Antibiotics for uncomplicated skin abscesses: a BMJ Rapid Recommendation

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Weak Recommendation

In patients with uncomplicated skin abscesses, we suggest trimethoprim/sulfamethoxazole or clindamycin in addition to incision and drainage rather than incision and drainage alone.

The desirable and undesirable consequences are closely balanced, necessitating shared decision making.

Strong Recommendation

In patients with uncomplicated skin abscesses who are initiating antibiotic therapy after incision and drainage, we recommend TMP/SMX or clindamycin over cephalosporins.

This strong recommendation applies to the most common situation where the risk of MRSA is more than 10%.

Weak Recommendation

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1 - Adults and children with uncomplicated skin abscesses

Weak Recommendation

In patients with uncomplicated skin abscesses, we suggest trimethoprim/sulfamethoxazole or clindamycin in addition to incision and drainage rather than incision and drainage alone.

The desirable and undesirable consequences are closely balanced, necessitating shared decision making.

Practical Info

Antibiotic choice
Please see recommendation #2 and #3 below for evidence about the different antibiotic options in patients who choose to use antibiotics. The evidence most directly applies to either TMP/SMX or clindamycin and there are small differences between these two options.

Antibiotic dosing
TMP/SMX is typically given to adults and children older than 12 years old as trimethoprim 160mg and sulfamethoxazole 800mg (one or two pills twice daily). The dosage needs to be adjusted by weight for younger children (but older than one month): 8 mg trimethoprim and 30mg sulphamethoxazole per kilogram per day, divided into two doses. A reasonable dose of clindamycin for adults is 600-1800mg daily, spread equally over three or four doses (e.g. 300mg three times daily). For children older than one month, a reasonable dose is 8-25 mg/kg/day, also in three to four doses.

Local antimicrobial resistance
The benefits of any antibiotic are probably lower in situations where the risk of resistance to that antibiotic is high. Therefore clinicians should consider local resistance patterns when choosing an appropriate therapy.

Probiotics
Probiotics may have a role in preventing antibiotic associated diarrhoea, including *Clostridium difficile* infection, although this is controversial.

Follow-up
If symptoms progress or worsen, the patient should be reassessed for treatment failure or recurrence. Rarely, the infection may progress to a deep tissue, invasive infection, or sepsis. If there are any systemic signs or symptoms of a severe infection, the patient should seek care as soon as possible.

Key Info

Benefits and harms

Small net benefit, or little difference between alternatives

TMP/SMX or clindamycin reduce treatment failure, early recurrence, late recurrence, and need for an additional surgical procedure by 5 to 7%. Counting both treatment failure and reucurrence, TMP/SMX or clindamycin benefit approximately 13% of people. Antibiotics reduce probably hospitalization and risk of infection in a household contact by approximately 2-3%. Antibiotics reduce the number of people with tenderness during treatment by 7%.

Some people will experience gastrointestinal side effects with TMP/SMX or clindamycin, including nausea by ~3-4%; diarrhoea by 2% to 10% (depending on antibiotic, more with clindamycin than TMP/SMX). Antibiotics have a small risk of anaphylaxis.

Quality of evidence

Moderate

The GRADE quality of evidence is moderate-to-high for almost all of the critical outcomes, suggesting that the overall interpretation is unlikely to change much with new studies.

Preference and values

Substantial variability is expected or uncertain

Overall, the panel felt that most patients would consider the benefits of antibiotics to be somewhat important, with moderate variability between patients; most would consider the adverse effects of antibiotics as somewhat important or of little importance,

with moderate variability between patients. Given that there is probably a high degree of variability between people in how much importance they attach to the expected desirable and undesirable consequences of antibiotic therapy compared to no antibiotic therapy, shared decision-making with each patient is crucial.

Resources and other considerations

Important issues, or potential issues not investigated

In many settings, antibiotics are associated with a higher up-front cost to the patient. The overall impact on costs when the impact on treatment failure, recurrence and other outcomes are considered is unclear.

Rationale

Rationale

There is a close balance between the expected benefits from antibiotics (a modest reduction in treatment failure, abscess recurrence, and pain) and the expected harms (gastrointestinal side effects), burdens of treatment, and costs. We expect that most but not all people will find the benefits sufficiently large that they will choose to use antibiotics, however there is probably a great deal of variation between people in how important people will consider the benefits.

Person-centred perspective

This guideline, like all *BMJ* Rapid Recommendations, takes a person-perspective rather than a societal, public health, or healthcare payer perspective. Increasing rates of antimicrobial resistance are a public health priority. From a societal perspective, it is possible that the modest benefits from adjuvant antibiotics in this scenario would not outweigh the risk of increased antimicrobial resistance in the community. However, the impact of an individual course of antibiotics on community resistance rates is unknown. Therefore, whether antibiotics in this situation provide a net benefit or harm to society is highly speculative.

Adaptation

Local antimicrobial resistance patterns

The benefits of any antibiotic are probably lower in situations where the risk of resistance to that antibiotic is high. Therefore clinicians should consider local resistance patterns when choosing an appropriate therapy.

