

Recent research: antibiotic therapy and resistance, understanding transmission

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Overview

- Trimethoprim-sulfamethoxazole
 - Clinical trials
 - Does it work for GAS?
 - Concerns over resistance
- Overall burden of SSTI
- Genomics and modelling for GAS

Treatment of impetigo

- Intramuscular benzathine benzylpenicillin
 - Works
 - Assured adherence
 - Painful



660 kids who join in

Consent

Randomisation



Chance

Group 1
Needle medicine
(Penicillin)
One shot



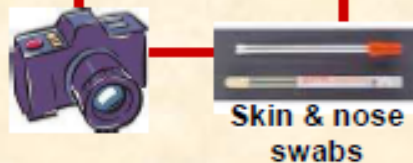
Group 2
Drink medicine
(Bactrim x 1)
5 days



Group 3
Drink medicine
(Bactrim x 2)
3 days



Check up
Day 0
Day 2
Day 7



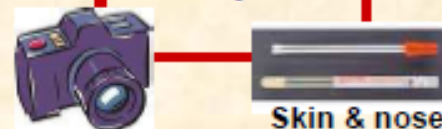
Skin & nose
swabs

Check up
Day 0
Day 2
Day 7



Skin
swabs

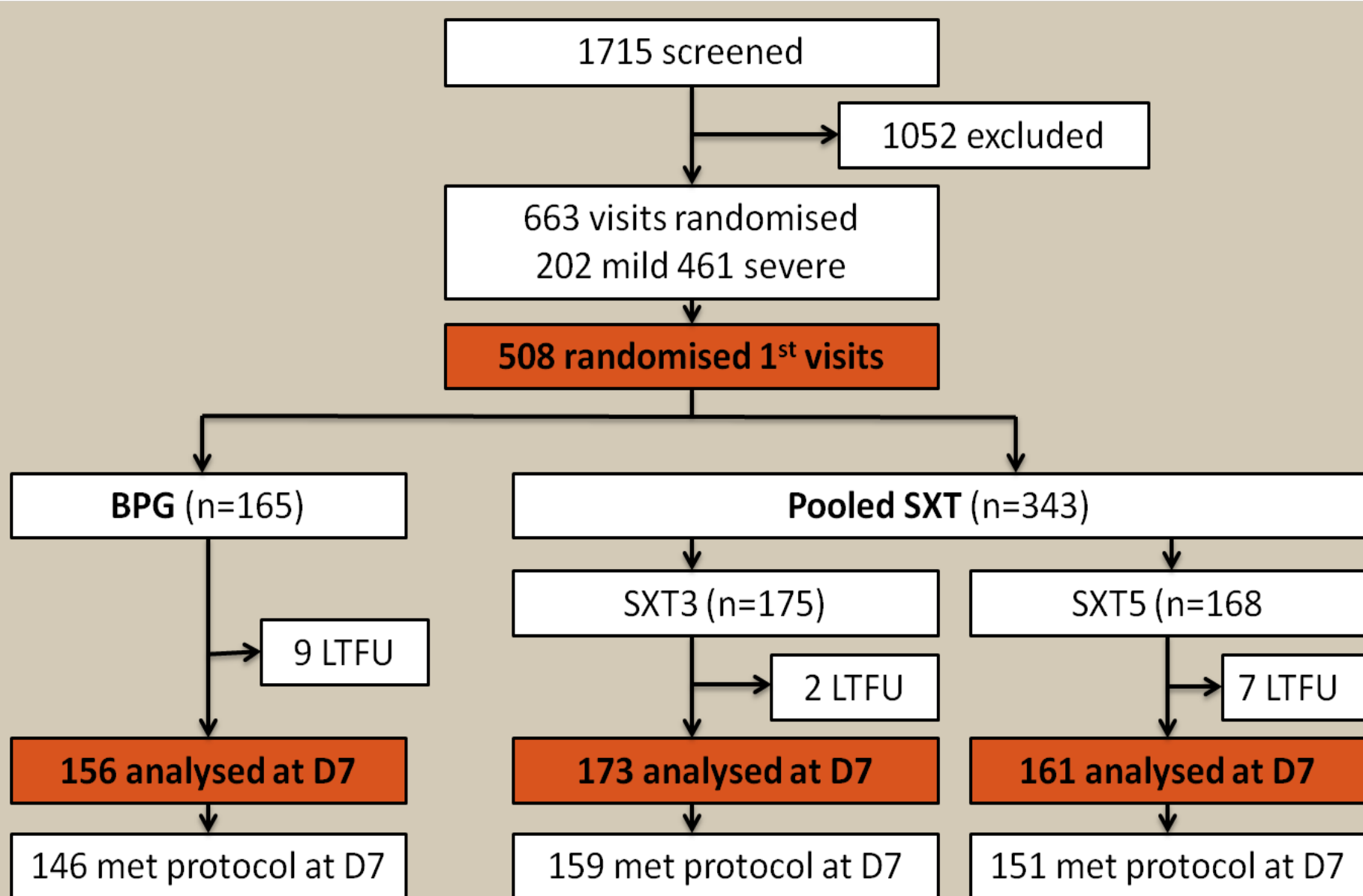
Check up
Day 0
Day 2
Day 7



Skin & nose
swabs



Screening, randomisation & follow up



Primary outcome

Is Image A compared to Image B?

Healed
 Improved
 Same
 Worse
 Unable to Determine

Is Image B compared to Image A?

