mean 12 months) | | | | | | | | | | | | |
| 1 | Observational study | No serious risk of bias | No serious inconsistency | No serious indirectness | Very serious ¹ | None | 1/1 (100%) | 0/2 (0%) | RR 4.5 (0.32 to 63.94) | — | ⊕○○○ VERY LOW | CRITICAL |

1 Single study, very small, post-hoc analysis of only 3 participants.

Table 1.5 Should HAART plus liposomal anthracyclines versus HAART alone be used for mild and moderate treatment-naive Kaposi sarcoma (RCTs)?

| No. of studies | Design | Quality assessment | | | | | No. of patients | | Effect | | Quality | Importance |
|---|------------------|-------------------------|--------------------------|----------------------|----------------------|----------------------|-------------------------------------|-------------|--------------------------|--|------------------|------------|
| | | Risk of bias | Inconsistency | Indirectness | Imprecision | Other considerations | HAART plus liposomal anthracyclines | HAART alone | Relative (95% CI) | Absolute | | |
| Overall response (complete + partial) (follow-up 48 weeks) | | | | | | | | | | | | |
| 1 | Randomized trial | No serious risk of bias | No serious inconsistency | Serious ¹ | Serious ² | None | 6/8 (75%) | 2/8 (25%) | RR 3 (0.85 to 10.63) | 500 more per 1000 (from 37 fewer to 1000 more) | ⊕⊕○○ LOW | CRITICAL |
| Adverse events (follow-up 48 weeks) | | | | | | | | | | | | |
| 1 | Randomized trial | Serious ³ | No serious inconsistency | Serious ¹ | Serious ² | None | 5/14 (35.7%) | 0/8 (0%) | OR 9.84 (0.47 to 205.62) | — | ⊕○○○ VERY LOW | IMPORTANT |

1 Post-hoc analysis of subgroup of patients with mild to moderate disease.

2 Single study of only 16 patients.

3 Adverse events only reported for intervention arm (PLD+ART), not for comparison arm (ART alone).

Table 1.6 Should HAART plus liposomal anthracyclines versus HAART alone be used for mild and moderate treatment-naive Kaposi sarcoma (observational studies)?

| No. of studies | Design | Quality assessment | | | | | No. of patients | | Effect | | Quality | Importance |
|--|---------------------|-------------------------|--------------------------|----------------------|----------------------|----------------------|-------------------------------------|-------------|-------------------------|---|------------------|------------|
| | | Risk of bias | Inconsistency | Indirectness | Imprecision | Other considerations | HAART plus liposomal anthracyclines | HAART alone | Relative (95% CI) | Absolute | | |
| Mortality¹ (follow-up 12 months) | | | | | | | | | | | | |
| 1 | Observational study | No serious risk of bias | No serious inconsistency | Serious ² | Serious ³ | None | 0/7 (0%) | 0/77 (0%) | Not pooled ¹ | Not pooled ¹ | ⊕○○○ VERY LOW | CRITICAL |
| Mortality¹ (follow-up 3 months) | | | | | | | | | | | | |
| 1 | Observational study | No serious risk of bias | No serious inconsistency | Serious ² | Serious ³ | None | 0/7 (0%) | 0/77 (0%) | Not pooled ¹ | Not pooled ¹ | ⊕○○○ VERY LOW | CRITICAL |
| KS IRIS (follow-up median 40.5 months) | | | | | | | | | | | | |
| 1 | Observational study | No serious risk of bias | No serious inconsistency | Serious ² | Serious ³ | None | 0/7 (0%) | 6/71 (8.5%) | RR 0.69 (0.04 to 11.18) | 26 fewer per 1000 (from 81 fewer to 860 more) | ⊕○○○ VERY LOW | IMPORTANT |

1 No deaths in either group.

2 Single study, where intervention group (liposomal anthracyclines plus ART) was not representative of patients with mild/moderate disease in general; UK cohort participants with mild/moderate disease only received liposomal anthracyclines above and beyond ART in exceptional circumstances per clinician's decision (standard of care at that site was considered to be ART alone).

3 Very few patients in intervention group (7) due to standard of care in UK cohort (see footnote above).

Severe or progressive Kaposi sarcoma

Table 1.7 Should HAART plus ABV versus HAART alone be used for severe or progressive Kaposi sarcoma?

| No. of studies | Design | Quality assessment | | | | | No. of patients | | Effect | | Quality | Importance |
|---|------------------|-------------------------|--------------------------|-------------------------|---------------------------|----------------------|-----------------|-------------|------------------------|---|---------------|------------|
| | | Risk of bias | Inconsistency | Indirectness | Imprecision | Other considerations | HAART + ABV | HAART alone | Relative (95% CI) | Absolute | | |
| Mortality | | | | | | | | | | | | |
| 1 | Randomized trial | No serious risk of bias | No serious inconsistency | No serious indirectness | Serious ¹ | None | 11/50 (22%) | 13/50 (26%) | RR 0.92 (0.45 to 1.88) | 21 fewer per 1000 (from 143 fewer to 229 more) | ⊕⊕⊕O MODERATE | CRITICAL |
| Progressive disease (follow-up mean 12 months) | | | | | | | | | | | | |
| 1 | Randomized trial | No serious risk of bias | No serious inconsistency | No serious indirectness | Serious ¹ | None | 1/50 (2%) | 10/50 (20%) | RR 0.1 (0.01 to 0.75) | 180 fewer per 1000 (from 50 fewer to 198 fewer) | ⊕⊕⊕O MODERATE | CRITICAL |
| Clinical response – complete response (follow-up mean 12 months) | | | | | | | | | | | | |
| 1 | Randomized trial | No serious risk of bias | No serious inconsistency | No serious indirectness | Very serious ¹ | None | 8/50 (16%) | 4/50 (8%) | RR 2 (0.64 to 6.22) | 80 more per 1000 (from 29 fewer to 418 more) | ⊕⊕OO LOW | CRITICAL |
| Clinical response – partial response (follow-up mean 12 months) | | | | | | | | | | | | |
| 1 | Randomized trial | No serious risk of bias | No serious inconsistency | No serious indirectness | Serious ¹ | None | 24/50 (48%) | 14/50 (28%) | RR 1.71 (1.01 to 2.91) | 199 more per 1000 (from 3 more to 535 more) | ⊕⊕⊕O MODERATE | CRITICAL |

¹ There were very few events with very wide CIs.

Table 1.8 Should HAART + ABV versus HAART alone be used for severe or progressive Kaposi sarcoma?

| No. of studies | Design | Quality assessment | | | | | No. of patients | | Effect | | Quality | Importance |
|---|------------------|-------------------------|--------------------------|-------------------------|---------------------------|----------------------|-----------------|-------------|------------------------|--|------------------|------------|
| | | Risk of bias | Inconsistency | Indirectness | Imprecision | Other considerations | HAART + ABV | HAART alone | Relative (95% CI) | Absolute | | |
| Clinical response – stable disease (follow-up mean 12 months) | | | | | | | | | | | | |
| 1 | Randomized trial | No serious risk of bias | No serious inconsistency | No serious indirectness | Very serious ¹ | none | 0/50 (0%) | 8/50 (16%) | RR 0.06 (0 to 0.99) | 150 fewer per 1000 (from 2 fewer to 160 fewer) | ⊕⊕⊕⊕ LOW | CRITICAL |
| Clinical response – overall response (complete and partial) (follow-up mean 12 months) | | | | | | | | | | | | |
| 1 | Randomized trial | No serious risk of bias | No serious inconsistency | No serious indirectness | Serious ¹ | None | 32/50 (64%) | 18/50 (36%) | RR 1.78 (1.16 to 2.72) | 281 more per 1000 (from 58 more to 619 more) | ⊕⊕⊕⊕ MODERATE | CRITICAL |
| Adverse events (follow-up mean 12 months) | | | | | | | | | | | | |
| 1 | Randomized trial | No serious risk of bias | No serious inconsistency | No serious indirectness | Serious ¹ | None | 23/50 (46%) | 26/50 (52%) | RR 0.88 (0.59 to 1.32) | 62 fewer per 1000 (from 213 fewer to 166 more) | ⊕⊕⊕⊕ MODERATE | IMPORTANT |

¹ There were very few events with very wide CIs.

Table 1.9 Should HAART + PLD versus HAART alone be used for severe or progressive Kaposi sarcoma?

| No. of studies | Design | Quality assessment | | | | | No. of patients | | Effect | | Quality | Importance |
|--|------------------|-------------------------|--------------------------|-------------------------|---------------------------|----------------------|-----------------|-------------|-----------------------|----------|----------|------------|
| | | Risk of bias | Inconsistency | Indirectness | Imprecision | Other considerations | HAART + PLD | HAART alone | Relative (95% CI) | Absolute | | |
| Clinical response (follow-up mean 48 weeks) | | | | | | | | | | | | |
| 1 | Randomized trial | No serious risk of bias | No serious inconsistency | No serious indirectness | Very serious ¹ | None | 4/5 (80%) | 0/5 (0%) | RR 9 (0.61 to 133.08) | — | ⊕⊕⊕⊕ LOW | IMPORTANT |

¹ There were very few events with very wide CIs.

Table 1.10 Should HAART + liposomal anthracycline versus HAART alone be used for severe or progressive Kaposi sarcoma?

| No. of studies | Design | Quality assessment | | | | | No. of patients | | Effect | | Quality | Importance |
|---|---------------------|-------------------------|--------------------------|--------------------------------------|----------------------|----------------------|---------------------------------|--------------|------------------------|---|---------------|------------|
| | | Risk of bias | Inconsistency | Indirectness | Imprecision | Other considerations | HAART + liposomal anthracycline | HAART alone | Relative (95% CI) | Absolute | | |
| Mortality (follow-up median 4 years) | | | | | | | | | | | | |
| 1 | Observational study | No serious risk of bias | No serious inconsistency | No serious indirectness ¹ | Serious ¹ | None | 5/65 (7.7%) | 4/64 (6.3%) | RR 1.23 (0.35 to 4.38) | 14 more per 1000 (from 41 fewer to 211 more) | ⊕⊕⊕⊕ VERY LOW | CRITICAL |
| KS IRIS (follow-up median 4 years) | | | | | | | | | | | | |
| 1 | Observational study | No serious risk of bias | No serious inconsistency | No serious indirectness | Serious ¹ | None | 4/65 (6.2%) | 8/64 (12.5%) | RR 0.49 (0.16 to 1.55) | 64 fewer per 1000 (from 105 fewer to 69 more) | ⊕⊕⊕⊕ VERY LOW | IMPORTANT |

¹ There were very few events with very wide CIs.

2. Seborrhoeic dermatitis

Table 2.1 Should lithium succinate versus placebo be used for seborrhoeic dermatitis in HIV-infected patients?

| No. of studies | Design | Quality assessment | | | | | No. of patients | | Effect | | Quality | Importance |
|---|------------------|-------------------------|--------------------------|-------------------------|----------------------------------|------------------|----------------------|-------------------|-------------------|----------|-------------------------------|------------|
| | | Risk of bias | Inconsistency | Indirectness | Imprecision | Publication bias | No lithium succinate | Lithium succinate | Relative (95% CI) | Absolute | | |
| Incidence assessed by clinical examination (follow-up 47 days) | | | | | | | | | | | | |
| 1 | Randomized Trial | No serious risk of bias | No serious inconsistency | No serious indirectness | Serious imprecision ¹ | Undetected | 10 | 10 | — | — | ⊕⊕⊕⊕ MODERATE ¹ | MODERATE |

1 Difference between the intervention and placebo groups could be observed only up to 6.8 days. Out of 10 subjects recruited, 9 were there until 6.8 days and only 5 until 47 days which was the maximum follow-up reported.