Clinical Question/ PICO

Population: Adults and children with uncomplicated skin abscesses

Intervention: Trimethoprim/sulfamethoxazole

Comparator: No antibiotics

Summary

Antibiotics, specifically, trimethoprim/sulfamethoxazole (TMP/SMX) or clindamycin, reduce treatment failure, early recurrence, late recurrence, and need for an additional surgical procedure by 5 to 7% (moderate-to-high certainty). Overall, antibiotics reduce the risk of treatment failure and recurrence by approximately 13%. Antibiotics reduce hospitalization and risk of infection in a household contact by 2-3% (moderate certainty). Reduce tenderness during therapy by 7% (moderate certainty). Antibiotics probably increase nausea by ~3-4% (moderate certainty); diarrhoea by 2% to 10% (depending on antibiotic). Antibiotics have a risk of anaphylaxis of up to 0.8% (low certainty).

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** No antibiotics	TMP-SMX	**Certainty in effect estimates** (Quality of evidence)	**Plain text summary**

Treatment failure 1 month	Odds Ratio 0.45 (CI 95% 0.33 - 0.62) Based on data from 2,305 patients in 6 studies. (Randomized controlled) Follow up 7 to 21 days	**90** per 1000 **43** per 1000 Difference: **47 fewer** per 1000 (CI 95% 58 fewer - 32 fewer)	**High** 1	Antibiotics with activity against MRSA reduce the risk of treatment failure.
Early recurrence 1 month	Odds Ratio 0.48 (CI 95% 0.3 - 0.77) Based on data from 2,134 patients in 6 studies. (Randomized controlled) Follow up 7 to 30 days	**129** per 1000 **66** per 1000 Difference: **63 fewer** per 1000 (CI 95% 86 fewer - 27 fewer)	**Moderate** Due to serious risk of bias and borderline inconsistency [2]	Antibiotics probably reduce the risk of early abscess recurrence.
Late recurrence 1 to 3 months	Odds Ratio 0.64 (CI 95% 0.48 - 0.85) Based on data from 1,155 patients in 2 studies. (Randomized controlled) Follow up 63 to 90 days	**267** per 1000 **189** per 1000 Difference: **78 fewer** per 1000 (CI 95% 118 fewer - 31 fewer)	**Moderate** Due to serious risk of bias, borderline imprecision [3]	Antibiotics probably reduce the risk of late abscess recurrence.
Hospitalisation 3 months	Odds Ratio 0.55 (CI 95% 0.32 - 0.94) Based on data from 1,206 patients in 2 studies. (Randomized controlled) Follow up 40 to 90 days	**39** per 1000 **22** per 1000 Difference: **17 fewer** per 1000 (CI 95% 26 fewer - 2 fewer)	**Moderate** Due to serious imprecision [4]	Antibiotics probably reduce the risk of hospitalisation.
Sepsis 1 month	Odds Ratio 7.24 (CI 95% 0.14 - 364.86) Based on data from 1,247 patients in 1 studies. (Randomized controlled) Follow up 49-63 days	**0** per 1000 **2** per 1000 Difference: **2 more** per 1000 (CI 95% 3 fewer - 6 more)	**Moderate** Due to serious imprecision [5]	Antibiotics probably do not decrease the risk of sepsis.
Serious complications (invasive infections) 1 months	Odds Ratio 1.02 (CI 95% 0.14 - 7.24) Based on data from 1,057 patients in 1 studies. (Randomized controlled) Follow up 14 days	**4** per 1000 **4** per 1000 Difference: **0 fewer** per 1000 (CI 95% 8 fewer - 8 more)	**Moderate** Due to serious imprecision [6]	Antibiotics probably do not reduce the risk of serious complications.
Additional surgical procedure 3 months	Odds Ratio 0.58 (CI 95% 0.38 - 0.88) Based on data from 1,013 patients in 1 studies. (Randomized controlled) Follow up 49 to 63 days	**136** per 1000 **84** per 1000 Difference: **52 fewer** per 1000 (CI 95% 78 fewer - 16 fewer)	**Moderate** Due to serious imprecision [7]	Antibiotics probably reduce the need for additional surgical procedures.