Healed
 Improved
 Same
 Worse
 Unable to Determine

Please comment on the quality of Image A

Adequate
 Suboptimal
 Unable to interpret

Please comment on the quality of Image B

Adequate
 Suboptimal
 Unable to interpret




Image A 4245


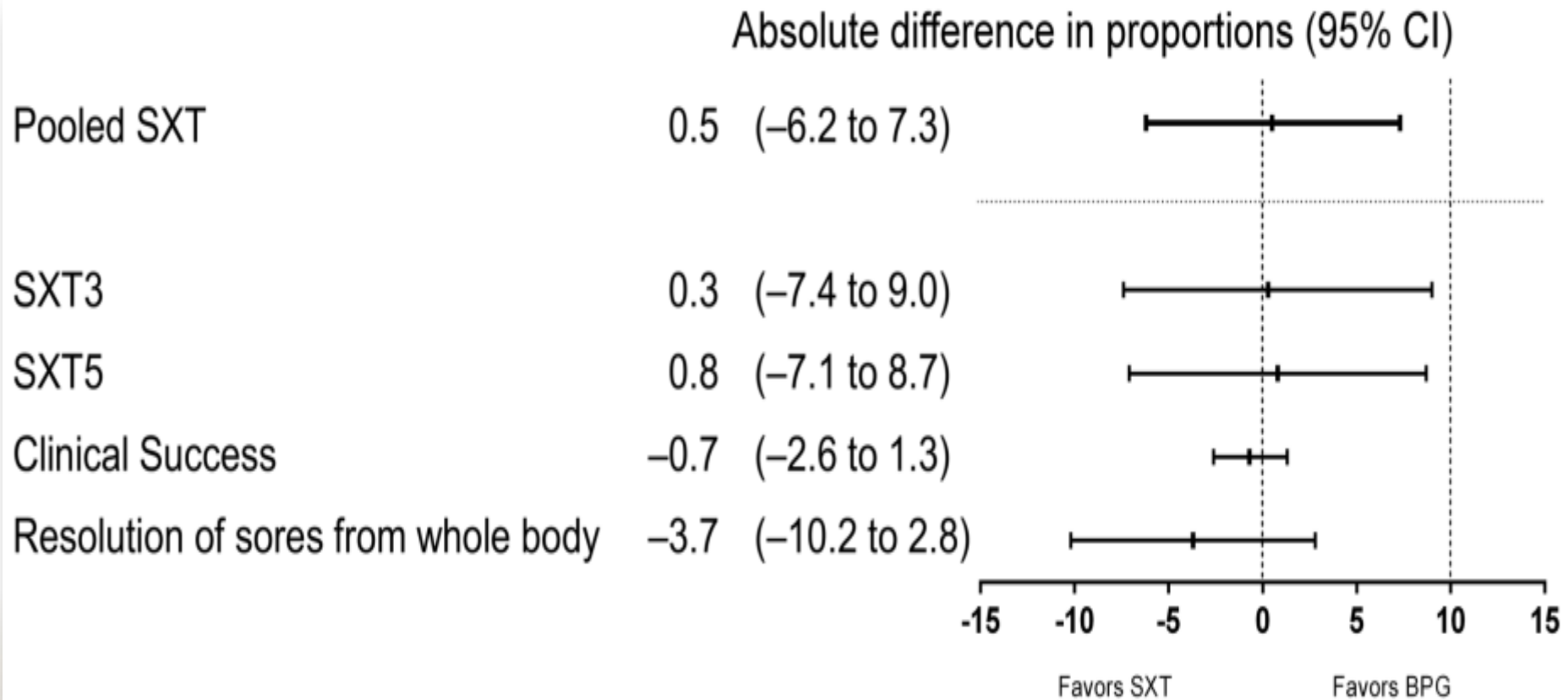


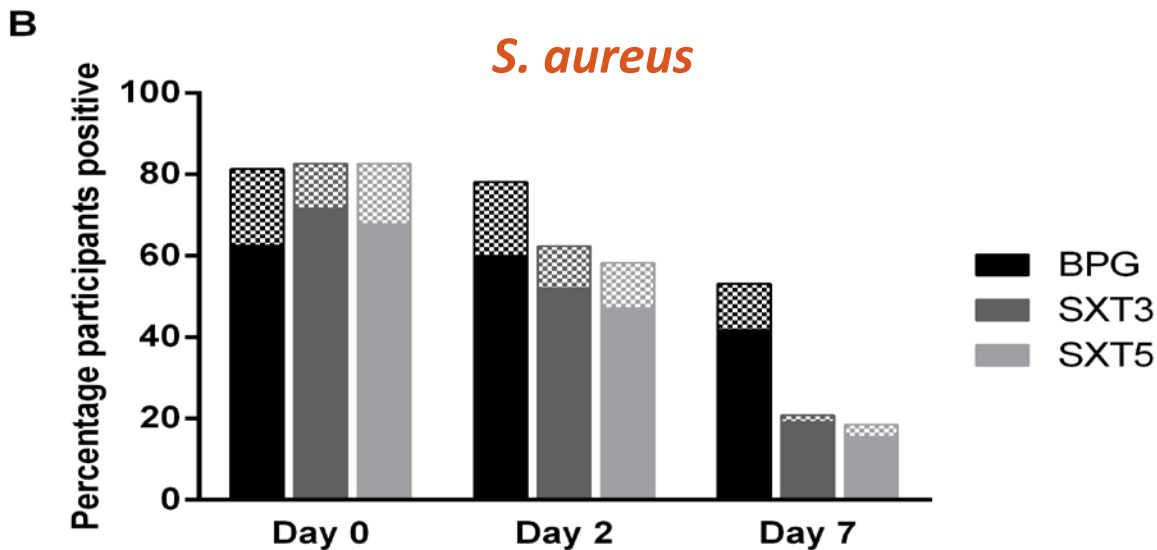