Table 2.2 Should pimecrolimus be used for seborrhoeic dermatitis in HIV-infected patients?

| No. of studies | Design | Quality assessment | | | | | No. of patients | | Effect | | Quality | Importance |
|---|---------------------|---------------------------|--------------------------|-------------------------|------------------------|------------------|-----------------|--------------|-------------------|----------|-------------------------------|------------|
| | | Risk of bias | Inconsistency | Indirectness | Imprecision | Publication bias | No pimecrolimus | Pimecrolimus | Relative (95% CI) | Absolute | | |
| Resolution (important outcome; assessed with clinical exam; follow-up 4 weeks) | | | | | | | | | | | | |
| 1 | Observational study | Very serious ¹ | No serious inconsistency | No serious indirectness | No serious imprecision | Undetected | — | 19/19 (100%) | — | — | ⊕○○○ VERY LOW ¹ | MODERATE |
| Relapse (not important outcome; follow-up 4 weeks) | | | | | | | | | | | | |
| 1 | Observational study | Very serious | No serious inconsistency | No serious indirectness | No serious imprecision | Undetected | — | 2/19 (10.5%) | — | — | ⊕○○○ VERY LOW ¹ | MODERATE |

1 Open label single group pilot study.

Table 2.3 Should bifonazole be used for seborrhoeic dermatitis in HIV-infected patients?

| No. of studies | Design | Quality assessment | | | | | No. of patients | | Effect | | Quality | Importance |
|---|---------------------|----------------------|--------------------------|-------------------------|------------------------|------------------|-----------------|-------------|-------------------|----------|----------------------------|------------|
| | | Risk of bias | Inconsistency | Indirectness | Imprecision | Publication bias | No bifonazole | Bifonazole | Relative (95% CI) | Absolute | | |
| Resolution (important outcome; assessed with clinical exam; follow-up 4 weeks) | | | | | | | | | | | | |
| 1 | Observational study | Serious ¹ | No serious inconsistency | No serious indirectness | No serious imprecision | Undetected | — | 12/15 (80%) | — | — | ⊕⊕○○ LOW | MODERATE |
| Relapse (not important outcome; follow-up 4 weeks) | | | | | | | | | | | | |
| 1 | Observational study | Serious ¹ | No serious inconsistency | No serious indirectness | No serious imprecision | Undetected | — | 9/12 (75%) | — | — | ⊕○○○ VERY LOW ¹ | MODERATE |

1 No explanation was provided.

Table 2.4 Should ART be used for seborrhoeic dermatitis in HIV-infected patients?

| No. of studies | Design | Quality assessment | | | | | No. of patients | | Effect | | Quality | Importance |
|---|---------------------|---------------------------|--------------------------|-------------------------|------------------------|------------------|-----------------|---------------|------------------------|--|----------------------------|------------|
| | | Risk of bias | Inconsistency | Indirectness | Imprecision | Publication bias | No ART | ART | Relative (95% CI) | Absolute | | |
| Resolution (important outcome; assessed with clinical exam; follow-up 22 months) | | | | | | | | | | | | |
| 1 | Observational study | Very serious ¹ | No serious inconsistency | Serious ² | No serious imprecision | Undetected | 7/17 (41.2%) | 16/19 (84.2%) | RR 2.05 (1.12 to 3.73) | 432 more per 1000 (from 49 more to 1000 more) | ⊕○○○ VERY LOW | MODERATE |
| Incidence assessed with clinical exam (follow-up 22 months) | | | | | | | | | | | | |
| 1 | Observational study | Very serious ³ | No serious inconsistency | No serious indirectness | No serious imprecision | Undetected | 17/44 (38.6%) | 19/76 (25%) | RR 0.65 (0.38 to 1.11) | 135 fewer per 1000 (from 240 fewer to 43 more) | ⊕○○○ VERY LOW ³ | MODERATE |

1 Prospective observational study.

2 This study reports resolution of seborrhoeic dermatitis among those on ART who got seborrhoeic dermatitis after a certain follow-up period.

3 No explanation was provided.

Table 2.5 Should ART be used for seborrhoeic dermatitis in HIV-infected patients?

| No. of studies | Design | Quality assessment | | | | | No. of patients | | Effect | | Quality | Importance |
|---|---------------------|---------------------------|--------------------------|----------------------|------------------------|------------------|-----------------|------------|-------------------|----------|------------------|------------|
| | | Risk of bias | Inconsistency | Indirectness | Imprecision | Publication bias | No ART | ART | Relative (95% CI) | Absolute | | |
| Incidence assessed by clinical examination (follow-up 5 years) | | | | | | | | | | | | |
| 1 | Observational study | Very serious ¹ | No serious inconsistency | Serious ² | No serious imprecision | Undetected | — | 9/878 (1%) | — | — | ⊕○○○ VERY LOW | MODERATE |

1 Subset of cohort.

2 No explanation was provided.

Table 2.6 Should ART be used for seborrhoeic dermatitis in HIV-infected patients?

| No. of studies | Design | Quality assessment | | | | | No. of patients | | Effect | | Quality | Importance |
|---|---------------------|-------------------------|--------------------------|---------------------------|------------------------|------------------|-----------------|------------|------------------------|---|------------------|------------|
| | | Risk of bias | Inconsistency | Indirectness | Imprecision | Publication bias | No ART | ART | Relative (95% CI) | Absolute | | |
| Incidence assessed by clinical examination (follow-up 8 weeks) | | | | | | | | | | | | |
| 1 | Observational study | No serious risk of bias | No serious inconsistency | Very serious ¹ | No serious imprecision | Undetected | 15/43 (34.9%) | 2/10 (20%) | RR 0.22 (0.05 to 0.89) | 272 fewer per 1000 (from 38 fewer to 331 fewer) | ⊕○○○ VERY LOW | MODERATE |

1 Subgroup analysis of late initiation of ART.

3. Papular pruritic eruption (PPE)

Table 3.1 Should ART alone or with other treatments versus no intervention be used in HIV-positive patients with PPE?

| No. of studies | Design | Quality assessment | | | | | No. of patients | | Effect | | Quality | Importance |
|--|---------------------|-------------------------|--------------------------|----------------------|----------------------|----------------------|------------------------------------|-----------------|-------------------|--|------------------|------------|
| | | Risk of bias | Inconsistency | Indirectness | Imprecision | Other considerations | ART alone or with other treatments | No Intervention | Relative (95% CI) | Absolute | | |
| Reduction in PPE severity (follow-up median 24 months; measured with: defined by sum of day and night itch scores; range of scores: 0-6; better indicated by higher values) | | | | | | | | | | | | |
| 1 | Observational study | No serious risk of bias | No serious inconsistency | Serious ¹ | Serious ² | None | 39 | 53 ³ | — | Mean 0.1 higher (0 to 6 higher) ⁴ | ⊕000 VERY LOW | IMPORTANT |

1 No comparison with no ART.

2 Small population size, no control.

3 Before and after study.

4 No CIs reported, this is the range of the scoring system.

Table 3.2 Should oral therapy with pentoxifylline versus no intervention be used in HIV-positive patients with PPE?

| No. of studies | Design | Quality assessment | | | | | No. of patients | | Effect | | Quality | Importance |
|--|---------------------|-------------------------|--------------------------|--------------------------------------|---------------------------|----------------------|----------------------------------|-----------------|-------------------|---|------------------|------------|
| | | Risk of bias | Inconsistency | Indirectness | Imprecision | Other considerations | Oral therapy with pentoxifylline | No intervention | Relative (95% CI) | Absolute | | |
| Pruritus score (follow-up 8 weeks; measured with: visual analog scale, investigator global assessment; range of scores: 0-10; better indicated by lower values) | | | | | | | | | | | | |
| 1 | Observational study | No serious risk of bias | No serious inconsistency | No serious indirectness ¹ | Very serious ¹ | None | 11 | 12 ² | — | Mean 3.6 higher (0 to 10 higher) ³ | ⊕000 VERY LOW | IMPORTANT |

1 Low size of population, no comparison group, no control group.

2 Before and after study.

3 No reported CI, this is the range of the scoring system.

Table 3.3 Should dapson versus antihistamines and topical clobetasol be used in HIV-positive patients with PPE?

| No. of studies | Design | Quality assessment | | | | | No. of patients | | Effect | | Quality | Importance |
|---|------------------|---------------------------|--------------------------|-------------------------|---------------------------|----------------------|-----------------|---------------------------------------|-------------------|--|------------------|------------|
| | | Risk of bias | Inconsistency | Indirectness | Imprecision | Other considerations | Dapsone | Antihistamines and topical clobetasol | Relative (95% CI) | Absolute | | |
| Favourable response (follow-up 14 weeks; better indicated by lower values) | | | | | | | | | | | | |
| 1 | Randomized trial | Very serious ¹ | No serious inconsistency | No serious indirectness | Very serious ² | None | 10 | 10 | — | MD 0 higher (0 to 0 higher) ³ | ⊕○○○ VERY LOW | IMPORTANT |
| Remission period (follow-up 14 weeks; better indicated by lower values) | | | | | | | | | | | | |
| 1 | Randomized trial | Very serious ¹ | No serious inconsistency | No serious indirectness | Very serious ⁴ | None | 10 | 10 | — | MD 0 higher (0 to 0 higher) ³ | ⊕○○○ VERY LOW | IMPORTANT |

- 1 There is no mention of randomization or blinding.
- 2 There is not enough data to support the result on faster response for each group. The study population is small.
- 3 No quantitative data reported for this outcome.
- 4 No data on duration of remission or evaluation of remission among the groups.

Table 3.4 Should oral promethazine versus 1% hydrocortisone be used in HIV-positive patients with PPE?

| No. of studies | Design | Quality assessment | | | | | No. of patients | | Effect | | Quality | Importance |
|--|---------------------|----------------------|--------------------------|-------------------------|---------------------------|----------------------|-------------------|-------------------|-------------------|--|------------------|------------|
| | | Risk of bias | Inconsistency | Indirectness | Imprecision | Other considerations | Oral promethazine | 1% hydrocortisone | Relative (95% CI) | Absolute | | |
| Reduction in itch score (measured with: subjective itching score; range of scores: 0–9; better indicated by lower values) | | | | | | | | | | | | |
| 1 | Observational study | Serious ¹ | No serious inconsistency | No serious indirectness | Very serious ² | None | 50 | 18 | — | Mean 3.9 higher (0 to 9 higher) ³ | ⊕○○○ VERY LOW | IMPORTANT |
| Reduction in clinical severity score (measured with: score system; range of scores: 1–3; better indicated by higher values) | | | | | | | | | | | | |
| 1 | Observational study | Serious ¹ | No serious inconsistency | No serious indirectness | Serious ⁴ | None | 50 | 18 | — | Mean 1.3 higher (1 to 3 higher) ³ | ⊕○○○ VERY LOW | IMPORTANT |

- 1 Did not specify time to follow-up, or patient characteristics such as adults or children, unclear inclusion criteria.
- 2 There was no reported value for significant difference between scores at the start and end of the treatment. No control group.
- 3 There was no CI data, this is the range of the score system.
- 4 No reported data on differences at the start and end of study.

4. Eosinophilic folliculitis*

Table 4.1 Should ART and isotretinoin versus no intervention be used in HIV-positive patients with eosinophilic folliculitis?

| No. of studies | Design | Quality assessment | | | | | No. of patients | | Effect | | Quality | Importance |
|--|----------------------------------|----------------------|--------------------------|-------------------------|------------------------|----------------------|----------------------|---------|-------------------|----------|------------------|------------|
| | | Risk of bias | Inconsistency | Indirectness | Imprecision | Other considerations | ART and isotretinoin | Control | Relative (95% CI) | Absolute | | |
| Resolution of lesions (follow-up 36 months) | | | | | | | | | | | | |
| 1 | Observational study ¹ | Serious ² | No serious inconsistency | No serious indirectness | Serious ^{2,3} | None | 16/23 (69.6%) | — | — | — | ⊕○○○ VERY LOW | IMPORTANT |
| | | | | | | | | 0% | | — | | |

1 Prospective study.

2 No controls.

3 No precise definition on complete response and partial response criteria.

* Only case reports and retrospective data available in the review. The recommendations were made on the basis of expert consensus.

5. Tinea infections

Table 5.1 Should terbinafine 1% cream/gel versus placebo cream/gel be used for *tinea cruris* and *tinea corporis*?

| No. of studies | Design | Quality assessment | | | | | No. of patients | | Effect | | Quality | Importance |
|---|-------------------|---------------------------|--------------------------|-------------------------|---------------------------|----------------------|--------------------------|-------------------|------------------------|--|------------------|------------|
| | | Risk of bias | Inconsistency | Indirectness | Imprecision | Other considerations | Terbinafine 1% cream/gel | Placebo cream/gel | Relative (95% CI) | Absolute | | |
| Mycological cure (assessed with: negative potassium hydroxide [KOH] microscopy, or culture, or both. Treatment duration 1–2 weeks) | | | | | | | | | | | | |
| 7 | Randomized trials | Very serious ¹ | Serious ² | No serious indirectness | No serious imprecision | None | 151/168 (89.9%) | 42/162 (25.9%) | Not pooled | Not pooled | ⊕⊕⊕⊕ VERY LOW | CRITICAL |
| | | | | | | | | 31.3% | | Not pooled | | |
| Clinical cure (follow-up 2-4 weeks; assessed with: resolution of clinical signs and symptoms. Treatment duration 1–2 weeks) | | | | | | | | | | | | |
| 5 | Randomized trials | Serious ³ | No serious inconsistency | No serious indirectness | Serious ⁴ | None ⁵ | 104/134 (77.6%) | 23/139 (16.5%) | RR 4.51 (3.1 to 6.56) | 581 more per 1000 (from 347 more to 920 more) | ⊕⊕⊕⊕ LOW | CRITICAL |
| | | | | | | | | 13.3% | | 467 more per 1000 (from 279 more to 739 more) | | |
| Adverse effects (follow-up 0-8 weeks; assessed with: reported by investigators and/or participants) | | | | | | | | | | | | |
| 7 | Randomized trials | Serious ¹ | No serious inconsistency | No serious indirectness | Very serious ⁶ | None | 8/232 (3.4%) | 23/237 (9.7%) | RR 0.43 (0.2 to 0.92) | 55 fewer per 1000 (from 8 fewer to 78 fewer) | ⊕⊕⊕⊕ VERY LOW | CRITICAL |
| | | | | | | | | 2.9% | | 17 fewer per 1000 (from 2 fewer to 23 fewer) | | |
| Relapse or recurrence (follow-up 1–8 weeks; assessed with: evidence of clinical or mycological infection in previously cured participants) | | | | | | | | | | | | |
| 3 | Randomized trials | Serious ⁷ | No serious inconsistency | No serious indirectness | Serious ⁸ | None | 0/81 (0%) | 0/87 (0%) | Not pooled | Not pooled | ⊕⊕⊕⊕ LOW | IMPORTANT |
| | | | | | | | | 0% | | Not pooled | | |
| Participant-judged cure (assessed with: judgement of treatment as 'good' or 'very good') | | | | | | | | | | | | |
| 2 | Randomized trials | Serious ⁹ | No serious inconsistency | No serious indirectness | Serious ¹⁰ | None ¹¹ | 110/122 (90.2%) | 26/131 (19.8%) | RR 4.46 (3.16 to 6.31) | 687 more per 1000 (from 429 more to 1000 more) | ⊕⊕⊕⊕ LOW | IMPORTANT |
| | | | | | | | | 0% | | — | | |

1 Random sequence generation, allocation concealment and blinding at unclear risk of bias across studies, with 2 studies (Lebwohl et al., 2001; Millikan, 1990) judged overall at high risk of bias. In both of these studies, there was a high dropout rate (20–25%) in already underpowered studies.