Pain (tenderness) 3 to 4 days	Odds Ratio 0.76 (CI 95% 0.61 - 0.97) Based on data from 1,057 patients in 1 studies. (Randomized controlled) Follow up 3 to 4 days	**559** per 1000	**491** per 1000	Difference: **68 fewer** per 1000 (CI 95% 126 fewer - 8 fewer)	**Moderate** Due to serious imprecision [8]	Antibiotics probably reduce pain during treatment.
Infection in a household member 1 month	Odds Ratio 0.58 (CI 95% 0.34 - 1.01) Based on data from 1,013 patients in 1 studies. (Randomized controlled) Follow up 49 to 63 days	**67** per 1000	**40** per 1000	Difference: **27 fewer** per 1000 (CI 95% 55 fewer - 1 more)	**Moderate** Due to serious imprecision [9]	Antibiotics probably reduce the risk of infection in people living in the same household.
Death 3 months	Odds Ratio 0.98 (CI 95% 0.06 - 15.68) Based on data from 2,194 patients in 3 studies. (Randomized controlled) Follow up 30 to 90 days	**1** per 1000	**1** per 1000	Difference: **0 fewer** per 1000 (CI 95% 4 fewer - 4 more)	**High** Borderline imprecision	Antibiotics do not reduce the risk of death.
Gastrointestinal side effects While taking antibiotics	Odds Ratio 1.28 (CI 95% 1.04 - 1.58) Based on data from 2,124 patients in 4 studies. (Randomized controlled) Follow up 30 to 90 days	**85** per 1000	**106** per 1000	Difference: **21 more** per 1000 (CI 95% 3 more - 43 more)	**Moderate** Due to serious imprecision [10]	TMP-SMX probably increases the risk of gastrointestinal side effects.
Nausea While taking antibiotics	Odds Ratio 1.49 (CI 95% 0.98 - 2.25) Based on data from 1,975 patients in 3 studies. (Randomized controlled) Follow up 30 to 63 days	**24** per 1000	**35** per 1000	Difference: **11 more** per 1000 (CI 95% 0 fewer - 28 more)	**Moderate** Due to serious imprecision [11]	TMP-SMX probably increases the risk of nausea.
Diarrhoea 3 months	Odds Ratio 0.92 (CI 95% 0.7 - 1.22) Based on data from 1,912 patients in 3 studies. (Randomized controlled) Follow up 30 to 63 days	**67** per 1000	**62** per 1000	Difference: **5 fewer** per 1000 (CI 95% 19 fewer - 14 more)	**Moderate** Due to serious imprecision [12]	TMP-SMX probably does not increase the risk of diarrhoea.
Anaphylaxis Minutes to days	Odds Ratio 2.32 (CI 95% 0.67 - 8.06) Based on data from 877 patients in 3 studies. (Randomized controlled) Follow up 30 to 90 days	**7** per 1000	**15** per 1000	Difference: **8 more** per 1000 (CI 95% 2 fewer - 44 more)	**Low** Due to serious risk of bias and imprecision [13]	Antibiotics probably increase the risk of anaphylaxis.

Practical issues	No antibiotics	Trimethoprim/ sulfamethoxazole	Both
 Medication routine	One or two pills, taken 2-3 times per day for 5-10 days.	No additional pills.	
 Tests and visits			May need additional visits if symptoms do not resolve or worsen.
 Adverse effects, interactions and antidote Drug-drug interactions	Antibiotics may interact with other medications.		
 Adverse effects, interactions and antidote Antimicrobial resistance	Antibiotics increase the rates of antibiotic resistance in the community and in the individual.	Avoiding antibiotics decreases the rates of antibiotic resistance in the community and in the individual.	
 Pregnancy and nursing	TMP-SMX should be avoided in pregnancy. It is known to cause birth defects and is an FDA class 4 medication in pregnancy (harm is likely).	The impact of an modestly increased risk of treatment failure and recurrence on pregnancy is uncertain, but unlikely to have an impact on the health of the child.	
 Food and drinks	May decrease appetite. Should be taken with a glass of water.		

1. **Risk of bias: Serious . Inconsistency: No serious . Indirectness: No serious . Imprecision: No serious . Publication bias: No serious .**
2. **Risk of bias: Serious .** There was substantial missing data/lost-to-follow-up: the results are not robust to worth plausible sensitivity analysis. ; **Inconsistency: No serious .** The magnitude of statistical heterogeneity was high, with I^2: 45%, but the direction of effect was similar in almost all trials, favouring antibiotics over no antibiotics. ; **Indirectness: No serious . Imprecision: No serious . Publication bias: No serious .**
3. **Risk of bias: Serious .** Incomplete data and/or large loss to follow up: results are not sensitive to worst plausible sensitivity analysis: RR 1.10 95%CI (0.77,1.57) ; **Inconsistency: No serious . Indirectness: No serious . Imprecision: No serious .** A single large

study, and one small study contributed data to this outcome. ; **Publication bias: No serious .**
4. **Inconsistency: No serious . Indirectness: No serious . Imprecision: Serious .** Confidence interval approaches no effect ; **Publication bias: No serious .**
5. **Inconsistency: No serious . Indirectness: No serious . Imprecision: Serious .** Due to serious imprecision ; **Publication bias: No serious .**
6. **Inconsistency: No serious . Indirectness: No serious . Imprecision: Serious .** Only data from one study ; **Publication bias: No serious .**
7. **Inconsistency: No serious . Indirectness: No serious . Imprecision: Serious .** Data from one study only. ; **Publication bias: No serious .**
8. **Inconsistency: No serious . Indirectness: No serious . Imprecision: Serious .** Only data from one study, confidence interval approaches no effect. ; **Publication bias: No serious .**
9. **Inconsistency: No serious . Indirectness: No serious . Imprecision: Serious .** Only data from one study; confidence interval include no effect. ; **Publication bias: No serious .**
10. **Inconsistency: No serious . Indirectness: No serious . Imprecision: Serious .** Confidence interval approaches no effect. ; **Publication bias: No serious .**
11. **Inconsistency: No serious . Indirectness: No serious . Imprecision: Serious .** Confidence interval approaches no effect ; **Publication bias: No serious .**
12. **Inconsistency: No serious . Indirectness: No serious . Imprecision: Serious .** Wide confidence intervals ; **Publication bias: No serious .**
13. **Risk of bias: Serious .** Selective outcome reporting: studies without any events are likely to have not reported this outcome, leading to overestimation of risk. ; **Inconsistency: No serious . Indirectness: No serious . Imprecision: Serious .** Few events. Not all studies reported anaphylaxis. ; **Publication bias: No serious .**

Strong Recommendation

In patients with uncomplicated skin abscesses who are initiating antibiotic therapy after incision and drainage, we recommend TMP/SMX or clindamycin over cephalosporins.