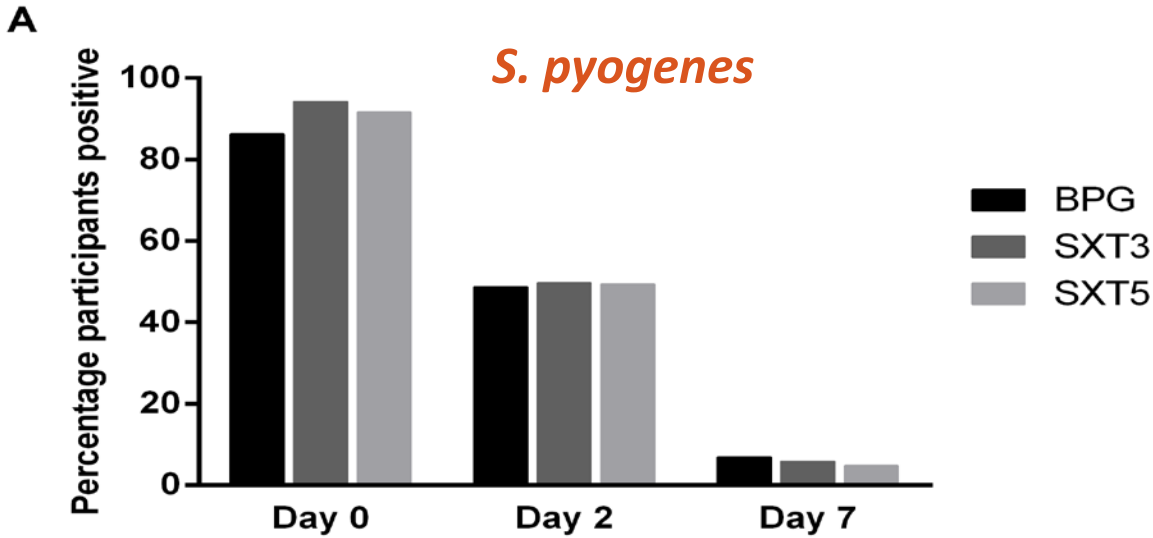
Image B 12941

Day 7 results

Outcome	BPG (n=165)	SXT3 (n=175)	SXT5 (n=168)	SXT pooled (n=343)
Success (mITT)	133/156 85.3%	147/173 85.0%	136/161 84.5%	284/334 84.7%
Success (per-protocol)	124/146 84.9%	135/159 84.9%	129/151 85.4%	264/310 85.2%
Clinical success	154/156 98.7%	171/173 98.8%	161/161 100.0%	332/334 99.4%