2 Substantial unexplained heterogeneity.

3 3 studies (Lebwohl et al., 2001; Millikan, 1990; Zaias et al., 1993) judged at high risk of bias overall.

4 Small sample size, optimal size would be 2790 participants.

5 Although there is a large effect (RR 4.51, in all studies RR > 4.00), there are threats to validity, see risk of bias.

- 6 CI includes the threshold for appreciable benefit (0.75) and nearly no effect (1.0), very low number of events, low sample size (optimal size would be 4238 participants).
- 7 Millikan (1990) judged at high risk of bias overall – high dropout rate in an underpowered study; sequence generation, allocation concealment and blinding judged at unclear risk of bias in remaining studies.
- 8 Low number of events, sample size is lower than optimal.
- 9 Blinding for both studies judged at unclear risk of bias, and Zaias and colleagues (1993) judged overall at high risk of bias – details on total number of randomized participants not given.
- 10 Number of events <300 and optimal size would be 2210 participants.
- 11 Although there is a large effect (RR > 2), there are threats to validity, see risk of bias.

Table 5.2 Should naftifine 1% cream once or twice daily versus placebo cream once or twice daily be used for *tinea cruris* and *tinea corporis*?

| No. of studies | Design | Quality assessment | | | | | No. of patients | | Effect | | Quality | Importance |
|---|-------------------|-------------------------|--------------------------|-------------------------|---------------------------|----------------------|--|-----------------------------------|------------------------|--|------------------|------------|
| | | Risk of bias | Inconsistency | Indirectness | Imprecision | Other considerations | Naftifine 1% cream once or twice daily | Placebo cream once or twice daily | Relative (95% CI) | Absolute | | |
| Mycological cure (assessed with: negative KOH microscopy and culture. Treatment duration 2–4 weeks) | | | | | | | | | | | | |
| 3 | Randomized trials | Serious ¹ | No serious inconsistency | No serious indirectness | Serious ² | None ³ | 83/95 (87.4%) | 33/92 (35.9%) | RR 2.38 (1.8 to 3.14) | 495 more per 1000 (from 287 more to 768 more) | ⊕⊕OO LOW | CRITICAL |
| | | | | | | | | 32.1% | | 443 more per 1000 (from 257 more to 687 more) | | |
| Clinical cure (follow-up 6 weeks; assessed with: resolution of clinical signs and symptoms at least 2 weeks from start of treatment) | | | | | | | | | | | | |
| 1 | Randomized trials | No serious risk of bias | No serious inconsistency | No serious indirectness | Very serious ⁴ | None ⁵ | 25/32 (78.1%) | 10/31 (32.3%) | RR 2.42 (1.41 to 4.16) | 458 more per 1000 (from 132 more to 1000 more) | ⊕⊕OO LOW | CRITICAL |
| | | | | | | | | 0% | | — | | |
| Adverse effects (follow-up 0–6 weeks; assessed with: reported by investigators and/or participants) | | | | | | | | | | | | |
| 3 | Randomized trials | Serious ¹ | No serious inconsistency | No serious indirectness | Very serious ⁶ | None | 3/99 (3%) | 7/96 (7.3%) | RR 0.44 (0.13 to 1.57) | 41 fewer per 1000 (from 63 fewer to 42 more) | ⊕OOO VERY LOW | CRITICAL |
| | | | | | | | | 5.4% | | 30 fewer per 1000 (from 47 fewer to 31 more) | | |
| Relapse or recurrence (follow-up 6 weeks; assessed with: evidence of clinical or mycological infection in previously cured participants) | | | | | | | | | | | | |
| 1 | Randomized trials | No serious risk of bias | No serious inconsistency | No serious indirectness | Very serious ⁷ | None | 0/30 (0%) | 3/14 (21.4%) | RR 0.07 (0 to 1.25) | 199 fewer per 1000 (from 214 fewer to 54 more) | ⊕⊕OO LOW | IMPORTANT |
| | | | | | | | | 0% | | — | | |
| | | | | | | | | 0% | | — | | |

1 Dobson and colleagues (1991) judged at high risk of bias overall – high dropout rate (27%) in an already underpowered study. Numbers of participants in each group after randomization unclear.

2 Low sample size, optimal size would be 938.

3 Although large treatment effect (RR > 2), there were threats to validity, see risk of bias.

4 Very low total number of participants, optimal size would be 1114, and wide CI.

5 Although large treatment effect (RR > 2), there were threats to validity, see imprecision.

6 CI includes appreciable harm, no effect and appreciable benefit. Furthermore, low number of events and small sample size (optimal size would be 5804 participants).

7 CI includes appreciable harm, no effect and appreciable benefit. Furthermore, low sample size (optimal size would be 1608 participants).

Table 5.3 Should azoles versus moderate-potent corticosteroid/azole combinations be used for *tinea cruris* and *tinea corporis*?

| Quality assessment | | | | | | | No. of patients | | Effect | | Quality | Importance |
|--|-------------------|---------------------------|--------------------------|-------------------------|---------------------------|----------------------|-----------------|---|------------------------|--|------------------|------------|
| No. of studies | Design | Risk of bias | Inconsistency | Indirectness | Imprecision | Other considerations | Azoles | Moderate-potent corticosteroid/azole combinations | Relative (95% CI) | Absolute | | |
| Mycological cure (assessed with: negative KOH microscopy and culture. Treatment duration 2–3 weeks) | | | | | | | | | | | | |
| 6 ¹ | Randomized trials | Serious ² | No serious inconsistency | Serious ³ | No serious imprecision | None | 245/313 (78.3%) | 248/312 (79.5%) | RR 0.99 (0.93 to 1.05) | 8 fewer per 1000 (from 56 fewer to 40 more) | ⊕⊕OO LOW | CRITICAL |
| | | | | | | | | 88.1% | | 9 fewer per 1000 (from 62 fewer to 44 more) | | |
| Clinical cure (immediately at end of treatment) (assessed with: resolution of clinical signs and symptoms at least 2 weeks from the start of treatment) | | | | | | | | | | | | |
| 4 ⁴ | Randomized trials | Serious ² | No serious inconsistency | Serious ³ | Serious ⁵ | None | 90/181 (49.7%) | 133/172 (77.3%) | RR 0.67 (0.53 to 0.84) | 255 fewer per 1000 (from 124 fewer to 363 fewer) | ⊕OOO VERY LOW | CRITICAL |
| | | | | | | | | 83.6% | | 276 fewer per 1000 (from 134 fewer to 393 fewer) | | |
| Adverse effects (follow-up 0–4 weeks; assessed with: reported by investigators and/or participants) | | | | | | | | | | | | |
| 5 ⁶ | Randomized trials | Serious ² | No serious inconsistency | No serious indirectness | Very serious ⁷ | None | 18/336 (5.4%) | 13/332 (3.9%) | RR 1.36 (0.68 to 2.69) | 14 more per 1000 (from 13 fewer to 66 more) | ⊕OOO VERY LOW | CRITICAL |
| | | | | | | | | 1.8% | | 6 more per 1000 (from 6 fewer to 30 more) | | |
| | | | | | | | | 0% | | — | | |
| Participant-judged cure (assessed with: 4 point symptom score scale) | | | | | | | | | | | | |
| 1 ⁸ | Randomized trials | Very serious ⁹ | No serious inconsistency | No serious indirectness | No serious imprecision | None | — | — | — | — | ⊕⊕OO LOW | IMPORTANT |
| | | | | | | | | 0% | | — | | |
| | | | | | | | | 0% | | — | | |

1 Katz et al., 1984; Li et al., 2004; Pariser & Pariser, 1995; Shen et al., 2002; Wang et al., 2000; Wortzel, 1982.

2 Sequence generation, allocation concealment and blinding at unclear risk of bias across all studies. Pariser & Pariser (1995) judged overall at high risk of bias.

3 4 different azole creams and 2 different corticosteroid/azole creams assessed in these studies.

4 Pariser & Pariser, 1995; Shen et al., 2002; Wang et al., 2000; Wortzel, 1982.

5 Low sample size, optimal sample size would be 500, CI includes threshold 0.75.

6 Katz et al., 1984; Li et al., 2004; Pariser & Pariser, 1995; Shen et al., 2002; Wortzel, 1982.

7 CI includes appreciable harm, no effect and appreciable benefit. Furthermore, low number of events and very small sample size (optimal sample size would be 10 310).

8 Pariser & Pariser, 1995.

9 Blinding judged at unclear risk of bias, and minimal data were reported on patient-judged cure.

Table 5.4 Should azoles versus allylamines be used for *tinea cruris* and *tinea corporis*?

| No. of studies | Design | Quality assessment | | | | | No. of patients | | Effect | | Quality | Importance |
|---|-------------------|----------------------|--------------------------|-------------------------|---------------------------|----------------------|-----------------|-----------------|-------------------------|---|------------------|------------|
| | | Risk of bias | Inconsistency | Indirectness | Imprecision | Other considerations | Azoles | Allylamines | Relative (95% CI) | Absolute | | |
| Mycological cure (assessed with: negative KOH microscopy and culture. Treatment duration 1–7 weeks) | | | | | | | | | | | | |
| 7 | Randomized trials | Serious ¹ | Serious ² | Serious ³ | No serious imprecision | None | 288/323 (89.2%) | 303/315 (96.2%) | Not pooled | Not pooled | ⊕○○○ VERY LOW | CRITICAL |
| | | | | | | | | 100% | | Not pooled | | |
| Clinical cure (assessed with: resolution of clinical signs and symptoms at least 2 weeks from the start of treatment. Treatment duration 1–7 weeks) | | | | | | | | | | | | |
| 6 | Randomized trials | Serious ⁴ | Serious ² | Serious ³ | No serious imprecision | None | 249/305 (81.6%) | 270/300 (90%) | Not pooled | Not pooled | ⊕○○○ VERY LOW | CRITICAL |
| | | | | | | | | 92.3% | | Not pooled | | |
| Adverse effects (follow-up 0–8 weeks; assessed with: reported by investigators and/or participants) | | | | | | | | | | | | |
| 5 | Randomized trials | Serious ¹ | No serious inconsistency | No serious indirectness | Very serious ⁵ | None | 2/197 (1%) | 4/189 (2.1%) | RR 0.7 (0.18 to 2.68) | 6 fewer per 1000 (from 17 fewer to 36 more) | ⊕○○○ VERY LOW | CRITICAL |
| | | | | | | | | 2.2% | | 7 fewer per 1000 (from 18 fewer to 37 more) | | |
| Relapse or recurrence (follow-up 2–4 weeks; assessed with: evidence of clinical and mycological relapse after the end of treatment. Assessed in 3 studies) | | | | | | | | | | | | |
| 3 ⁶ | Randomized trials | Serious ¹ | No serious inconsistency | No serious indirectness | Very serious ⁷ | None | 1/61 (1.6%) | 0% | RR 2.33 (0.21 to 26.23) | — | ⊕○○○ VERY LOW | IMPORTANT |
| Duration of treatment until clinical cure (range of scores: 21–77; better indicated by lower values) | | | | | | | | | | | | |
| 1 | Randomized trial | Serious ⁸ | No serious inconsistency | No serious indirectness | Very serious ⁹ | None | 2 | 5 | — | MD 33.60 lower (46.91 to 20.29 lower) | ⊕○○○ VERY LOW | IMPORTANT |

- 1 Haroon and colleagues (1996) and Jerajani and colleagues (2013) were both open trials, and blinding was therefore judged at high risk of bias. In addition, the attrition rate was also high in both studies (20% and 25% respectively). Sequence generation, allocation concealment and blinding all judged at an unclear risk of bias in remaining studies.
- 2 Substantial heterogeneity ($I^2 = 75\%$).
- 3 Six different azole creams used across the studies. Allylamine treatment regimens different across all studies.
- 4 Jerajani and colleagues (2013) judged at high risk of bias due to lack of blinding and high attrition rate. Sequence generation, allocation concealment and blinding for the remaining studies all judged at an unclear risk of bias.
- 5 Low number of events, CI is wide, including appreciable harm, no effect and appreciable benefit, optimal size would be 15 414 participants.
- 6 Hantschke & Reichenberger (1980); Haroon et al., 1996; Jerajani et al., 2013.
- 7 Low total number of participants and wide CI including no effect and appreciable harm.
- 8 Sequence generation, allocation concealment and blinding all judged at unclear risk of bias.
- 9 Only 9 participants in total.