This strong recommendation applies to the most common situation where the risk of MRSA is more than 10%.

Practical Info

MRSA risk
This recommendation applies most strongly to settings with a high (i.e., >10%) risk of MRSA infection. Whether or not cephalosporins and other beta-lactams are effective for abscesses not caused by MRSA is unclear. In almost all settings.

Cellulitis and other skin and soft tissue infections
While abscesses are more likey to be caused by *Staphylococcus aureus*, especially MRSA, cellulitis and other skin and soft tissue infection are probably more often caused by *Streptococcus spp.*, in which cephalosporins and other beta-lactams are probably more effective. Indeed, there is RCT evidence to suggest that cephalexin is just as effective as cephalexin plus TMP-SMX for uncomplicated cellulitis.*[1]*

Key Info

Benefits and harms

Substantial net benefits of the recommended alternative

Both trimethoprim/sulfamethoxazole (TMP/SMX) and clindamycin probably reduce the risk of treatment failure compared to early and late generation cephalosporins. There is no evidence that cephalosporins reduce the risk of treatment failure compared to placebo.

There was no direct evidence for other key outcomes, including pain, abscess recurrence, and hospitalisation. However, the panel felt that it would be unlikely that cephalosporins had a beneficial effects on other related outcomes but not on teratment failure.

All antibiotics are associated with adverse effects, including antibiotic associated diarrhea. There was no direct evidence to suggest that cephalosporins have higher or lower risks of adverse effects than TMP/SMX and clindamycin.

Quality of evidence Moderate

There is moderate quality evidence that cephalosporins confer a higher risk of treatment failure than TMP/SMX and clindamycin. The evidence is lower because of imprecision around the absolute effect -- the confidence interval includes no effect. Evidence for other outcomes, assuming it is consistent with treatment failure is low quality, further rated down for indirectness.

Preference and values No substantial variability expected

The panel believes that almost all patients would find the expected benefits with TMP/SMX or clindamycin compared to cephalosporins important, with little variability between patients.

Resources and other considerations No important issues with the recommended alternative

Many of the options are off-patent, inexpensive, and widely available. In most places, TMP/SMX will be less expensive than both clindamycin and most cephalosporins.

Rationale

There is no evidence that cephalosporins reduce the risk of treatment failure more than placebo (moderate certainty), and either TMP/SMX or clindamycin both probably reduce the risk of treatment failure compared to cephalosporins (moderate certainty). There was no direct evidence from RCTs to inform any of the other outcomes. However, it is unlikely that cephalosporins would confer benefits for abscess recurrence, hospitalisations, and other related outcomes given that cephalosporins are probably not effective for treatment failure compared to placebo (low certainty for all related outcomes because evidence is indirect).

Clinical Question/ PICO

Population: Adults and children with uncomplicated skin abscesses who are initiating antibiotics
Intervention: Trimethoprim/sulfamethoxazole
Comparator: First and second generation cephalosporins

Summary

Trimethoprim and sulfamethoxazole (TMP/SMX) probably reduces treatment failure compared to cephalosporins, by approximately 16%.

Outcome Timeframe	Study results and measurements	Absolute effect estimates Cephalosporins	 TMP/SMX	Certainty in effect estimates (Quality of evidence)	Plain text summary
Treatment failure 1 month	Odds Ratio 0.42 (CI 95% 0.12 - 1.07) Based on data from 1,436	**280**	**119**	**Moderate** Due to serious imprecision [1]	TMP/SMX probably reduces the risk of treatment failure.

	patients in 5 studies. (Randomized controlled) Follow up 7 to 21 days	per 1000 per 1000 Difference: **162 fewer** per 1000 (CI 95% 392 fewer - 7 more)		

1. **Inconsistency: No serious . Indirectness: No serious . Imprecision: Serious .** Confidence interval includes no difference. ;

Clinical Question/ PICO

Population: Adults and children with uncomplicated skin abscesses who are initiating antibiotics
Intervention: Clindamycin
Comparator: First and second generation cephalosporins

Summary

Clindamycin probably reduces treatment failure compared to cephalosporins, by approximately 16%.

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Cephalosporins Clindamycin	**Certainty in effect estimates** (Quality of evidence)	**Plain text summary**
Treatment failure 1 month	Odds Ratio 0.39 (CI 95% 0.11 - 1.02) Based on data from 1,572 patients in 5 studies. (Randomized controlled) Follow up 7 to 21 days	**280** per 1000 **109** per 1000 Difference: **171 fewer** per 1000 (CI 95% 401 fewer - 2 more)	**Moderate** Due to serious imprecision [1]	Clindamycin probably reduces the risk of treatment failure.