Non-inferiority demonstrated





GAS clearance
predicts treatment
success,
OR 5.2

BPG 49/160 (30.6%)

- Injection site pain at 48 hours
- Abscess requiring drainage
- No anaphylaxis

SXT 5/343 (1.5%)

- Vomiting
- Rash
- No Stevens-Johnson syndrome

Short-course oral co-trimoxazole versus intramuscular benzathine benzylpenicillin for impetigo in a highly endemic region: an open-label, randomised, controlled, non-inferiority trial



Asha C Bowen, Steven Y C Tong, Ross M Andrews, Irene M O'Meara, Malcolm I McDonald, Mark D Chatfield, Bart J Currie, Jonathan R Carapetis

Summary

Background Impetigo affects more than 110 million children worldwide at any one time. The major burden of disease is in developing and tropical settings where topical antibiotics are impractical and lead to rapid emergence of

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OTHER STUDIES

Clinda vs TMP/SMX

- Abscess >5cm, cellulitis
- Not impetigo
- Cellulitis 50%

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Clindamycin versus Trimethoprim–Sulfamethoxazole
for Uncomplicated Skin Infections

. Miller, M.D., M.P.H., Robert S. Daum, M.D., C.M., C. Buddy Creech, M.D., M.P.H., David Youn
Michele D. Downing, R.N., M.S.N., Samantha J. Eells, M.P.H., Stephanie Pettibone, B.S.,
Rebecca J. Hoagland, M.S., and Henry F. Chambers, M.D., for the DMID 07-0051 Team*

