CLINICAL TRIAL RESULTS

Sponsor: National Institute of Allergy and Infectious Diseases (NIAID)

Medicine(s) Studied: Clindamycin, Trimethoprim-Sulfamethoxazole (TMP-SMX)

Protocol Number: NCT00730028

Dates of Trial: April 2009 to February 2015

Title of this Trial: Randomized, Double-Blind Trial of Clindamycin, Trimethoprim-Sulfamethoxazole, or Placebo for Uncomplicated Skin and Soft Tissue Infections Caused by Community-Associated Methicillin-Resistant Staphylococcus Aureus

Date of this Report: 13 June 2017

~ *Thank You* ~

The NIAID, the Sponsor, would like to thank you for participating in this clinical trial, or for allowing your child to participate, and provide you a summary of results representing everyone who participated. If you have any questions about the study or results please contact the doctor or staff at your study site (or your child's study site).

This summary of results represents a single trial only.

WHY WAS THIS STUDY DONE?

MRSA stands for **m**ethicillin-**r**esistant ***S****taphylococcus* ***a****ureus*. MRSA is a type of bacteria that can cause infection in the skin and many other parts of the body. You may have heard MRSA called a "staph infection." MRSA can be very hard for doctors to treat, so it is important to find out which medications will work best for this infection.

This study looked at 2 different medications for MRSA called antibiotics. The medications are clindamycin (CLINDA) and trimethoprim-sulfamethoxazole (TMP-SMX). Both of these medications are taken by mouth and work by fighting infections in the body. Some patients in this study took placebo instead of CLINDA or TMP-SMX. A placebo does not have any medicine in it, but looks just like the medicine.

The main purpose of this study was to compare TMP-SMX, CLINDA, and placebo for the treatment of patients with MRSA.

Researchers wanted to know: **How many patients who took TMP-SMX, CLINDA, or placebo would have their MRSA infections under control?**

To answer this question, researchers looked at 2 different groups of patients:

- Group 1: All patients in the study
- Group 2: Patients who the researchers collected enough information from to get a good idea of how well the medications worked. These patients are called "evaluable."

Researchers tested the area of skin that had MRSA 7 to 10 days after patients finished treatment. Patients who still had symptoms of MRSA in that area did not have their infections under control. Patients who had MRSA in a new area, or had certain other problems, also did not have their MRSA controlled.

WHAT HAPPENED DURING THE STUDY?

The study included 1310 patients with 2 types of MRSA infection in their skin:

- Abscess: A pocket of pus in the skin. An abscess is usually red and painful.
- Cellulitis: A red, swollen area of skin that feels warm and painful.

Patients were 6 months to 85 years old. 436 patients were children, and 874 were adults. A total of 588 women/girls and 722 men/boys participated.

The patients and researchers did not know who took CLINDA or TMP-SMX and who took the placebo. This is called a "double-blind" study. Researchers use a double-blind study to make sure that the results are not influenced in any way.

First, patients were placed into 2 groups based on the size and type of their MRSA infection. The 2 groups are listed in the chart below:

Smaller Skin Infection: **"Limited Abscess Group"**	• Adults with abscess 5 centimeters (cm) or smaller • Children 9 years and older with abscess 5 cm or smaller • Children 1-8 years old with abscess 4 cm or smaller • Children under 1 year old with abscess 3 cm or smaller
Larger Skin Infection: **"Cellulitis or Larger Abscess Group"**	• Adults with abscess larger than 5 cm • Children 9 years and older with abscess larger than 5 cm • Children 1-8 years old with abscess larger than 4 cm • Children under 1 year old with abscess larger than 3 cm • Adults and children with abscesses in more than 1 area • Adults and children with cellulitis only (no abscess)

Patients in the smaller skin infection group were then placed in 1 of 3 treatment groups. Patients were picked for each treatment by chance alone. This is known as a "randomized" study, and it makes the groups more even to compare. The chart below shows the 3 treatment groups and the medications they took:

