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

WEB APPENDIX 1: GRADE TABLES

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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?

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	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)	⊕OOO 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)	⊕OOO 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)	⊕OOO 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)	⊕OOO 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)	⊕OOO 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	⊕OOO 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?

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	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)	⊕OOO 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)	⊕OOO 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)	⊕OOO 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)	⊕OOO 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)	⊕OOO 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-naive Kaposi sarcoma?

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	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)	⊕⊕OO 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)	—	⊕⊕OO 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)	⊕⊕OO 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)	⊕⊕OO 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)	⊕⊕OO 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	⊕⊕OO 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	⊕⊕OO 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 detailled 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)?

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	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)	—	⨁OOO 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)?

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	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)	⨁⨁OO 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)	—	⨁OOO 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)?

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	HAART plus liposomal anthracyclines	HAART alone	Relative (95% CI)	Absolute		
Mortality[1] (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]	⨁OOO VERY LOW	CRITICAL
Mortality[1] (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]	⨁OOO 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)	⨁OOO 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?

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	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?

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	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)	⨁⨁OO 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)	⨁⨁⨁O 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)	⨁⨁⨁O 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?

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	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)	—	⨁⨁OO 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?

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	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)	⨁OOO 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)	⨁OOO 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?

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	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	—	—	⊕⊕⊕O 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?

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	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%)	—	—	⊕OOO 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%)	—	—	⊕OOO 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?

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	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%)	—	—	⨁⨁OO 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%)	—	—	⨁OOO VERY LOW[1]	MODERATE

1 No explanation was provided.

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

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	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)	⨁OOO 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)	⨁OOO 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?

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	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%)	—	—	⨁OOO 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?

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	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)	⨁OOO 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?

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	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]	⊕OOO 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?

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	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]	⊕OOO 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 dapsone versus antihistamines and topical clobetasol be used in HIV-positive patients with PPE?

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	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]	⨁OOO 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]	⨁OOO 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?

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	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]	⨁OOO 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]	⨁OOO 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?

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	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%)	—	—	—	⊕OOO 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*?

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	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	⊕OOO 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)	⊕⊕OO 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)	⊕OOO 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	⊕⊕OO 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)	⊕⊕OO 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*?

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	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*?

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	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	⊕OOO 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	⊕OOO 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)	⊕OOO 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)	—	⊕OOO 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)	⊕OOO 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*?

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	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)	⊕⊕OO 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	⊕⊕OO 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)	⊕OOO 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)	⊕OOO 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*?

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	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	⊕OOO 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	⊕OOO 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)	⊕OOO 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 Spiekernann & 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?

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												
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)	⨁⨁OO 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)	⨁⨁OO 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)	⨁⨁OO 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)	⨁⨁OO 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)	⨁⨁OO 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)	⨁⨁OO 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?

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	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	⨁⨁OO 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)	⨁⨁OO 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?

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	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)	⨁⨁OO 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	⨁⨁OO 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?

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	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)	⨁⨁OO 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?

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Oral ivermectin with antihista-minics	Permethrin with anti-histaminics	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)	⨁OOO 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?

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	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)	⨁OOO 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]	⨁OOO 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]	⨁OOO 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)	⊕OOO 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]	⊕OOO 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?

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	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)	⨁OOO 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?

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	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)	⨁OOO 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)	⨁OOO 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)	⨁⨁OO LOW	CRITICAL
								0%		—		

1 Not blinded.
2 No HIV test was performed before or after, or immunological essay.

8. Molluscum contagiosum

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

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Cryotheraphy	Cryotheraphy and podo-phyllotoxin	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)	⨁OOO 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 contagiosun?

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	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]	⨁OOO 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?

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	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)	⊕⊕OO 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)	⊕⊕OO 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)	⊕⊕⊕O 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)	⊕⊕OO 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)	⊕⊕OO 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?

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	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)	⊕OOO 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)	⊕OOO 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)	⊕OOO 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)	⊕⊕OO 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?

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	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)	⨁⨁OO 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)	⨁⨁OO 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)	⨁⨁OO 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?

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	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 fluconazole150 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)	⨁⨁OO 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)	⨁⨁OO 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)	⨁⨁OO 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)	⨁⨁OO 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?

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	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?

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	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?

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	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)	⨁OOO 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)	⨁OOO 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?

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	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)	—	⊕⊕OO 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)	⊕⊕OO 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?

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	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)	⊕⊕OO 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)	⊕⊕OO 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?

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	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)	⨁⨁OO 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)	⨁⨁OO 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?

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	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)	⨁⨁OO 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)	⨁⨁OO 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?

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	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)	⨁⨁OO 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)	⨁⨁OO 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?

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	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)	⨁⨁OO 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)	⨁⨁OO 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?

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	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)	⨁⨁⨁O 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?

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	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)	⨁⨁OO 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)	⨁⨁OO 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)	⨁⨁OO 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?

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	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)	⨁⨁OO 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)	⨁⨁OO 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?

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	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)	⨁⨁OO 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)	⨁⨁OO 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?

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	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)	⨁⨁OO 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)	⨁⨁OO 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?

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	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)	⨁⨁⨁O 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)	⨁⨁⨁O 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)	⨁⨁⨁O 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

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