Table 5.5 Should azoles versus benzylamines be used for *tinea cruris* and *tinea corporis*?

| No. of studies | Design | Quality assessment | | | | | No. of patients | | Effect | | Quality | Importance |
|---|-------------------|-------------------------|--------------------------|-------------------------|---------------------------|----------------------|-----------------|-----------------|------------------------|--|------------------|------------|
| | | Risk of bias | Inconsistency | Indirectness | Imprecision | Other considerations | Azoles | Benzylamines | Relative (95% CI) | Absolute | | |
| Mycological cure (assessed with: negative KOH microscopy and culture. Treatment duration 2–4 weeks) | | | | | | | | | | | | |
| 3 ¹ | Randomized trials | Serious ² | No serious inconsistency | Serious ³ | No serious imprecision | None | 107/112 (95.5%) | 101/107 (94.4%) | RR 1.01 (0.94 to 1.07) | 9 more per 1000 (from 57 fewer to 66 more) | ⊕⊕⊕⊕ LOW | CRITICAL |
| | | | | | | | | 93.1% | | 9 more per 1000 (from 56 fewer to 65 more) | | |
| Clinical cure (assessed with: resolution of clinical signs and symptoms at least 2 weeks from the start of treatment) | | | | | | | | | | | | |
| 2 ⁴ | Randomized trials | No serious risk of bias | Serious ⁵ | No serious indirectness | Serious ⁶ | None | 47/84 (56%) | 45/85 (52.9%) | Not pooled | Not pooled | ⊕⊕⊕⊕ LOW | CRITICAL |
| | | | | | | | | 0% | | Not pooled | | |
| Adverse effects (follow-up 0–8 weeks; assessed with: reported by investigators and/or participants) | | | | | | | | | | | | |
| 3 ¹ | Randomized trials | Serious ² | No serious inconsistency | No serious indirectness | Very serious ⁷ | None | 12/131 (9.2%) | 14/132 (10.6%) | RR 0.85 (0.41 to 1.76) | 16 fewer per 1000 (from 63 fewer to 81 more) | ⊕⊕⊕⊕ VERY LOW | CRITICAL |
| | | | | | | | | 10.3% | | 15 fewer per 1000 (from 61 fewer to 78 more) | | |
| Relapse or recurrence (follow-up 4–8 weeks; assessed with: evidence of clinical or mycological disease after successful treatment) | | | | | | | | | | | | |
| 3 ¹ | Randomized trials | Serious ² | No serious inconsistency | Serious ³ | Serious ⁸ | None | 4/110 (3.6%) | 2/105 (1.9%) | RR 1.84 (0.35 to 9.6) | 16 more per 1000 (from 12 fewer to 164 more) | ⊕⊕⊕⊕ VERY LOW | IMPORTANT |
| | | | | | | | | 0% | | — | | |
| | | | | | | | | 0% | | — | | |

- 1 Ramam et al., 2003; Singal et al., 2005; Li et al., 2006.
- 2 Ramam and colleagues (2003) judged at high risk of bias overall – high attrition rate and study funded by industry supplying both interventions.
- 3 Different azoles assessed in the studies.
- 4 Singal et al., 2005; Li et al., 2006.
- 5 Substantial heterogeneity apparent.
- 6 Low total number of participants.
- 7 Low sample size, optimal size is around 5500, and CI includes both no effect and appreciable harm.
- 8 Very wide CI, low event rate, small sample size.

Table 5.6 Should azoles versus placebo be used for *tinea cruris* and *tinea corporis*?

| No. of studies | Design | Quality assessment | | | | | No. of patients | | Effect | | Quality | Importance |
|---|-------------------|----------------------|--------------------------|-------------------------|---------------------------|----------------------|-----------------|----------------|------------------------|--|------------------|------------|
| | | Risk of bias | Inconsistency | Indirectness | Imprecision | Other considerations | Azoles | Placebo | Relative (95% CI) | Absolute | | |
| Mycological cure (assessed with: negative KOH microscopy and culture. Treatment duration 2–4 weeks) | | | | | | | | | | | | |
| 4 ^{1,2} | Randomized trials | Serious ³ | Serious ⁴ | Serious ⁵ | No serious imprecision | None | 257/284 (90.5%) | 72/206 (35%) | Not pooled | Not pooled | ⊕000 VERY LOW | CRITICAL |
| | | | | | | | | 0% | | Not pooled | | |
| Clinical cure (assessed with: resolution of clinical signs and symptoms. Treatment duration 2–4 weeks) | | | | | | | | | | | | |
| 3 ^{2,6} | Randomized trials | Serious ⁷ | Serious ⁴ | Serious ⁵ | No serious imprecision | None | 153/211 (72.5%) | 34/125 (27.2%) | Not pooled | Not pooled | ⊕000 VERY LOW | CRITICAL |
| | | | | | | | | 0% | | Not pooled | | |
| Adverse effects (follow-up 0–5 weeks; assessed with: reported by investigators and/or participants) | | | | | | | | | | | | |
| 3 ^{2,6} | Randomized trials | Serious ⁷ | No serious inconsistency | No serious indirectness | Very serious ⁸ | None | 2/132 (1.5%) | 11/134 (8.2%) | RR 0.25 (0.06 to 0.99) | 62 fewer per 1000 (from 1 fewer to 77 fewer) | ⊕000 VERY LOW | CRITICAL |
| | | | | | | | | 0% | | — | | |
| | | | | | | | | 0% | | — | | |

1 Bagatell, 1986; Miura et al., 1979; Spiekermann & Young, 1976; Tanenbaum et al., 1989.

2 Miura and colleagues (1979) – 2 comparisons (econazole versus placebo and clotrimazole versus placebo).

3 Spiekermann & Young (1976) judged at high risk of bias overall due to high attrition rate (33%) and industry funded study. Sequence generation, allocation concealment and blinding all judged at unclear risk of bias across remaining studies.

4 Substantial unexplained heterogeneity, data not pooled.

5 4 different azoles.

6 Bagatell, 1986; Miura et al., 1979; Tanenbaum et al., 1989.

7 Sequence generation, allocation concealment and blinding all judged at unclear risk of bias across all studies.

8 Wide CI including appreciable harm and low sample size, optimal size around 4724.

6. Herpes zoster

Table 6.1 Should acyclovir versus placebo be used for herpes zoster in HIV-infected adults and children?

| No. of studies | Design | Quality assessment | | | | | No. of patients | | Effect | | Quality | Importance |
|---|-------------------|-----------------------------------|--------------------------|-----------------------------------|------------------------|------------------|-----------------|-----------------|------------------------|---|-------------|------------|
| | | Risk of bias | Inconsistency | Indirectness | Imprecision | Publication bias | No acyclovir | Acyclovir | Relative (95% CI) | Absolute | | |
| Cessation of new lesions | | | | | | | | | | | | |
| 5 | Randomized trials | Serious risk of bias ¹ | No serious inconsistency | Serious indirectness ² | No serious imprecision | Undetected | 122/200 (61%) | 127/206 (61.7%) | HR 1.54 (1.21 to 1.97) | 155 more per 1000 (from 70 more to 234 more) | ⊕⊕⊕⊕ LOW | CRITICAL |
| Mean time new lesion stoppage (better indicated by lower values) | | | | | | | | | | | | |
| 2 | Randomized trials | Serious risk of bias ¹ | No serious inconsistency | Serious indirectness ² | No serious imprecision | Undetected | 53 | 55 | — | Mean time to new lesion stoppage in intervention group was 0.59 lower (1.11 to 0.08 lower) | ⊕⊕⊕⊕ LOW | CRITICAL |
| Lesion healing (critical outcome) | | | | | | | | | | | | |
| 3 | Randomized trials | Serious risk of bias ¹ | No serious inconsistency | Serious indirectness ² | No serious imprecision | Undetected | 78/148 (52.7%) | 66/135 (48.9%) | HR 1.48 (1.06 to 2.05) | 143 more per 1000 (from 21 more to 257 more) | ⊕⊕⊕⊕ LOW | CRITICAL |
| Mean time to full crusting (better indicated by lower values) | | | | | | | | | | | | |
| 1 | Randomized trial | Serious risk of bias ¹ | No serious inconsistency | Serious indirectness ² | No serious imprecision | Undetected | 29 | 29 | | Mean time to full crusting in intervention group was 7.4 lower (15.78 lower to 0.98 higher) | ⊕⊕⊕⊕ LOW | CRITICAL |

1 Details of randomization not provided or incomplete outcome data.

2 Studies involved non-HIV populations.

Table 6.2 Should famciclovir versus acyclovir be used for herpes zoster in HIV-infected adults and children?

| Quality assessment | | | | | | | No. of patients | | Effect | | Quality | Importance |
|--|-------------------|-----------------------------------|--------------------------|-----------------------------------|------------------------|------------------|-----------------|-----------------|------------------------|--|----------|------------|
| No. of studies | Design | Risk of bias | Inconsistency | Indirectness | Imprecision | Publication bias | Acyclovir | Famciclovir | Relative (95% CI) | Absolute | | |
| Lesion healing (critical outcome) | | | | | | | | | | | | |
| 3 | Randomized trials | Serious risk of bias ¹ | No serious inconsistency | Serious indirectness ² | No serious imprecision | Undetected | 291/294 (99%) | 271/275 (98.5%) | HR 1.18 (0.98 to 1.41) | 6 more per 1000 (from 1 fewer to 9 more) | ⊕⊕○○ LOW | CRITICAL |

- 1 Details of randomization not provided.
 2 Studies involved non-HIV populations.

Table 6.3 Should famciclovir versus acyclovir be used for stoppage of new herpes zoster lesions in HIV-infected adults and children?

| Quality assessment | | | | | | | No. of patients | | Effect | | Quality | Importance |
|--|------------------|-----------------------------------|--------------------------|-----------------------------------|------------------------|------------------|-----------------|--------------|------------------------|---|----------|------------|
| No. of studies | Design | Risk of bias | Inconsistency | Indirectness | Imprecision | Publication bias | No acyclovir | Acyclovir | Relative (95% CI) | Absolute | | |
| Cessation of new lesions (critical outcome) | | | | | | | | | | | | |
| 1 | Randomized trial | Serious risk of bias ¹ | No serious inconsistency | Serious indirectness ² | No serious imprecision | Undetected | 77/128 (60.2%) | 69/121 (57%) | HR 1.45 (0.93 to 2.26) | 135 more per 1000 (from 27 fewer to 273 more) | ⊕⊕○○ LOW | CRITICAL |

- 1 Details of randomization not provided.
 2 Studies involved non-HIV populations.

Table 6.4 Should brivudin versus acyclovir be used for herpes zoster in HIV-infected adults and children?

| No. of studies | Design | Quality assessment | | | | | No. of patients | | Effect | | Quality | Importance |
|--|-------------------|-----------------------------------|--------------------------|-----------------------------------|------------------------|------------------|-----------------|-----------------|------------------------|---|-------------|------------|
| | | Risk of bias | Inconsistency | Indirectness | Imprecision | Publication bias | Acyclovir | Brivudin | Relative (95% CI) | Absolute | | |
| Cessation of new lesions (critical outcome) | | | | | | | | | | | | |
| 2 | Randomized trials | Serious risk of bias ¹ | No serious inconsistency | Serious indirectness ² | No serious imprecision | Undetected | 633/633 (100%) | 635/635 (100%) | HR 1.11 (0.99 to 1.24) | 0 fewer per 1000 | ⊕⊕○○ LOW | CRITICAL |
| Lesion healing (critical outcome) | | | | | | | | | | | | |
| 3 | Randomized trials | Serious risk of bias ¹ | No serious inconsistency | Serious indirectness ² | No serious imprecision | Undetected | 653/657 (99.4%) | 653/658 (99.2%) | HR 0.95 (0.85 to 1.06) | 2 fewer per 1000 (from 7 fewer to 2 more) | ⊕⊕○○ LOW | CRITICAL |

1 Details of randomization not provided.

2 Studies involved non-HIV populations.

Table 6.5 Should valacyclovir versus acyclovir be used for herpes zoster in HIV-infected adults and children?

| No. of studies | Design | Quality assessment | | | | | No. of patients | | Effect | | Quality | Importance |
|--|-------------------|-----------------------------------|--------------------------|-----------------------------------|------------------------|------------------|-----------------|-----------------|------------------------|--|-------------|------------|
| | | Risk of bias | Inconsistency | Indirectness | Imprecision | Publication bias | Acyclovir | Brivudin | Relative (95% CI) | Absolute | | |
| Lesion healing (critical outcome) | | | | | | | | | | | | |
| 2 | Randomized trials | Serious risk of bias ¹ | No serious inconsistency | Serious indirectness ² | No serious imprecision | Undetected | 391/406 (96.3%) | 403/414 (97.3%) | HR 1.01 (0.88 to 1.16) | 1 more per 1000 (from 18 fewer to 15 more) | ⊕⊕○○ LOW | CRITICAL |
| Cessation of new lesions (critical outcome) | | | | | | | | | | | | |
| 1 | Randomized trial | Serious risk of bias ¹ | No serious inconsistency | Serious indirectness ² | No serious imprecision | Undetected | 376/376 (100%) | 384/384 (100%) | HR 1.03 (0.89 to 1.2) | 1000 per 1000 | ⊕⊕○○ LOW | CRITICAL |

1 Details of randomization not provided or incomplete outcome data.

2 Studies involved non-HIV populations.

7. Scabies

Table 7.1 Should permethrin (topical) versus ivermectin (oral 1 dose) be used for scabies?

| No. of studies | Design | Quality assessment | | | | | No. of patients | | Effect | | Quality | Importance |
|--|------------------|-------------------------|--------------------------|-------------------------|---------------------------|----------------------|--------------------|------------------------|------------------------|--|----------|------------|
| | | Risk of bias | Inconsistency | Indirectness | Imprecision | Other considerations | Permethrin topical | Ivermectin oral 1 dose | Relative (95% CI) | Absolute | | |
| Complete cure (follow-up 4 weeks; assessed with: reduction in both the number of lesions as well as the grade of pruritus by more than or equal to 50%) | | | | | | | | | | | | |
| 1 | Randomized trial | No serious risk of bias | No serious inconsistency | No serious indirectness | Very serious ¹ | None | 36/38 (94.7%) | 36/40 (90%) | RR 1.06 (0.95 to 1.67) | 54 more per 1000 (from 45 fewer to 603 more) | ⊕⊕○○ LOW | CRITICAL |
| | | | | | | | | 0% | | — | | |

1 Poor confirmation of diagnosis, unclear definition of complete clinical cure, and rate of cure defined as >50% improvement in lesion count.