1. **Inconsistency: No serious . Indirectness: No serious . Imprecision: Serious .** Confidence interval includes no difference. ;

Clinical Question/ PICO

Population: Adults and children with uncomplicated skin abscesses who are initiating antibiotics after incision and drainage
Intervention: First and second generation cephalosporins
Comparator: No antibiotics

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** No antibiotics Cephalosporins	**Certainty in effect estimates** (Quality of evidence)	**Plain text summary**

Treatment failure 1 month	Odds Ratio 1.91 (CI 95% 0.6 - 4.66) Based on data from 3,285 patients in 12 studies. (Randomized controlled) Follow up 7 to 21 days	**180** per 1000	**295** per 1000 Difference: **115 more** per 1000 (CI 95% 64 fewer - 326 more)	**Moderate** Due to serious imprecision [1]	Cephalosporins probably do not reduce the risk of treatment failure.

1. **Inconsistency: No serious . Indirectness: No serious . Imprecision: Serious .** Confidence interval includes important benefit. ; **Publication bias: No serious .**

Weak Recommendation

In patients with uncomplicated skin abscesses who are initiating antibiotic therapy after incision and drainage, we suggest TMP/SMX over clindamycin.

Practical Info

Antibiotic dosing
TMP/SMX is typically given to adults and children older than 12 years old as trimethoprim 160mg and sulfamethoxazole 800mg (one or two pills twice daily). The dosage needs to be adjusted by weight for younger children (but older than one month): 8 mg trimethoprim and 30mg sulphamethoxazole per kilogram per day, divided into two doses. A reasonable dose of clindamycin for adults is 600-1800mg daily, spread equally over three or four doses (e.g. 300mg three times daily). For children older than one month, a reasonable dose is 8-25 mg/kg/day, also in three to four doses. A reasonable antibiotic duration is 5 to 10 days.

Local antimicrobial resistance
The benefits of any antibiotic are probably lower in situations where the risk of resistance to that antibiotic is high. Therefore clinicians should consider local resistance patterns when choosing an appropriate therapy.

Probiotics
Probiotics may have a role in preventing antibiotic associated diarrhoea, including *Clostridium difficile* infection, although this is controversial.

Key Info

Benefits and harms

Small net benefit, or little difference between alternatives

TMP/SMX and clindamycin confer a similar reduction in treatment failure compared to no antibiotics. TMP/SMX probably has a ~7% higher risk of abscess recurrence compared to clindamycin, but has a ~11% lower risk of antibiotic associated diarrhoea. The severity of diarrhoea is variable.

Quality of evidence

Moderate

There is moderate quality evidence for a difference in abscess recurrence, and high quality difference for diarrhoea.

Preference and values

Substantial variability is expected or uncertain

The panel felt that the typical patient would consider the reduction in abscess recurrence with clindamycin as somewhat important-to-important, with moderate variability; and the increase in diarrhoea as important, with moderate variability.

People who place a higher value on avoiding abscess recurrence may choose clindamycin, while patients who place a higher value on

avoiding diarrhoea and on minimizing costs may preferentially opt for TMP/SMX.

Resources and other considerations

No important issues with the recommended alternative

Both TMP/SMX and clindamycin are off-patent around the world and for many people cost differences will be unimportant. Both are widely available. However, TMP/SMX is typically more inexpensive than clindamycin. Where cost is an important consideration, TMP/SMX is likely to be preferred over clindamycin.

Rationale

We believe that most people would rather avoid the 11% increased risk of diarrhoea, and accept an ~7% increased risk of abcsess recurrence. Clindamycin is also more expensive than TMP/SMX and must be taken at least three times per day compared to twice daily with TMP/SMX. However, the recommendation is weak rather than strong because there is a close balance between the desirable and undesirable consequences, burdens, and costs. Different people are likely to choose different options on the basis of this evidence.

Clinical Question/ PICO

Population: Adults and children with uncomplicated skin abscesses who are initiating antibiotics

Intervention: Trimethoprim and sulfamethoxazole

Comparator: Clindamycin

Summary

TMP/SMX probably has an ~7% higher risk of recurrence within 1 month compared to clindamycin. TMP/SMX probably has a ~11% lower risk of diarrhea compared to clindamycin. There is no difference for treatment failure, or nausea.