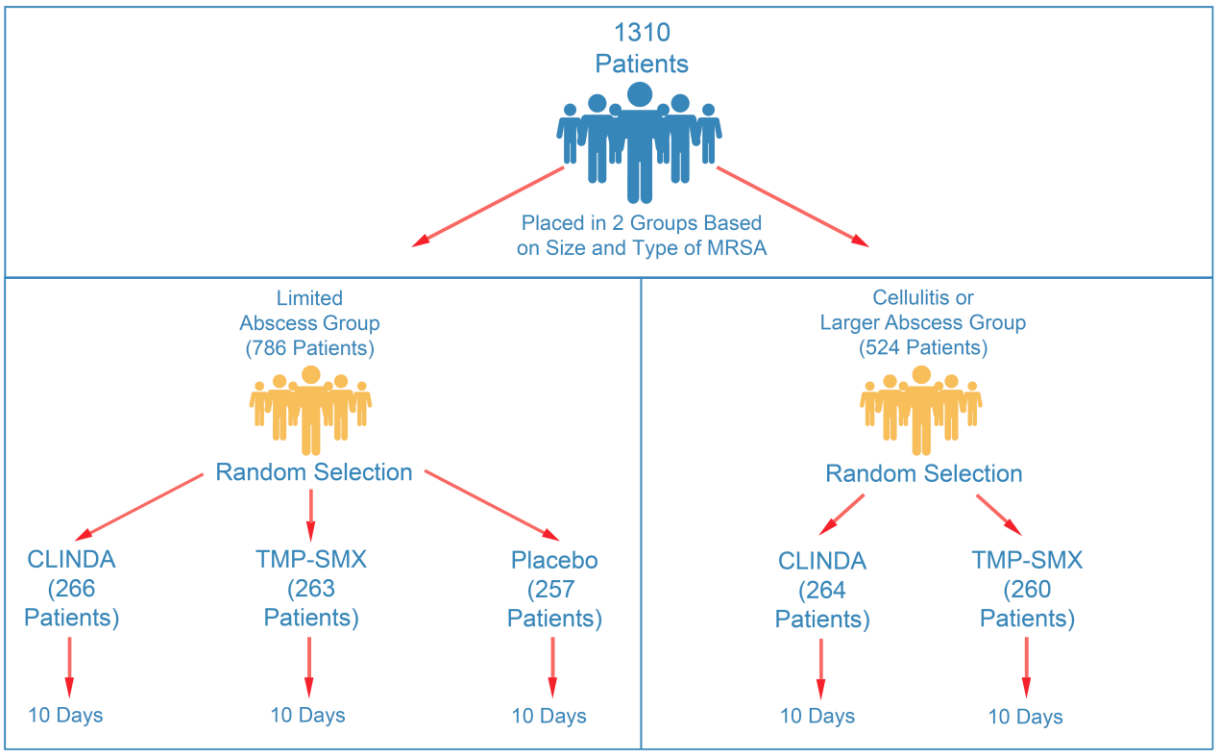
Smaller Skin Infection: Limited Abscess Group	
CLINDA Group (266 Patients)	**Adults:** 300 milligrams (mg) 3 times a day for 10 days **Children:** 25-30 mg per kilogram (kg) of weight, up to 900 mg a day. The medicine was divided into 3 daily doses. They took the medicine for 10 days.
TMP-SMX Group (263 Patients)	**Adults and children who weigh more than 40 kg:** 160 mg of TMP and 800 mg of SMX 2 times a day. They took the medicine for 10 days. **Children who weigh less than 40 kg:** 8-10 mg TMP based on weight, and 40-50 mg SMX based on weight. The medicine was divided into 2 daily doses. They took the medicine for 10 days.
Placebo Group (257 Patients)	Adults and children took placebo pills 3 times a day for 10 days.

Patients in the larger skin infection group were given 1 of 2 treatments. Patients were picked for each treatment by chance alone. The chart below shows the 2 treatment groups and the medications they took:

Larger Skin Infection: Cellulitis or Larger Abscess Group	
TMP-SMX Group (260 Patients)	**Adults and children who weigh more than 40 kg:** 160 mg of TMP and 800 mg of SMX 2 times a day. They took the medicine for 10 days. **Children who weigh less than 40 kg:** 8-10 mg TMP based on weight, and 40-50 mg SMX based on weight. The medicine was divided into 2 daily doses. They took the medicine for 10 days.
CLINDA Group (264 Patients)	**Adults:** 300 mg 3 times a day for 10 days **Children:** 25-30 mg based on weight, up to 900 mg a day. The medicine was divided into 3 daily doses. They took the medicine for 10 days.