Table 7.2 Should oral ivermectin with antihistaminics versus permethrin with antihistaminics be used for scabies?

| No. of studies | Design | Quality assessment | | | | | No. of patients | | Effect | | Quality | Importance |
|---|------------------|------------------------|--------------------------|-------------------------|-----------------------------|----------------------|--------------------------------------|---------------------------------|-------------------|--------------------------------------|---------------|------------|
| | | Risk of bias | Inconsistency | Indirectness | Imprecision | Other considerations | Oral ivermectin with antihistaminics | Permethrin with antihistaminics | Relative (95% CI) | Absolute | | |
| Clinical cure rate (follow-up 4 weeks; measured with: number of lesions;¹ better indicated by lower values) | | | | | | | | | | | | |
| 1 | Randomized trial | Serious ^{1,2} | No serious inconsistency | No serious indirectness | Very serious ^{1,2} | None | 100 | 103 | — | RR 1.01 higher (0.95 to 1.08 higher) | ⊕○○○ VERY LOW | CRITICAL |

1 Rate of clinical cure not clearly defined.

2 Mention of a single dose in methodology and repeated dose in discussion for oral ivermectin.

Table 7.3 Should oral ivermectin (two applications) versus topical permethrin (two applications) be used for scabies?

| No. of studies | Design | Quality assessment | | | | | No. of patients | | Effect | | Quality | Importance |
|---|------------------|----------------------|--------------------------|-------------------------|---------------------------|----------------------|----------------------------------|-------------------------------------|------------------------|--|---------------|------------|
| | | Risk of bias | Inconsistency | Indirectness | Imprecision | Other considerations | Oral ivermectin two applications | Topical permethrin two applications | Relative (95% CI) | Absolute | | |
| Cure (follow-up 4 weeks; assessed with: disappearance of itching, clearance of skin lesions and absence of mites on microscopy skin lesions) | | | | | | | | | | | | |
| 1 | Randomized trial | Serious ¹ | No serious inconsistency | No serious indirectness | Very serious ² | None | 44/50 (88%) | 42/50 (84%) | RR 1.06 (0.92 to 1.33) | 50 more per 1000 (from 67 fewer to 277 more) | ⊕○○○ VERY LOW | CRITICAL |
| | | | | | | | | 0% | | — | | |

1 Not blinded.

2 Unclear definition of number of lesions considered as cure. Second dose of each treatment only provided to non-responsive patients.

Table 7.4 Should topical permethrin (two applications) versus oral ivermectin (two applications) be used for scabies?

| Quality assessment | | | | | | | No. of patients | | Effect | | Quality | Importance |
|---|------------------|----------------------|--------------------------|-------------------------|-------------------------------|----------------------|-------------------------------------|----------------------------------|-------------------|--|------------------|------------|
| No. of studies | Design | Risk of bias | Inconsistency | Indirectness | Imprecision | Other considerations | Topical permethrin two applications | Oral ivermectin two applications | Relative (95% CI) | Absolute | | |
| Cure rate (follow-up 2 weeks; measured with: lesion count;¹ better indicated by lower values) | | | | | | | | | | | | |
| 1 | Randomized trial | Serious ² | No serious inconsistency | No serious indirectness | Very serious ^{1,3,4} | None | 28 | 27 | — | Rate % 96.43 higher (0 to 100 higher) ⁵ | ⊕○○○ VERY LOW | CRITICAL |

- 1 Not clearly defined, "The participants who did not have any new lesions were considered as cured".
- 2 Not blinded.
- 3 Does not state how many patients received treatment with azithromycin.
- 4 Only patients who did not improve at week 1 received second application.
- 5 The rate of cure can go from 0% to 100%.

Table 7.5 Should topical permethrin (two applications) versus benzyl benzoate (two applications) be used for scabies?

| Quality assessment | | | | | | | No. of patients | | Effect | | Quality | Importance |
|---|------------------|----------------------|--------------------------|-------------------------|-------------------------------|----------------------|-------------------------------------|----------------------------------|-------------------|--|------------------|------------|
| No. of studies | Design | Risk of bias | Inconsistency | Indirectness | Imprecision | Other considerations | Topical permethrin two applications | Benzyl benzoate two applications | Relative (95% CI) | Absolute | | |
| Cure rate (follow-up 2 weeks; measured with: lesion count;¹ better indicated by lower values) | | | | | | | | | | | | |
| 1 | Randomized trial | Serious ² | No serious inconsistency | No serious indirectness | Very serious ^{3,4,5} | None | 34 | 35 | — | Rate % 96.46 higher (0 to 100 higher) ⁶ | ⊕○○○ VERY LOW | CRITICAL |

- 1 Not clearly defined, "The participants who did not have any new lesions were considered as cured".
- 2 Not blinded.
- 3 Not clearly defined, "The participants who did not have any new lesions were considered as cured".
- 4 Does not state how many patients received treatment with azithromycin.
- 5 Only patients who did not improve at week 1 received second application.
- 6 The rate of cure can go from 0% to 100%.

Table 7.6 Should oral ivermectin (two applications) versus benzyl benzoate (two applications) be used for scabies?

| Quality assessment | | | | | | | No. of patients | | Effect | | Quality | Importance |
|---|------------------|----------------------|--------------------------|-------------------------|-------------------------------|----------------------|----------------------------------|----------------------------------|-------------------|-------------------------------------|------------------|------------|
| No. of studies | Design | Risk of bias | Inconsistency | Indirectness | Imprecision | Other considerations | Oral ivermectin two applications | Benzyl benzoate two applications | Relative (95% CI) | Absolute | | |
| Cure rate (follow-up 2 weeks; measured with: lesion count;¹ better indicated by lower values) | | | | | | | | | | | | |
| 1 | Randomized trial | Serious ² | No serious inconsistency | No serious indirectness | Very serious ^{1,3,4} | None | 34 | 35 | — | Rate % 100 higher (0 to 100 higher) | ⊕○○○ VERY LOW | CRITICAL |

- 1 Not clearly defined, "The participants who did not have any new lesions were considered as cured".
- 2 Not blinded.
- 3 Does not state how many patients received treatment with azithromycin.
- 4 Only patients who did not improve at week 1 received second application.

Table 7.7 Should ivermectin be used in HIV-positive patients with scabies?

| Quality assessment | | | | | | | No. of patients | | Effect | | Quality | Importance |
|---|---------------------|----------------------|--------------------------|-------------------------|------------------------|----------------------|-----------------|---------------|---------------------|---|------------------|------------|
| No. of studies | Design | Risk of bias | Inconsistency | Indirectness | Imprecision | Other considerations | Ivermectin | Control | Relative (95% CI) | Absolute | | |
| Cure (follow-up 4 months; assessed with: patients with no pruritus, no dermatological evidence of scabies and no positive scrapings) | | | | | | | | | | | | |
| 1 | Observational study | Serious ¹ | No serious inconsistency | No serious indirectness | No serious imprecision | None | 11/11 (100%) | 11/13 (84.6%) | RR 3 (0.13 to 66.5) | 1000 more per 1000 (from 736 fewer to 1000 more) ² | ⊕○○○ VERY LOW | CRITICAL |
| | | | | | | | | 0% | | — | | |

- 1 Not randomized, small study population.

Table 7.8 Should oral ivermectin versus benzyl benzoate solution be used in HIV-positive patients with scabies?

| No. of studies | Design | Quality assessment | | | | | No. of patients | | Effect | | Quality | Importance |
|--|----------------------------------|----------------------|--------------------------|-------------------------|----------------------|----------------------|-----------------|--------------------------|------------------------|---|---------------|------------|
| | | Risk of bias | Inconsistency | Indirectness | Imprecision | Other considerations | Oral ivermectin | Benzyl benzoate solution | Relative (95% CI) | Absolute | | |
| Complete clinical response (follow-up 4 weeks; assessed with: resolution of itching and dermatological or microbiological cure) | | | | | | | | | | | | |
| 1 | Observational study ¹ | Serious ² | No serious inconsistency | No serious indirectness | Serious ³ | None | 12/21 (57.1%) | 10/22 (45.5%) | RR 0.78 (0.42 to 1.46) | 100 fewer per 1000 (from 264 fewer to 209 more) | ⊕○○○ VERY LOW | CRITICAL |
| | | | | | | | | 0% | | — | | |

- 1 Observational.
- 2 Retrospective study, small study population.
- 3 No clear definition of dermatological cure in respect to the number of lesions.

Table 7.9 Should oral ivermectin versus a combination of topical benzyl benzoate and oral ivermectin be used in HIV-positive patients with scabies?

| No. of studies | Design | Quality assessment | | | | | No. of patients | | Effect | | Quality | Importance |
|--|----------------------------------|----------------------|--------------------------|-------------------------|------------------------|----------------------|-----------------|--|-------------------------|--|---------------|------------|
| | | Risk of bias | Inconsistency | Indirectness | Imprecision | Other considerations | Oral ivermectin | Combination of topical benzyl benzoate and oral ivermectin | Relative (95% CI) | Absolute | | |
| Complete clinical response (follow-up 4 weeks; assessed with: resolution of itching and dermatological or microbiological cure) | | | | | | | | | | | | |
| 1 | Observational study ¹ | Serious ¹ | No serious inconsistency | No serious indirectness | Serious ^{1,2} | None | 12/21 (57.1%) | 17/17 (100%) | RR 0.06 (0.004 to 1.03) | 940 fewer per 1000 (from 996 fewer to 30 more) | ⊕○○○ VERY LOW | CRITICAL |
| | | | | | | | | 0% | | — | | |

- 1 Retrospective study.
- 2 Small study population.

Table 7.10 Should ivermectin versus combined therapy (ivermectin, permethrin, salicylic acid) be used for crusted scabies?

| Quality assessment | | | | | | | No. of patients | | Effect | | Quality | Importance |
|---|----------------------------------|---------------------------|--------------------------|-------------------------|----------------------|----------------------|-----------------|--|------------------------|---|------------------|------------|
| No. of studies | Design | Risk of bias | Inconsistency | Indirectness | Imprecision | Other considerations | Ivermectin | Combined therapy of ivermectin, permethrin, salicylic acid | Relative (95% CI) | Absolute | | |
| Cure (assessed with: elimination of lesions) | | | | | | | | | | | | |
| 1 | Observational study ¹ | Very serious ² | No serious inconsistency | No serious indirectness | Serious ³ | None | 6/8 (75%) | 2/2 (100%) | RR 1.66 (0.10 to 25.8) | 660 more per 1000 (from 900 fewer to 1000 more) | ⊕○○○ VERY LOW | |
| | | | | | | | | 0% | | — | | |

1 Retrospective.

2 Small study population.

3 Repeated doses were administered to unresponsive patients. The combination group received 3 doses of ivermectin and only received combined therapy when single doses of ivermectin did not resolve completely.