Outcome Timeframe	Study results and measurements	Absolute effect estimates Clindamycin	 TMP/SMX	Certainty in effect estimates (Quality of evidence)	Plain text summary
Treatment failure 1 month	Odds Ratio 1.08 (CI 95% 0.69 - 1.75) Based on data from 2,673 patients in 7 studies. (Randomized controlled) Follow up 7 to 30 days	**109** per 1000	**119** per 1000 Difference: **10 more** per 1000 (CI 95% 53 fewer - 41 more)	**High** Borderline imprecision [1]	There is no important difference in treatment failure.
Early recurrence 1 month	Odds Ratio 2.14 (CI 95% 1.11 - 4.12) Based on data from 436 patients in 1 studies. (Randomized controlled) Follow up 30 days	**68** per 1000	**135** per 1000 Difference: **67 more** per 1000 (CI 95% 7 more - 163 more)	**Low** Due to serious imprecision and serious inconsistency [2]	TMP/SMX may result in higher risk of early abscess recurrence.
Diarrhoea 1 month	Odds Ratio 0.29 (CI 95% 0.16 - 0.55) Based on data from 526 patients in 1 studies.	**162** per 1000	**53** per 1000	**High** [3]	TMP/SMX has a lower risk of diarrhoea.

	(Randomized controlled) Follow up 30 days	Difference: **109 fewer** per 1000 (CI 95% 132 fewer - 66 fewer)			
Nausea 1 month	Odds Ratio 1.9 (CI 95% 0.69 - 5.21) Based on data from 526 patients in 1 studies. (Randomized controlled) Follow up 30 days	**23** per 1000	**43** per 1000 Difference: **20 more** per 1000 (CI 95% 7 fewer - 86 more)	**Moderate** Due to serious imprecision [4]	There is probably not an important difference in risk of nausea.

Practical issues	Clindamycin	Trimethoprim and sulfamethoxazole	Both
Medication routine	One or two pills twice daily.	One or two pills three-to-four times daily.	
Costs and access	Inexpensive in almost all settings.	Typically quite a bit more expensive than TMP/SMX.	
Pregnancy and nursing	FDA class D: evidence of harm in pregnancy. Some studies have suggested the possibility of a slightly increased risk of congenital malformations such as neural tube defects. Should be avoided whenever possible, especially during the first trimester.	FDA class B: no evidence of harm in pregnancy. Crosses the placenta and into breastmilk. No dose adjustment required in pregnancy.	
Food and drinks	Take with or without meals. Take with at least 250mL of water.	Take with or without meals. Take with at least 250mL of water.	
Medication routine Formulations	Available as a suspension in water, or tablets.	Availale as a solution to be reconstituted in water, or capsules.	

1. **Inconsistency: No serious . Indirectness: No serious . Imprecision: No serious .** Borderline wide confidence intervals ; **Publication bias: No serious .**

2. **Inconsistency: Serious .** These results from the only trial comparing TMP-SMX to clindamycin are not consistent with several other studies that compare TMP-SMX to placebo. In every other study, TMP-SMX reduced the risk of recurrence compared to placebo, but it did not in this same study. ; **Indirectness: No serious . Imprecision: Serious .** Data from one study only; confidence interval approaches no difference ; **Publication bias: No serious .**
3. **Inconsistency: No serious . Indirectness: No serious . Imprecision: No serious .** Direct data from one study only. However, we did not rate down for imprecision because of high certainty indirect evidence from other conditions that clindamycin has a higher risk of diarrhoea than TMP/SMX. ; **Publication bias: No serious .**
4. **Inconsistency: No serious . Indirectness: No serious . Imprecision: Serious .** Data from one study only; wide confidence intervals ; **Publication bias: No serious .**

2 - BMJ Rapid Recommendations: Background and Methods

About *BMJ* Rapid Recommendations

Translating research to clinical practice is challenging. Trustworthy clinical practice recommendations are one useful knowledge translation strategy. Organisations creating systematic reviews and guidelines often struggle to deliver timely and trustworthy recommendations in response to potentially practice-changing evidence. *BMJ* Rapid Recommendations aims to create trustworthy clinical practice recommendations based on the highest quality evidence in record time. The project is supported by an international network of systematic review and guideline methodologists, people with lived experience of the diseases or conditions, clinical specialists, and front-line clinicians. This overview is one of a package that includes recommendations and one or more systematic reviews published by the *BMJ* group and in MAGICapp (http://www.magicapp.org). The goal is to translate evidence into recommendations for clinical practice in a timely and transparent way, minimizing bias and centred around the experience of patients. *BMJ* Rapid Recommendations will consider both new and old evidence that might alter established clinical practice.

Process overview

1. On a daily basis, we monitor the literature for practice-changing evidence:
   a. Formal monitoring through McMaster Premium LiteratUre Service (PLUS)
   b. Informal monitoring the literature by *BMJ* Rapid Recommendations expert groups, including clinician specialists and patients
2. The *RapidRecs* executive team and editors at *The BMJ* choose which clinical questions to pursue among the identified potentially-practice changing evidence, based on relevance to a wide audience, widespread interest, and likelihood to change practice.
3. We incorporate the evidence into the existing body of evidence and broader context of clinical practice via:
   a. a rapid and high-quality systematic review and meta-analysis on the benefits and harms with a focus on the outcomes that matter to patients
   b. parallel rapid recommendations that meet the standards for trustworthy guidelines[1] by an international panel of people with relevant lived experience, front-line clinicians, clinical content experts, and methodologists.
d. Further research may be conducted including:
   i. A systematic review of observational studies to identify baseline risk estimates that most closely represent the population at the heart of the clinical question, a key component when calculating the estimates of absolute effects of the intervention
   ii. A systematic review on the preferences and values of patients on the topic.
4. Disseminate the rapid recommendations through
a. publication of the research in *BMJ* journals
b. short summary of recommendations for clinicians published in *The BMJ*
c. press release and/or marketing to media outlets and relevant parties such as patient groups
d. Links to BMJ Group's *Best Practice* point of care resource
e. MAGICapp which provides recommendations and all underlying content in digitally structured multilayered formats for clinicians and others who wish to re-examine or consider national or local adaptation of the recommendations.