Patients were supposed to take medication for 10 days and come to 4 visits at the study center. Some patients also had a minor surgery to remove fluid from their infected skin, in addition to taking medication. Of the 1310 patients who started the study, 1001 patients came to their 1 month follow-up visit and finished the study. A total of 309 patients left before the study was over by their choice or because a doctor decided it was best for them to stop the study.

While patients were only in the study for about 6 weeks, the entire study took almost 6 years to complete. The Sponsor ran this study at 6 locations in 6 cities in the United States. It began in April 2009 and ended in February 2015. This study was completed as planned.



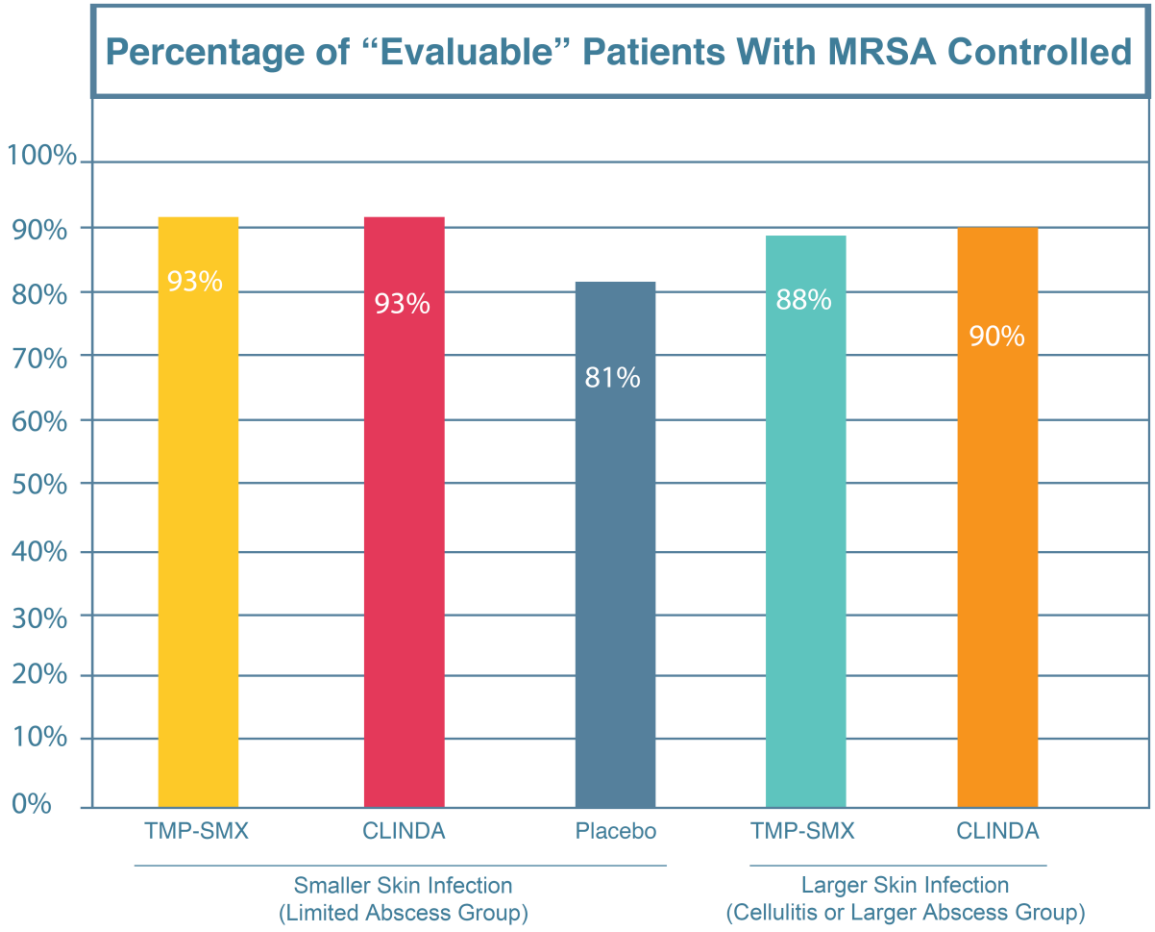
When the study ended in February 2015, the Sponsor began reviewing the information collected. The Sponsor then created a report of the results. This is a summary of that report.