Table 7.11 Should ivermectin (single dose) versus benzyl benzoate (two applications) be used for scabies?

| Quality assessment | | | | | | | No. of patients | | Effect | | Quality | Importance |
|--|------------------|----------------------|--------------------------|-------------------------|----------------------|----------------------|------------------------|----------------------------------|------------------------|--|-------------|------------|
| No. of studies | Design | Risk of bias | Inconsistency | Indirectness | Imprecision | Other considerations | Ivermectin single dose | Benzyl benzoate two applications | Relative (95% CI) | Absolute | | |
| Cure (follow-up median 28 days; assessed with: not clearly defined) | | | | | | | | | | | | |
| 1 | Randomized trial | Serious ¹ | No serious inconsistency | No serious indirectness | Serious ² | None | 16/65 (24.6%) | 37/68 (54.4%) | OR 0.23 (0.10 to 0.50) | 329 fewer per 1000 (from 170 fewer to 437 fewer) | ⊕⊕○○ LOW | CRITICAL |
| | | | | | | | | 0% | | — | | |

1 Not blinded.

2 No HIV test was performed before or after, or immunological assay.

8. Molluscum contagiosum

Table 8.1 Should cryotherapy versus cryotherapy and podophyllotoxin be used in HIV-positive patients with molluscum contagiosum?

| No. of studies | Design | Quality assessment | | | | | No. of patients | | Effect | | Quality | Importance |
|---|---------------------|----------------------|--------------------------|-------------------------|----------------------|----------------------|-----------------|---------------------------------|-------------------|--------------------------------|------------------|------------|
| | | Risk of bias | Inconsistency | Indirectness | Imprecision | Other considerations | Cryotherapy | Cryotherapy and podophyllotoxin | Relative (95% CI) | Absolute | | |
| Lesion elimination (follow-up 1 month; measured with: does not mention method of assessment; better indicated by lower values) | | | | | | | | | | | | |
| 1 | Observational study | Serious ¹ | No serious inconsistency | No serious indirectness | Serious ² | None | 21 | 19 | — | P 0.136 higher (0 to 0 higher) | ⊕○○○ VERY LOW | IMPORTANT |

1 Does not mention randomization.

2 Does not mention status of HIV infection (e.g. CD4 cell count, viral load).

Table 8.2 Should tricholoacetic acid versus cryotherapy be used in HIV-positive patients with molluscum contagiosum?

| No. of studies | Design | Quality assessment | | | | | No. of patients | | Effect | | Quality | Importance |
|---|-------------------------------|---------------------------|--------------------------|-------------------------|----------------------|----------------------|---------------------|-------------|-------------------|---|------------------|------------|
| | | Risk of bias | Inconsistency | Indirectness | Imprecision | Other considerations | Tricholoacetic acid | Cryotherapy | Relative (95% CI) | Absolute | | |
| Reduction in number of lesions (follow-up 8 weeks; measured with: method of evaluation of reduction not specified; better indicated by lower values) | | | | | | | | | | | | |
| 1 | Randomized trial ¹ | Very serious ² | No serious inconsistency | No serious indirectness | Serious ² | None | 20 | 20 | — | Median (%) 90 higher (0 to 0 higher) ³ | ⊕○○○ VERY LOW | IMPORTANT |

1 No randomization, each patient received both treatments, one on each side of the face.

2 Not clear if patients were on ART or not.

3 P≤.05 reported but CI was not reported.

9. Oropharyngeal candidiasis

Table 9.1 Should fluconazole versus ketoconazole be used for the management of oropharyngeal candidiasis associated with HIV infection in adults and children?

| No. of studies | Design | Quality assessment | | | | | No. of patients | | Effect | | Quality | Importance |
|---|-------------------|----------------------|--------------------------|-------------------------|------------------------|----------------------|-----------------|---------------|------------------------|--|------------------|------------|
| | | Risk of bias | Inconsistency | Indirectness | Imprecision | Other considerations | Fluconazole | Ketoconazole | Relative (95% CI) | Absolute | | |
| Clinical cure (follow-up mean 1 month) | | | | | | | | | | | | |
| 2 | Randomized trials | Serious ¹ | No serious inconsistency | No serious indirectness | Serious ² | None | 38/42 (90.5%) | 29/41 (70.7%) | RR 1.27 (0.97 to 1.66) | 191 more per 1000 (from 21 fewer to 467 more) | ⊕⊕⊕⊕ LOW | CRITICAL |
| Clinical cure – adults (follow-up mean 1 month) | | | | | | | | | | | | |
| 1 | Randomized trial | Serious ¹ | No serious inconsistency | No serious indirectness | Serious ² | None | 17/18 (94.4%) | 12/19 (63.2%) | RR 1.5 (1.04 to 2.15) | 316 more per 1000 (from 25 more to 726 more) | ⊕⊕⊕⊕ LOW | IMPORTANT |
| Clinical cure – children (follow-up mean 4 weeks) | | | | | | | | | | | | |
| 1 | Randomized trial | Serious | No serious inconsistency | No serious indirectness | No serious imprecision | None | 21/24 (87.5%) | 17/22 (77.3%) | RR 1.13 (0.86 to 1.49) | 100 more per 1000 (from 108 fewer to 379 more) | ⊕⊕⊕⊕ MODERATE | CRITICAL |
| Mycological cure (follow-up mean 1 month) | | | | | | | | | | | | |
| 1 | Randomized trial | Serious ¹ | No serious inconsistency | No serious indirectness | Serious ² | None | 13/18 (72.2%) | 9/19 (47.4%) | RR 1.52 (0.88 to 2.65) | 246 more per 1000 (from 57 fewer to 782 more) | ⊕⊕⊕⊕ LOW | CRITICAL |
| Clinical + mycological cure (follow-up mean 1 month) | | | | | | | | | | | | |
| 1 | Randomized trial | Serious ¹ | No serious inconsistency | No serious indirectness | Serious ² | None | 17/24 (70.8%) | 12/22 (54.5%) | RR 1.3 (0.82 to 2.06) | 164 more per 1000 (from 98 fewer to 578 more) | ⊕⊕⊕⊕ LOW | IMPORTANT |

1 Method of randomization not described. Baseline imbalance.

2 Wide CI (includes null and appreciable benefits).

Table 9.2 Should fluconazole versus itraconazole be used for the management of HIV-infected adults and children with oral candidiasis?

| No. of studies | Design | Quality assessment | | | | | No. of patients | | Effect | | Quality | Importance |
|--|-------------------|---------------------------|--------------------------|-------------------------|---------------------------|----------------------|-----------------|-----------------|------------------------|---|------------------|------------|
| | | Risk of bias | Inconsistency | Indirectness | Imprecision | Other considerations | Fluconazole | Itraconazole | Relative (95% CI) | Absolute | | |
| Clinical cure: with De Wit et al., 1998 (follow-up mean 1 month) | | | | | | | | | | | | |
| 5 | Randomized trials | Very serious ¹ | Serious ² | No serious indirectness | Serious ³ | None | 133/168 (79.2%) | 218/306 (71.2%) | RR 1.12 (0.92 to 1.36) | 85 more per 1000 (from 57 fewer to 256 more) | ⊕○○○ VERY LOW | CRITICAL |
| | | | | | | | | 68.4% | | 82 more per 1000 (from 55 fewer to 246 more) | | |
| Clinical cure: without De Wit et al., 1998 (follow-up mean 1 month) | | | | | | | | | | | | |
| 4 | Randomized trials | Very serious ¹ | No serious inconsistency | No serious indirectness | Serious ⁴ | None | 118/148 (79.7%) | 214/286 (74.8%) | RR 1.05 (0.94 to 1.16) | 37 more per 1000 (from 45 fewer to 120 more) | ⊕○○○ VERY LOW | CRITICAL |
| | | | | | | | | 74.8% | | 37 more per 1000 (from 45 fewer to 120 more) | | |
| Mycological cure (follow-up mean 1 month) | | | | | | | | | | | | |
| 5 | Randomized trials | Serious ³ | No serious inconsistency | No serious indirectness | Very serious ⁵ | None | 85/168 (50.6%) | 145/306 (47.4%) | RR 1.14 (0.9 to 1.46) | 66 more per 1000 (from 47 fewer to 218 more) | ⊕○○○ VERY LOW | CRITICAL |
| | | | | | | | | 43% | | 60 more per 1000 (from 43 fewer to 198 more) | | |
| Relapse (follow-up mean 1 month) | | | | | | | | | | | | |
| 5 | Randomized trials | Serious ⁵ | Serious ⁵ | No serious indirectness | No serious imprecision | None | 50/126 (39.7%) | 90/207 (43.5%) | RR 0.92 (0.71 to 1.21) | 35 fewer per 1000 (from 126 fewer to 91 more) | ⊕⊕○○ LOW | CRITICAL |
| | | | | | | | | 44.2% | | 35 fewer per 1000 (from 128 fewer to 93 more) | | |

1 Lack of blinding of outcome assessors. Method of allocation concealment not reported in De Wit and colleagues (1998). No blinding in De Wit and colleagues (1998).

2 Heterogeneity I² = 68%; CI includes null.

3 Total number of events is less than 300. 95% CI is wide and includes null.

4 95% CI includes null.

5 No explanation was provided.

Table 9.3 Should fluconazole versus clotrimazole be used for the management of oropharyngeal candidiasis associated with HIV infection in adults and children?

| No. of studies | Design | Quality assessment | | | | | No. of patients | | Effect | | Quality | Importance |
|--|-------------------|----------------------|--------------------------|-------------------------|----------------------|----------------------|-----------------|-----------------|------------------------|--|----------|------------|
| | | Risk of bias | Inconsistency | Indirectness | Imprecision | Other considerations | Fluconazole | Clotrimazole | Relative (95% CI) | Absolute | | |
| Clinical cure (follow-up mean 14 days) | | | | | | | | | | | | |
| 2 | Randomized trials | Serious ¹ | No serious inconsistency | No serious indirectness | Serious ² | None | 151/189 (79.9%) | 124/169 (73.4%) | RR 1.13 (0.92 to 1.37) | 95 more per 1000 (from 59 fewer to 271 more) | ⊕⊕○○ LOW | CRITICAL |
| | | | | | | | | 73.1% | | 95 more per 1000 (from 58 fewer to 270 more) | | |
| Mycological cure (follow-up mean 14 days) | | | | | | | | | | | | |
| 2 | Randomized trials | Serious ¹ | No serious inconsistency | No serious indirectness | Serious ² | None | 100/189 (52.9%) | 61/169 (36.1%) | RR 1.47 (1.16 to 1.87) | 170 more per 1000 (from 58 more to 314 more) | ⊕⊕○○ LOW | CRITICAL |
| | | | | | | | | 40.5% | | 190 more per 1000 (from 65 more to 352 more) | | |
| Relapse (follow-up mean 14 days) | | | | | | | | | | | | |
| 2 | Randomized trials | Serious ¹ | No serious inconsistency | No serious indirectness | Serious ³ | None | 24/143 (16.8%) | 50/107 (46.7%) | RR 0.36 (0.24 to 0.54) | 299 fewer per 1000 (from 215 fewer to 355 fewer) | ⊕⊕○○ LOW | CRITICAL |
| | | | | | | | | 34.1% | | 218 fewer per 1000 (from 157 fewer to 259 fewer) | | |

- 1 Lack of blinding.
- 2 Total number of events less than 300.
- 3 No explanation was provided.

Table 9.4 Should fluconazole versus fluconazole stat be used for the management of oropharyngeal candidiasis associated with HIV infection in adults and children?

| No. of studies | Design | Quality assessment | | | | | No. of patients | | Effect | | Quality | Importance |
|--|------------------|---------------------------|--------------------------|-------------------------|------------------------|----------------------|-----------------|------------------|------------------------|---|----------|------------|
| | | Risk of bias | Inconsistency | Indirectness | Imprecision | Other considerations | Fluconazole | Fluconazole stat | Relative (95% CI) | Absolute | | |
| Clinical cure – fluconazole 50 mg daily for 7 days vs fluconazole 150 mg stat (follow-up mean 2 weeks) | | | | | | | | | | | | |
| 1 | Randomized trial | Very serious ¹ | No serious inconsistency | No serious indirectness | No serious imprecision | None | 26/28 (92.9%) | 21/28 (75%) | RR 1.24 (0.98 to 1.57) | 180 more per 1000 (from 15 fewer to 428 more) | ⊕⊕○○ LOW | CRITICAL |
| | | | | | | | | 75% | | 180 more per 1000 (from 15 fewer to 428 more) | | |
| Clinical cure – fluconazole 150 mg daily for 14 days vs fluconazole 750 mg stat (follow-up mean 42 days) | | | | | | | | | | | | |
| 1 | Randomized trial | Very serious ¹ | No serious inconsistency | No serious indirectness | No serious imprecision | None | 105/110 (95.5%) | 105/110 (95.5%) | RR 1 (0.94 to 1.06) | 0 fewer per 1000 (from 57 fewer to 57 more) | ⊕⊕○○ LOW | CRITICAL |
| | | | | | | | | 95.5% | | 0 fewer per 1000 (from 57 fewer to 57 more) | | |
| Mycological cure – fluconazole 50 mg daily for 7 days vs fluconazole 150 mg stat (follow-up mean 2 weeks) | | | | | | | | | | | | |
| 1 | Randomized trial | Very serious ¹ | No serious inconsistency | No serious indirectness | No serious imprecision | None | 13/28 (46.4%) | 6/28 (21.4%) | RR 2.17 (0.96 to 4.89) | 251 more per 1000 (from 9 fewer to 834 more) | ⊕⊕○○ LOW | CRITICAL |
| | | | | | | | | 21.4% | | 250 more per 1000 (from 9 fewer to 832 more) | | |
| Mycological cure – fluconazole 150 mg daily for 14 days vs fluconazole 750 mg stat (follow-up mean 42 days) | | | | | | | | | | | | |
| 1 | Randomized trial | Very serious ¹ | No serious inconsistency | No serious indirectness | No serious imprecision | None | 83/110 (75.5%) | 93/110 (84.5%) | RR 0.89 (0.78 to 1.02) | 93 fewer per 1000 (from 186 fewer to 17 more) | ⊕⊕○○ LOW | CRITICAL |
| | | | | | | | | 84.6% | | 93 fewer per 1000 (from 186 fewer to 17 more) | | |