Who is involved?
Researchers, systematic review and guideline authors, clinicians, and patients often work in silos. Academic journals may publish work from any one or combinations of these groups of people and findings may also be published in the media. But it is rare that these groups work together to produce a comprehensive package. *BMJ-RapidRecs* circumvents organisational barriers in order to provide clinicians with guidance for potentially practice-changing evidence.
Our collaboration involves
   a. The *RapidRecs* group with a designated Executive team responsible for recruiting and coordinating the network of researchers who perform the systematic reviews and the recommendation panels.. The *RapidRecs* group is part of MAGIC (www.magicproject.org), a non for profit organization that provides MAGICapp (www.magicapp.org) an authoring and publication platform for evidence summaries, guidelines and decision aids, which are disseminated online for all devices.[5]
   b. *The BMJ* helps identifiying practice-changing evidence on key clinical questions, coordinates the editorial process and publishes the package of content linking to the MAGICapp that is presented in a user friendly way.

METHODS FOR THE RAPID RECOMMENDATIONS

The formation of these recommendations adheres to standards for trustworthy guidelines with an emphasis on patient involvement, strict management of conflicts of interests, as well as transparent and systematic processes for assessing the quality of evidence and for moving from evidence to recommendations. [1,2,6]

Guidance on how the panel is picked and how they contribute
Panel members are sought and screened through an informal process.
The following panel members are important

- At least one author of the individual systematic reviews
- At least one patient representative with lived experience of the disease or condition. This person receives patient-oriented documents to explain the process and is allocated a linked panel member to empower their contribution.
- A full spectrum of practicing clinicians involved in the management of the clinical problem and patients it affects, including front-line clinicians with generalist experience and those with deep content clinical and research expertise in the particular topic.
- Methodological experts in health research methodology and guideline development

Any potential conflicts of interest are managed with extreme prudence:

- No panel member can have a financial interest – as assessed by the panel chair, the *Rapidrecs* executive team or *The BMJ* editors as relevant to the topic
- No more than two panel members with an intellectual interest on the topic (typically having published statements favouring one of the interventions).

Illustrative example: For this BMJ Rapid Recommendation, no one was included on the panel who had, or planned to have, any financial relationship with a pharmaceutical company that makes oral antibiotics.

How the panel meets and works

The international panel communicates via teleconferences and e-mail exchange of written documents throughout the process. Minutes from teleconferences are audiorecorded, transcribed, and stored for later documentation (available for peer-reviewers on request). Teleconferences typically occur at three timepoints, with circulated documents by e-mail in advance:

1. At the initiation of the process to provide feedback on the systematic review protocol (for example, on selection of patient-important outcomes and appropriate prespecified analysis of results) before it is performed.
2. At the evidence summary stage with discussion, feedback and agreement on draft evidence (GRADE evidence profile) prepared by the Chair and the methods editor based on the systematic review.
3. At the recommendation formulation phase with discussion, feedback and agreement on draft recommendations and other content underlying the recommendation (e.g. GRADE SoF-table, key information, rationale, practical advice)

Following the last teleconference the final version of the recommendations is circulated by e-mail specifically requesting feedback from all panel members to document agreement before submission to *The BMJ*. Additional teleconferences are arranged as needed.

How we move from research findings to recommendations

What information is considered?

The panel considers best current evidence from available research. Beyond systematic reviews - performed in the context of the *BMJ* Rapid Recommendations - the panel may also include a number of other research papers to further inform the recommendations.

How is a trustworthy guideline made?

The Institute of Medicine (IOM)'s guidance on out how trustworthy guidelines should be developed and articulated key standards as outlined in the table below.[1] The standards are similar to those developed by the Guideline International Network (G-I-N).[2] These standards have been widely adopted by the international guideline community. Peer reviewers of the recommendation article are asked whether they found the guideline trustworthy (in accordance with IOM standards). The table below lays out how we hope to meet the standards for our rapid recommendations:

1. Establishing transparency **"The processes by which a CPG is developed and funded should be detailed explicitly and publicly accessible"***
• This method is available and published as a supplementary file as well as in MAGICapp where all recommendations and underlying content is available. • We ask the peer-reviewers to judge whether the guidance is trustworthy and will respond to concerns raised.
2. Managing conflicts of interest **"Prior to selection of the guideline development group, individuals being considered for membership should declare all interests and activities potentially resulting in COI with development group activity....",**

- Interests of each panel member are declared prior to involvement and published with the rapid recommendations
- No one with any potential financial interests in the past three years, or forthcoming 12 months will participate - as judged by the panel chair and *The BMJ*
- No more than two panel members have declared an intellectual conflict of interest. Such conflicts include having taken a position on the issue for example by a written an editorial, commentary, or conflicts related to performing a primary research study or written a prior systematic review on the topic.
- The Chair must have methods expertise, a clinical background and no financial or intellectual interests.
- Funders and pharmaceutical companies have no role in these recommendations.