WHAT WERE THE RESULTS OF THE STUDY?

How many patients in the *"evaluable" group* had their MRSA infections under control?

Overall, about 88% to 93% of evaluable patients who took CLINDA or TMP-SMX had MRSA infections that were controlled. Based on these results, the researchers decided that any differences between the CLINDA and TMP-SMX groups were likely the result of chance. These results show that CLINDA and TMP-SMX worked about the same for treating patients with smaller or larger MRSA infections in their skin.

More of the smaller MRSA infections were under control in patients who took CLINDA or TMP-SMX than patients who took placebo. About 81% of the evaluable patients had their smaller MRSA infections controlled with placebo. Researchers determined this difference (81% in placebo, compared to about 93% in either antibiotic group) was not likely the result of chance.

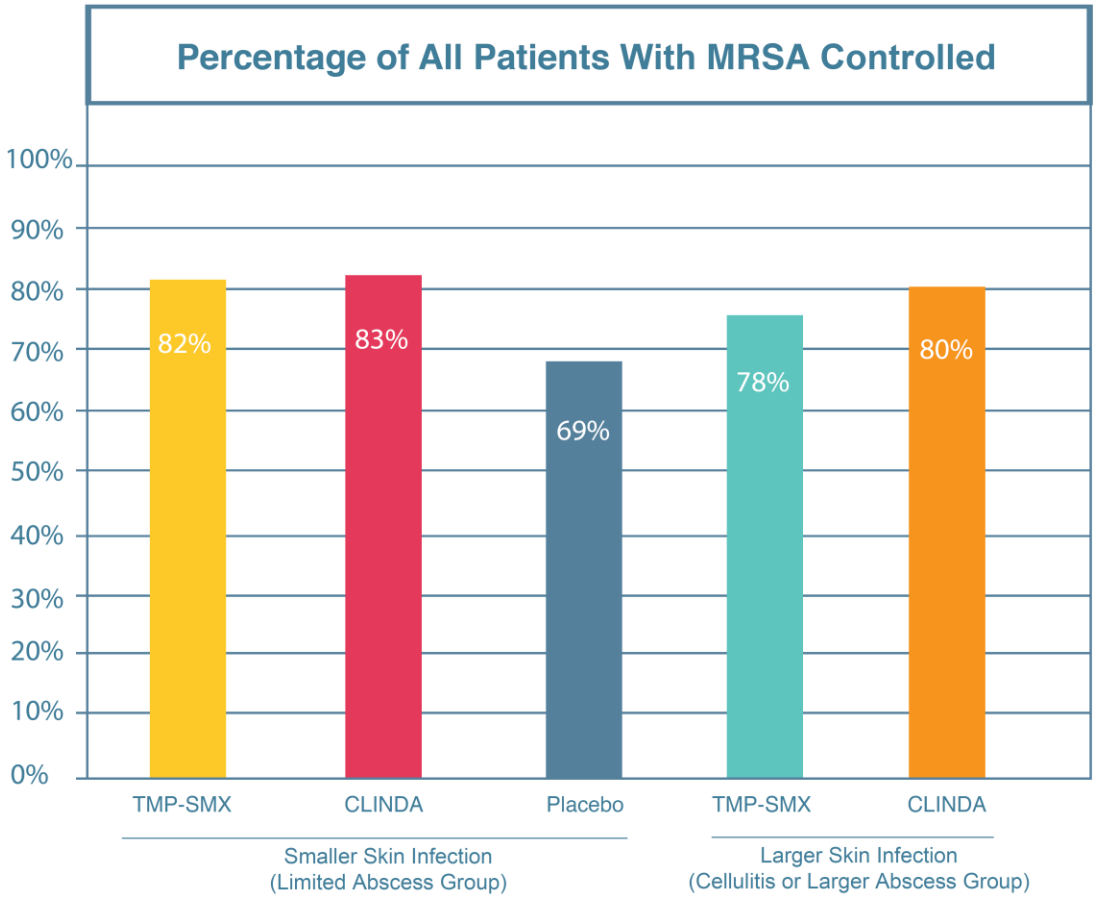


Out of *all the patients* in the study, how many had their MRSA infections under control after treatment?

Overall, about 78% to 83% of all patients in the CLINDA or TMP-SMX groups had MRSA infections that were controlled. Based on these results, the researchers decided that any differences between the CLINDA and TMP-SMX groups were likely the result of chance. These results show that CLINDA and

TMP-SMX worked about the same for treating patients with smaller or larger MRSA infections in their skin.

About 69% of all patients with smaller MRSA infections who took placebo had their infections under control. 82% of patients taking TMP-SMX, and about 83% of patients taking CLINDA had MRSA controlled. Researchers determined this difference (69% compared to about 82% to 83% in either antibiotic group) was not likely the result of chance.



This does not mean that everyone in this study had these results, and individual results could be better or worse than the overall group. Other studies may find different results. These are just some of the main findings of the study, and more information may be available on the websites listed at the end of this summary.

WHAT MEDICAL PROBLEMS DID PATIENTS HAVE DURING THE STUDY?