1 Allocation concealment not reported; no blinding; random sequence generation not specified.

Table 9.5 Should fluconazole versus nystatin be used for the management of oropharyngeal candidiasis associated with HIV infection in adults and children?

| No. of studies | Design | Risk of bias | Quality assessment | | | | Other considerations | No. of patients | | Effect | | Quality | Importance |
|--|------------------|---------------------------|--------------------------|-------------------------|------------------------|-------------|----------------------|-----------------|--------------------------|--|----------|----------|------------|
| | | | Inconsistency | Indirectness | Imprecision | Fluconazole | | Nystatin | Relative (95% CI) | Absolute | | | |
| Clinical cure (follow-up mean 4 days) | | | | | | | | | | | | | |
| 1 | Randomized trial | Very serious ¹ | No serious inconsistency | No serious indirectness | No serious imprecision | None | 60/83 (72.3%) | 36/84 (42.9%) | RR 1.69 (1.27 to 2.23) | 296 more per 1000 (from 116 more to 527 more) | ⊕⊕○○ LOW | CRITICAL | |
| | | | | | | | | 42.9% | | 296 more per 1000 (from 116 more to 528 more) | | | |
| Mycological cure (follow-up mean 48 days) | | | | | | | | | | | | | |
| 1 | Randomized trial | Very serious ¹ | No serious inconsistency | No serious indirectness | No serious imprecision | None | 41/83 (49.4%) | 4/84 (4.8%) | RR 10.37 (3.89 to 27.66) | 446 more per 1000 (from 138 more to 1000 more) | ⊕⊕○○ LOW | CRITICAL | |
| | | | | | | | | 4.8% | | 450 more per 1000 (from 139 more to 1000 more) | | | |

1 Random sequence generation not reported; allocation concealment not reported; single blind – clinical evaluator at trial sites.

Table 9.6 Should D0870 25 mg versus D0870 10 mg be used for the management of oropharyngeal candidiasis associated with HIV infection in adults and children?

| No. of studies | Design | Risk of bias | Quality assessment | | | | Other considerations | No. of patients | | Effect | | Quality | Importance |
|---|------------------|-------------------------|--------------------------|-------------------------|----------------------------------|--------------|----------------------|-----------------|------------------------|--|---------------|-----------|------------|
| | | | Inconsistency | Indirectness | Imprecision | D0870: 25 mg | | D0870: 10 mg | Relative (95% CI) | Absolute | | | |
| Clinical cure (follow-up mean 2 weeks) | | | | | | | | | | | | | |
| 1 | Randomized trial | No serious risk of bias | No serious inconsistency | No serious indirectness | Serious imprecision ¹ | None | 2/13 (15.4%) | 3/14 (21.4%) | RR 0.97 (0.59 to 1.58) | 6 fewer per 1000 (from 88 fewer to 124 more) | ⊕⊕⊕○ MODERATE | CRITICAL | |
| | | | | | | | | 71.4% | | 21 fewer per 1000 (from 293 fewer to 414 more) | | | |
| Relapse (follow-up mean 2 weeks) | | | | | | | | | | | | | |
| 1 | Randomized trial | No serious risk of bias | No serious inconsistency | No serious indirectness | Serious imprecision ² | None | 2/13 (15.4%) | 3/14 (21.4%) | RR 0.72 (0.14 to 3.64) | 60 fewer per 1000 (from 184 fewer to 566 more) | ⊕⊕⊕○ MODERATE | IMPORTANT | |
| | | | | | | | | 0% | | — | | | |

1 Small sample size.

2 95% CI includes null. Single study.

Table 9.7 Should itraconazole versus clotrimazole be used for the management of oropharyngeal candidiasis associated with HIV infection in adults and children?

| No. of studies | Design | Quality assessment | | | | | No. of patients | | Effect | | Quality | Importance |
|--|-------------------|----------------------|----------------------|-------------------------|----------------------|----------------------|-----------------|---------------|-----------------------|---|------------------|------------|
| | | Risk of bias | Inconsistency | Indirectness | Imprecision | Other considerations | Itraconazole | Clotrimazole | Relative (95% CI) | Absolute | | |
| Clinical and mycological cure (follow-up 43 days) | | | | | | | | | | | | |
| 2 | Randomized trials | Serious ¹ | Serious ² | No serious indirectness | Serious ² | None | 43/75 (57.3%) | 28/77 (36.4%) | RR 1.34 (0.56 to 3.2) | 124 more per 1000 (from 160 fewer to 800 more) | ⊕○○○ VERY LOW | CRITICAL |
| | | | | | | | | 50.4% | | 171 more per 1000 (from 222 fewer to 1000 more) | | |
| Mycological cure (follow-up 43 days) | | | | | | | | | | | | |
| 1 | Randomized trial | Serious | Serious | No serious indirectness | Serious | None | 39/61 (63.9%) | 18/62 (29%) | RR 2.2 (1.43 to 3.39) | 348 more per 1000 (from 125 more to 694 more) | ⊕○○○ VERY LOW | CRITICAL |
| | | | | | | | | 29% | | 348 more per 1000 (from 125 more to 693 more) | | |

1 Linpiyawan and colleagues (2000): allocation concealment not reported, single blinded, sequence generation not reported.

2 95% CI includes 1. I2 = 85%, p < 0.05.

Table 9.8 Should melaleuca alcohol-free oral solution versus alcohol-based oral solution be used for the management of oropharyngeal candidiasis associated with HIV infection in adults and children?

| No. of studies | Design | Risk of bias | Quality assessment | | | | Other considerations | No. of patients | | Effect | | Quality | Importance |
|--|------------------|----------------------|--------------------------|-------------------------|----------------------|---------------------------------------|----------------------|-----------------|--------------------------|--|-------------|----------|------------|
| | | | Inconsistency | Indirectness | Imprecision | Melaleuca oral solution: alcohol-free | | Alcohol-based | Relative (95% CI) | Absolute | | | |
| Clinical cure (follow-up mean 4 weeks) | | | | | | | | | | | | | |
| 1 | Randomized trial | Serious | No serious inconsistency | No serious indirectness | Serious ¹ | None | 3/14 (21.4%) | 0/13 (0%) | RR 6.53 (0.37 to 115.49) | — | ⊕⊕⊕⊕ LOW | CRITICAL | |
| | | | | | | | | 0% | | — | | | |
| Mycological cure (follow-up mean 4 weeks) | | | | | | | | | | | | | |
| 1 | Randomized trial | Serious ² | No serious inconsistency | No serious indirectness | Serious ³ | None | 9/14 (64.3%) | 5/13 (38.5%) | RR 1.67 (0.76 to 3.69) | 258 more per 1000 (from 92 fewer to 1000 more) | ⊕⊕⊕⊕ LOW | CRITICAL | |
| | | | | | | | | 38.5% | | 258 more per 1000 (from 92 fewer to 1000 more) | | | |

- 1 Small sample size, event rate low and 95% CI includes null.
- 2 Random sequence generation not reported, no blinding. Allocation concealment not reported.
- 3 No explanation was provided.

Table 9.9 Should amphotericin fat emulsion versus glucose solution be used for the management of oropharyngeal candidiasis associated with HIV infection in adults and children?

| No. of studies | Design | Risk of bias | Quality assessment | | | | Other considerations | No. of patients | | Effect | | Quality | Importance |
|---|------------------|----------------------|--------------------------|-------------------------|----------------------|---------------------------|----------------------|------------------|---------------------|--|-------------|----------|------------|
| | | | Inconsistency | Indirectness | Imprecision | Amphotericin fat emulsion | | Glucose solution | Relative (95% CI) | Absolute | | | |
| Clinical score reduction (follow-up mean 4 days; better indicated by lower values) | | | | | | | | | | | | | |
| 1 | Randomized trial | Serious ¹ | No serious inconsistency | No serious indirectness | Serious ² | None | 11 | 11 | — | Mean difference (MD) 1.1 lower (5.72 lower to 3.52 higher) | ⊕⊕⊕⊕ LOW | CRITICAL | |
| Mycological cure (follow-up mean 4 days) | | | | | | | | | | | | | |
| 1 | Randomized trial | Serious ¹ | No serious inconsistency | No serious indirectness | Serious | None | 2/11 (18.2%) | 2/11 (18.2%) | RR 1 (0.17 to 5.89) | 0 fewer per 1000 (from 151 fewer to 889 more) | ⊕⊕⊕⊕ LOW | CRITICAL | |
| | | | | | | | | 18.2% | | 0 fewer per 1000 (from 151 fewer to 890 more) | | | |

- 1 No blinding was used. Unclear sequence generation and allocation concealment.
- 2 Small study (95% CI wide including null). Small effect size.

Table 9.10 Should ketoconazole versus miconazole be used for the management of oropharyngeal candidiasis associated with HIV infection in adults and children?

| No. of studies | Design | Risk of bias | Quality assessment | | | | Other considerations | No. of patients | | Effect | | Quality | Importance |
|---|------------------|----------------------|--------------------------|-------------------------|----------------------|--------------|----------------------|-----------------|-----------------------|---|-------------|-----------|------------|
| | | | Inconsistency | Indirectness | Imprecision | Ketoconazole | | Miconazole | Relative (95% CI) | Absolute | | | |
| Clinical cure (follow-up mean 14 days) | | | | | | | | | | | | | |
| 1 | Randomized trial | Serious ¹ | No serious inconsistency | No serious indirectness | Serious ² | None | 159/179 (88.8%) | 155/178 (87.1%) | RR 1.02 (0.94 to 1.1) | 17 more per 1000 (from 52 fewer to 87 more) | ⊕⊕○○ LOW | CRITICAL | |
| | | | | | | | | 0% | | — | | | |
| Relapse (follow-up mean 14 days) | | | | | | | | | | | | | |
| 1 | Randomized trial | Serious ¹ | No serious inconsistency | No serious indirectness | Serious ² | None | 34/148 (23%) | 45/146 (30.8%) | RR 0.75 (0.51 to 9) | 77 fewer per 1000 (from 151 fewer to 1000 more) | ⊕⊕○○ LOW | IMPORTANT | |
| | | | | | | | | 0% | | — | | | |

1 Allocation concealment and blinding unclear. Attrition unclear.
2 Small effect size, 95% CI includes null.

Table 9.11 Should gentian violet versus ketoconazole be used for the management of oropharyngeal candidiasis associated with HIV infection in adults and children?

| No. of studies | Design | Risk of bias | Quality assessment | | | | Other considerations | No. of patients | | Effect | | Quality | Importance |
|--|------------------|----------------------|--------------------------|-------------------------|----------------------|----------------|----------------------|-----------------|------------------------|---|-------------|----------|------------|
| | | | Inconsistency | Indirectness | Imprecision | Gentian violet | | Ketoconazole | Relative (95% CI) | Absolute | | | |
| Clinical cure (follow-up mean 14 days) | | | | | | | | | | | | | |
| 1 | Randomized trial | Serious ¹ | No serious inconsistency | No serious indirectness | Serious ² | None | 11/49 (22.4%) | 10/45 (22.2%) | RR 1.01 (0.47 to 2.15) | 2 more per 1000 (from 118 fewer to 256 more) | ⊕⊕○○ LOW | CRITICAL | |
| | | | | | | | | 22.2% | | 2 more per 1000 (from 118 fewer to 255 more) | | | |
| Mycological cure (follow-up mean 14 days) | | | | | | | | | | | | | |
| 1 | Randomized trial | Serious | No serious inconsistency | No serious indirectness | Serious | None | 16/49 (32.7%) | 13/45 (28.9%) | RR 1.13 (0.61 to 2.08) | 38 more per 1000 (from 113 fewer to 312 more) | ⊕⊕○○ LOW | CRITICAL | |
| | | | | | | | | 28.9% | | 38 more per 1000 (from 113 fewer to 312 more) | | | |

1 No blinding due to character of drug – dye. Small study. 95% CI includes null.
2 Small study, less than 300 events. 95% CI includes null.