3. Guideline Development Group Composition
"The guideline development group should be multidisciplinary and balanced, comprising a variety of methodological experts and clinicians, and populations expected to be affected by the CPG"

- *The RapidRecs* group will aim to include representation from most or every major geographic region in the world, with specific efforts made to achieve gender-balance.
- We will facilitate patient and public involvement by including patient experience, via patient-representatives and systematic reviews addressing values and preferences to guide outcome choices and relative weights of each outcome, where available
- Patient-representatives will be given priority during panel meetings and will have an explicit role in vetting the panel's judgements of values and preferences.

4. Clinical Practice Guideline–Systematic Review Intersection
"CPG developers should use systematic reviews that meet standards set by the IOM. Guideline development group and systematic review team should interact regarding the scope, approach, and output of both processes".

- Each rapid recommendation will be based on one or more high-quality SRs either developed and published in parallel with our *BMJ* Rapid Recommendations or produced by other authors and available at the time of making the recommendaiton.
- The recommendation panel and SR teams will interact, with up to three members participating in both teams to facilitate communication and continuity in the process

5. Establishing Evidence Foundations for and Rating Strength of Recommendations
"For each recommendation: explain underlying reasoning, including a clear description of potential benefits and harms, a summary of relevant available evidence and description of the quality., explain the part played by values, opinion, theory, and clinical experience in deriving the recommendation, "provide rating of strength of recommendations"

- The GRADE approach will provide the framework for establishing evidence foundations and rating strength of recommendations.[6] For each recommendation systematic and transparent assessments are made across the following key factors:
  - Absolute benefit and harms for all patient-important outcomes through structured evidence summaries (e.g. GRADE Summary of Findings tables) [4]

- Quality of the evidence [7]
- Values and preferences of patients
- Resources and other considerations (e.g. feasibility, applicability, equity)

- Each outcome will - if data are available through systematic reviews - include an effect estimate and confidence interval, with a measure of certainty in the evidence, as presented in Summary of Findings tables. If such data are not available narrative summaries will be provided.
- A summary of the underlying reasoning and all additional information (e.g. key factors, practical advice, references) will be available online in an interactive format at www.magicapp.org. This summary will include descriptions of how theory (e.g. patophysiology) and clinical experience played into the evidence assessment and recommendation development.
- Recommendations will be rated either weak or strong, as defined by GRADE. [8]
- If the panel members disagree regarding evidence assessment or strength of recommendations, we will follow a structured consensus process customized to the GRADE system and report any final differences in opinion, with their rationale, in the online supplement and online at www.magicapp.org.

6. Articulation of recommendations
"Recommendations should be articulated in a standardized form detailing precisely what the recommended action is, and under what circumstances it should be performed, and so that compliance with the recommendation(s) can be evaluated"

- Each recommendation will appear at the top of the guideline infographic, published in *The BMJ*, and will be available in standardised formats in MAGICapp, articulated to be actionable based on best current evidence on presentation formats of guidelines.[9]
- There will be a statement included in each summary article in *The BMJ* and in the MAGICapp that these are recommendations to provide clinicians with guidance. They do not form a mandate of action and should be contextualised in the healthcare system a clinician's works in, and or with an individual patient.

7. External review
"External reviewers should comprise a full spectrum of relevant stakeholders...., authorship should be kept confidential....., all reviewer comments should be considered....a rationale for modifying or not should be recorded in writing.... a draft of the recommendation should be made available to general public for comment.."

- At least two external peer-reviewers and one patient reviewer will review the article for *The BMJ* and provide open peer review. Each will have access to all the information in the package. They will be asked for general feedback as well as to make an overall judgement on whether they view the guidelines as trustworthy
- A *BMJ* series adviser with methodological and/or statistical expertise will review the *BMJ* Rapid Recommendations publication and the systematic reviews.
- The *Rapidrecs* panel will be asked to read and respond to the peer review comments and make amendments where they judge reasonable
- *The BMJ* and *RapidRecs* executive team may, on a case-by-case basis, choose to invite key organizations, agencies, or patient/public representatives to provide and submit public peer-review.
- There will be post-publication public review process through which people can provide comments and feedback through MAGICapp (or through *The BMJ*). The

Chair will, on behalf of panel authors, aim to respond to each publicly-available peer-review within 30 days, for a period of six months after publication.

8. Updating
"The date for publication, systematic review and proposed date for future review should be documented, the literature should be monitored regularly and the recommendation should be updated when warranted by new evidence"

· The *Rapidrecs* panel will, through monitoring of new research evidence for published *BMJ* Rapid Recommendations, aim to provide updates of the recommendations in situations in which the evidence suggests a change in practice. These updates will be initially performed in MAGICapp and submitted to *The BMJ* for consideration of publication of a new Rapid Recommendation.

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