The researchers recorded any medical problems the patients had during the study. Patients could have had medical problems for reasons not related to the study (for example, caused by the patient's disease or by chance). Also, medical problems could have been caused by TMP-SMX or CLINDA, or by another medication the patient was taking. Sometimes the cause of a medical problem is unknown. By comparing medical problems across many treatment groups in many studies, doctors try to understand what the side effects of a medication might be.

A total of 128 patients left the study due to medical problems. A total of 304 out of 1310 patients (23%) in this study had at least 1 medical problem. The most common are listed in this chart:

Most Common Medical Problems (More Than 5% of Patients)

Medical Problem	CLINDA	TMP-SMX	Placebo	CLINDA	TMP-SMX
	Smaller Skin Infection			Larger Skin Infection	
	(266 Patients)	(263 Patients)	(257 Patients)	(264 Patients)	(260 Patients)
Diarrhea	46 (17%)	17 (6%)	20 (8%)	27 (10%)	28 (11%)
New Abscess	13 (5%)	29 (11%)	35 (14%)	21 (8%)	39 (15%)
New Cellulitis	3 (1%)	6 (2%)	9 (4%)	16 (6%)	23 (9%)

WERE THERE ANY SERIOUS MEDICAL PROBLEMS?

A medical problem is considered "serious" when it is life-threatening, causes lasting problems, or needs hospital care. A total of 17 out 1310 patients (1%) had at least 1 serious medical problem. 1 patient who took CLINDA (0.4%) and 1 patient who took placebo (0.4%) had an infection near the anal area. 2 patients who took TMP-SMX (0.8%) and 1 patient who took CLINDA (0.4%) had a new or worsening infection. 1 patient who took CLINDA (0.4%) and 3 patients who took TMP-SMX (0.6% total; 1 patient in the smaller infection group and 2 patients in the larger infection group) had new or worsening cellulitis. No patients died during the study.

WHERE CAN I LEARN MORE ABOUT THIS STUDY?

If you have questions about the results of your study, please speak with the doctor or staff at your study site.

The full study results are available online at:

www.clinicaltrials.gov: Use the study identifier **NCT00730028**

www.ncbi.nlm.nih.gov/pubmed/28657870

www.ncbi.nlm.nih.gov/pubmed/25785967

Please remember that researchers look at the results of many studies to find out which medicines work best and are safest for patients. Findings from this study may be used in other studies to learn more about how CLINDA and TMP-SMX help patients.

Again, **thank you** for volunteering or for allowing your child to volunteer.
We do research to try to find the best ways to help patients, and you helped us to do that!