Table 9.12 Should gentian violet versus nystatin be used for the management of oropharyngeal candidiasis associated with HIV infection in adults and children?

| No. of studies | Design | Quality assessment | | | | | No. of patients | | Effect | | Quality | Importance |
|--|------------------|----------------------|--------------------------|-------------------------|----------------------|----------------------|------------------|----------------|----------------------------|---|-------------|------------|
| | | Risk of bias | Inconsistency | Indirectness | Imprecision | Other considerations | Gentian violet | Nystatin | Relative (95% CI) | Absolute | | |
| Clinical cure (follow-up mean 14 days) | | | | | | | | | | | | |
| 1 | Randomized trial | Serious ¹ | No serious inconsistency | No serious indirectness | Serious ² | None | 11/49 (22.4%) | 2/47 (4.3%) | RR 5.28 (1.23 to 22.55) | 182 more per 1000 (from 10 more to 917 more) | ⊕⊕○○ LOW | CRITICAL |
| | | | | | | | | 4.3% | | 184 more per 1000 (from 10 more to 927 more) | | |
| Mycological cure (follow-up mean 14 days) | | | | | | | | | | | | |
| 1 | Randomized trial | Serious | No serious inconsistency | No serious indirectness | Serious ² | None | 16/49 (32.7%) | 3/47 (6.4%) | RR 5.12 (1.59 to 16.42) | 263 more per 1000 (from 38 more to 984 more) | ⊕⊕○○ LOW | CRITICAL |
| | | | | | | | | 6.4% | | 264 more per 1000 (from 38 more to 987 more) | | |

1 No blinding was used.

2 Small study, less than 300 events.

Table 9.13 Should ketoconazole versus nystatin be used for the management of oropharyngeal candidiasis associated with HIV infection in adults and children?

| No. of studies | Design | Quality assessment | | | | | No. of patients | | Effect | | Quality | Importance |
|--|------------------|------------------------|--------------------------|-------------------------|----------------------|----------------------|------------------|----------------|----------------------------|---|-------------|------------|
| | | Risk of bias | Inconsistency | Indirectness | Imprecision | Other considerations | Ketoconazole | Nystatin | Relative (95% CI) | Absolute | | |
| Clinical cure (follow-up mean 14 days) | | | | | | | | | | | | |
| 1 | Randomized trial | Serious ¹ | No serious inconsistency | No serious indirectness | Serious ² | None | 10/45 (22.2%) | 2/47 (4.3%) | RR 5.22 (1.21 to 22.53) | 180 more per 1000 (from 9 more to 916 more) | ⊕⊕○○ LOW | CRITICAL |
| | | | | | | | | 4.3% | | 181 more per 1000 (from 9 more to 926 more) | | |
| Mycological cure (follow-up mean 14 days) | | | | | | | | | | | | |
| 1 | Randomized trial | Serious ^{1,2} | No serious inconsistency | No serious indirectness | Serious | None | 13/45 (28.9%) | 3/47 (6.4%) | RR 4.53 (1.38 to 14.83) | 225 more per 1000 (from 24 more to 883 more) | ⊕⊕○○ LOW | CRITICAL |
| | | | | | | | | 6.4% | | 226 more per 1000 (from 24 more to 885 more) | | |

1 No blinding was used, small study.

2 Small study, less than 300 events.

Table 9.14 Should caspofungin versus amphotericin B be used for the management of oropharyngeal candidiasis associated with HIV infection in adults and children?

| No. of studies | Design | Quality assessment | | | | | No. of patients | | Effect | | Quality | Importance |
|--|------------------|-------------------------|--------------------------|-------------------------|----------------------|----------------------|-----------------|-----------------|---------------------------|--|------------------|------------|
| | | Risk of bias | Inconsistency | Indirectness | Imprecision | Other considerations | Caspofungin | Amphotericin B | Relative (95% CI) | Absolute | | |
| Clinical cure (follow-up 7–14 days) | | | | | | | | | | | | |
| 1 | Randomized trial | No serious risk of bias | No serious inconsistency | No serious indirectness | Serious ¹ | None | 36/40 (90%) | 8/12 (66.7%) | RR 1.35 (0.89 to 2.04) | 233 more per 1000 (from 73 fewer to 693 more) | ⊕⊕⊕○ MODERATE | CRITICAL |
| | | | | | | | | 66.7% | | 233 more per 1000 (from 73 fewer to 694 more) | | |

1 Small study with only 52 participants. Small estimate of effect and 95% CI includes null.

Table 9.15 Should posaconazole versus fluconazole be used for the management of oropharyngeal candidiasis associated with HIV infection in adults and children?

| No. of studies | Design | Quality assessment | | | | | No. of patients | | Effect | | Quality | Importance |
|---|------------------|----------------------|--------------------------|-------------------------|----------------------|----------------------|-----------------|-----------------|------------------------|---|-------------|------------|
| | | Risk of bias | Inconsistency | Indirectness | Imprecision | Other considerations | Posaconazole | Fluconazole | Relative (95% CI) | Absolute | | |
| Clinical cure (follow-up mean 14 days) | | | | | | | | | | | | |
| 1 | Randomized trial | Serious ¹ | No serious inconsistency | No serious indirectness | Serious ² | None | 130/135 (96.3%) | 139/143 (97.2%) | RR 1.32 (0.36 to 4.83) | 311 more per 1000 (from 622 fewer to 1000 more) | ⊕⊕○○ LOW | CRITICAL |
| | | | | | | | | 97.2% | | 311 more per 1000 (from 622 fewer to 1000 more) | | |
| Mycological cure (follow-up mean 14 days) | | | | | | | | | | | | |
| 1 | Randomized trial | Serious | No serious inconsistency | No serious indirectness | Serious ² | None | 24/91 (26.4%) | 41/101 (40.6%) | RR 1.24 (1.01 to 1.52) | 97 more per 1000 (from 4 more to 211 more) | ⊕⊕○○ LOW | IMPORTANT |
| | | | | | | | | 40.6% | | 97 more per 1000 (from 4 more to 211 more) | | |
| Mycological eradication (follow-up mean 14 days) | | | | | | | | | | | | |
| 1 | Randomized trial | Serious ¹ | No serious inconsistency | No serious indirectness | Serious ³ | None | 22/91 (24.2%) | 36/101 (35.6%) | RR 1.18 (0.98 to 1.42) | 64 more per 1000 (from 7 fewer to 150 more) | ⊕⊕○○ LOW | IMPORTANT |
| | | | | | | | | 35.6% | | 64 more per 1000 (from 7 fewer to 150 more) | | |

- 1 No indication of how randomization was done. Allocation concealment not reported. Patients not blinded.
- 2 Small estimate of effect. 95% CI includes null. Less than 300 events.
- 3 No explanation was provided.

Table 9.16 Should lemon juice versus gentian violet be used for the management of oropharyngeal candidiasis associated with HIV infection in adults and children?

| No. of studies | Design | Quality assessment | | | | | No. of patients | | Effect | | Quality | Importance |
|--|------------------|----------------------|--------------------------|-------------------------|----------------------|----------------------|-----------------|----------------|------------------------|--|----------|------------|
| | | Risk of bias | Inconsistency | Indirectness | Imprecision | Other considerations | Lemon juice | Gentian violet | Relative (95% CI) | Absolute | | |
| Clinical cure (follow-up mean 10 days) | | | | | | | | | | | | |
| 1 | Randomized trial | Serious ¹ | No serious inconsistency | No serious indirectness | Serious ² | None | 16/30 (53.3%) | 9/30 (30%) | RR 1.78 (0.94 to 3.37) | 234 more per 1000 (from 18 fewer to 711 more) | ⊕⊕○○ LOW | CRITICAL |
| | | | | | | | | 30% | | 234 more per 1000 (from 18 fewer to 711 more) | | |
| Clinical failure (follow-up mean 10 days) | | | | | | | | | | | | |
| 1 | Randomized trial | Serious ³ | No serious inconsistency | No serious indirectness | Serious ³ | None | 2/30 (6.7%) | 8/30 (26.7%) | RR 0.25 (0.06 to 1.08) | 200 fewer per 1000 (from 251 fewer to 21 more) | ⊕⊕○○ LOW | CRITICAL |
| | | | | | | | | 26.7% | | 200 fewer per 1000 (from 251 fewer to 21 more) | | |

- 1 No blinding reported, intervention is a dye and difficult to blind.
- 2 Small study with less than 300 events, small estimate of effect.
- 3 Small study with less than 300 events, 95% CI includes null.

Table 9.17 Should lemon grass versus gentian violet be used for the management of oropharyngeal candidiasis associated with HIV infection in adults and children?

| No. of studies | Design | Risk of bias | Quality assessment | | | | Other considerations | No. of patients | | Effect | | Quality | Importance |
|--|------------------|----------------------|--------------------------|-------------------------|----------------------|------|----------------------|-----------------|------------------------|--|-------------|-----------|------------|
| | | | Inconsistency | Indirectness | Imprecision | | | Lemon grass | Gentian violet | Relative (95% CI) | Absolute | | |
| Clinical cure (follow-up mean 10 days) | | | | | | | | | | | | | |
| 1 | Randomized trial | Serious ¹ | No serious inconsistency | No serious indirectness | Serious ¹ | None | 15/30 (50%) | 9/30 (30%) | RR 1.67 (0.87 to 3.2) | 201 more per 1000 (from 39 fewer to 660 more) | ⊕⊕○○ LOW | CRITICAL | |
| | | | | | | | | 30% | | 201 more per 1000 (from 39 fewer to 660 more) | | | |
| Clinical failure (follow-up mean 10 days) | | | | | | | | | | | | | |
| 1 | Randomized trial | Serious | No serious inconsistency | No serious indirectness | Serious | None | 2/30 (6.7%) | 8/30 (26.7%) | RR 0.25 (0.06 to 1.08) | 200 fewer per 1000 (from 251 fewer to 21 more) | ⊕⊕○○ LOW | IMPORTANT | |
| | | | | | | | | 26.7% | | 200 fewer per 1000 (from 251 fewer to 21 more) | | | |

1 Small study with less than 300 events. 95% CI includes null.

Table 9.18 Should lemon juice versus lemon grass be used for the management of oropharyngeal candidiasis associated with HIV infection in adults and children?

| No. of studies | Design | Risk of bias | Quality assessment | | | | Other considerations | No. of patients | | Effect | | Quality | Importance |
|--|------------------|----------------------|--------------------------|-------------------------|----------------------|-------------|----------------------|-----------------|------------------------|---|-------------|----------|------------|
| | | | Inconsistency | Indirectness | Imprecision | Lemon juice | | Lemon grass | Relative (95% CI) | Absolute | | | |
| Clinical cure (follow-up mean 10 days) | | | | | | | | | | | | | |
| 1 | Randomized trial | Serious ¹ | No serious inconsistency | No serious indirectness | Serious ² | None | 16/30 (53.3%) | 15/30 (50%) | RR 1.07 (0.65 to 1.74) | 35 more per 1000 (from 175 fewer to 370 more) | ⊕⊕⊕⊕ LOW | CRITICAL | |
| | | | | | | | | 50% | | 35 more per 1000 (from 175 fewer to 370 more) | | | |
| Clinical failure (follow-up mean 10 days) | | | | | | | | | | | | | |
| 1 | Randomized trial | Serious ¹ | No serious inconsistency | No serious indirectness | Serious | None | 2/30 (6.7%) | 2/30 (6.7%) | RR 1 (0.15 to 6.64) | 0 fewer per 1000 (from 57 fewer to 376 more) | ⊕⊕⊕⊕ LOW | CRITICAL | |
| | | | | | | | | 6.7% | | 0 fewer per 1000 (from 57 fewer to 378 more) | | | |

1 No blinding reported.

2 Small study, few events. Small estimate of effect and 95% CI includes null.

Table 9.19 Should miconazole versus clotrimazole be used for the management of oropharyngeal candidiasis associated with HIV infection in adults and children?

| No. of studies | Design | Quality assessment | | | | | No. of patients | | Effect | | Quality | Importance |
|--|------------------|-------------------------|--------------------------|-------------------------|----------------------|----------------------|-----------------|-----------------|------------------------|---|------------------|------------|
| | | Risk of bias | Inconsistency | Indirectness | Imprecision | Other considerations | Miconazole | Clotrimazole | Relative (95% CI) | Absolute | | |
| Clinical cure (follow-up mean 14 days) | | | | | | | | | | | | |
| 1 | Randomized trial | No serious risk of bias | No serious inconsistency | No serious indirectness | Serious ¹ | None | 176/290 (60.7%) | 187/287 (65.2%) | RR 0.93 (0.82 to 1.06) | 46 fewer per 1000 (from 117 fewer to 39 more) | ⊕⊕⊕○ MODERATE | CRITICAL |
| | | | | | | | | 65.2% | | 46 fewer per 1000 (from 117 fewer to 39 more) | | |
| Mycological cure (follow-up mean 35 days) | | | | | | | | | | | | |
| 1 | Randomized trial | No serious risk of bias | No serious inconsistency | No serious indirectness | Serious ¹ | None | 79/290 (27.2%) | 71/287 (24.7%) | RR 1.1 (0.84 to 1.45) | 25 more per 1000 (from 40 fewer to 111 more) | ⊕⊕⊕○ MODERATE | IMPORTANT |
| | | | | | | | | 24.7% | | 25 more per 1000 (from 40 fewer to 111 more) | | |
| Relapse (follow-up mean 35 days) | | | | | | | | | | | | |
| 1 | Randomized trial | No serious risk of bias | No serious inconsistency | No serious indirectness | Serious ¹ | None | 48/172 (27.9%) | 52/185 (28.1%) | RR 0.99 (0.71 to 1.38) | 3 fewer per 1000 (from 82 fewer to 107 more) | ⊕⊕⊕○ MODERATE | IMPORTANT |
| | | | | | | | | 28.1% | | 3 fewer per 1000 (from 81 fewer to 107 more) | | |

¹ Small estimate of effect with 95% CI including null.

10. Stevens-Johnson syndrome and toxic epidermal necrolysis

Studies not appropriate for GRADE.

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¹ This list only includes references cited in footnotes. The studies included in the GRADE tables are listed in the systematic reviews.

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