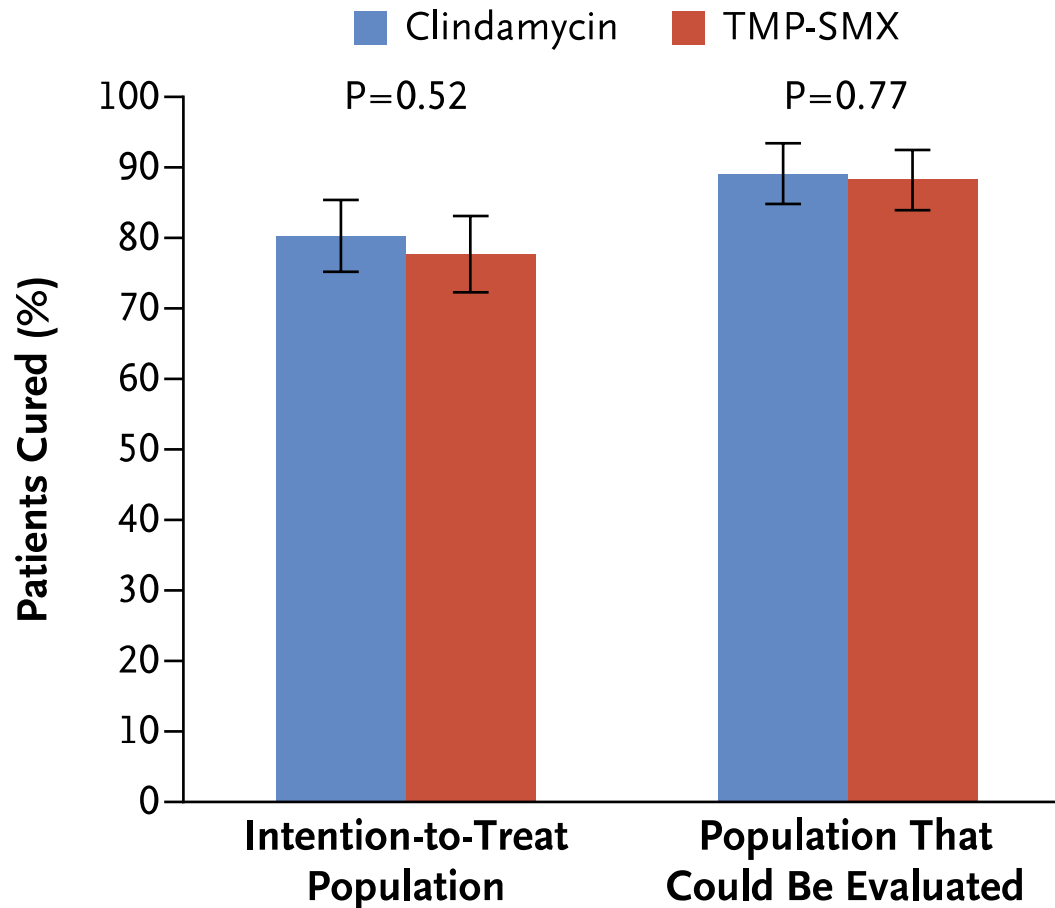
Clindamycin 300mg 3x/d for 10 days

Vs

TMP/SMX 160/800mg 2x/d for 10 days

Clinda vs TMP/SMX

524 patients – 264 clinda; 260 TMP/SMX



Clinda vs TMP/SMX

Expert opinion and empirical data^{21,22} suggest that cellulitis is most commonly caused by *Streptococcus pyogenes*. Our findings are provocative, because TMP-SMX has been considered a poor empirical choice for the treatment of cellulitis. Recent data show that *S. pyogenes* strains may be TMP-SMX–susceptible if low-concentration thymidine agar is used for testing.²³ Our results showing that TMP-SMX and clindamycin have similar efficacy in patients with cellulitis are consistent with these in vitro data.

TMP/SMX vs placebo

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- Abscess >2cm, drained

ORIGINAL ARTICLE

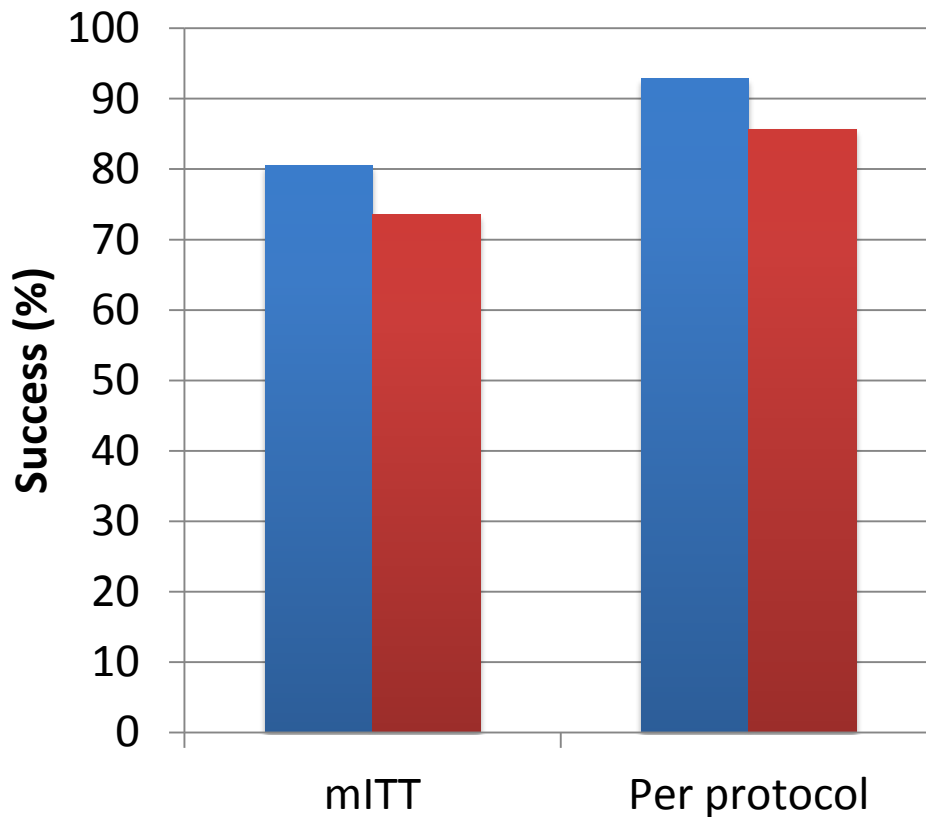
Trimethoprim–Sulfamethoxazole versus Placebo for Uncomplicated Skin Abscess

David A. Talan, M.D., William R. Mower, M.D., Ph.D.,
Anusha Krishnadasan, Ph.D., Fredrick M. Abrahamian, D.O.,
Frank Lovecchio, D.O., M.P.H., David J. Karras, M.D., Mark T. Steele, M.D.,
Richard E. Rothman, M.D., Ph.D., Rebecca Hoagland, M.S.,
and Gregory J. Moran, M.D.

TMP/SMX 320/1600mg 2x/d for 7 days
Vs
Placebo

TMP/SMX vs placebo

1247 patients – 617 TMP/SMX; 630 placebo



	Difference (%)	P
mITT	6.9 (2.1-11.7)	0.005
Per protocol	7.2 (3.2-11.2)	<0.001

■ TMP/SMX
■ Placebo

TMP/SMX vs clindamycin

- Wound infections

Clinical Infectious Diseases

MAJOR ARTICLE



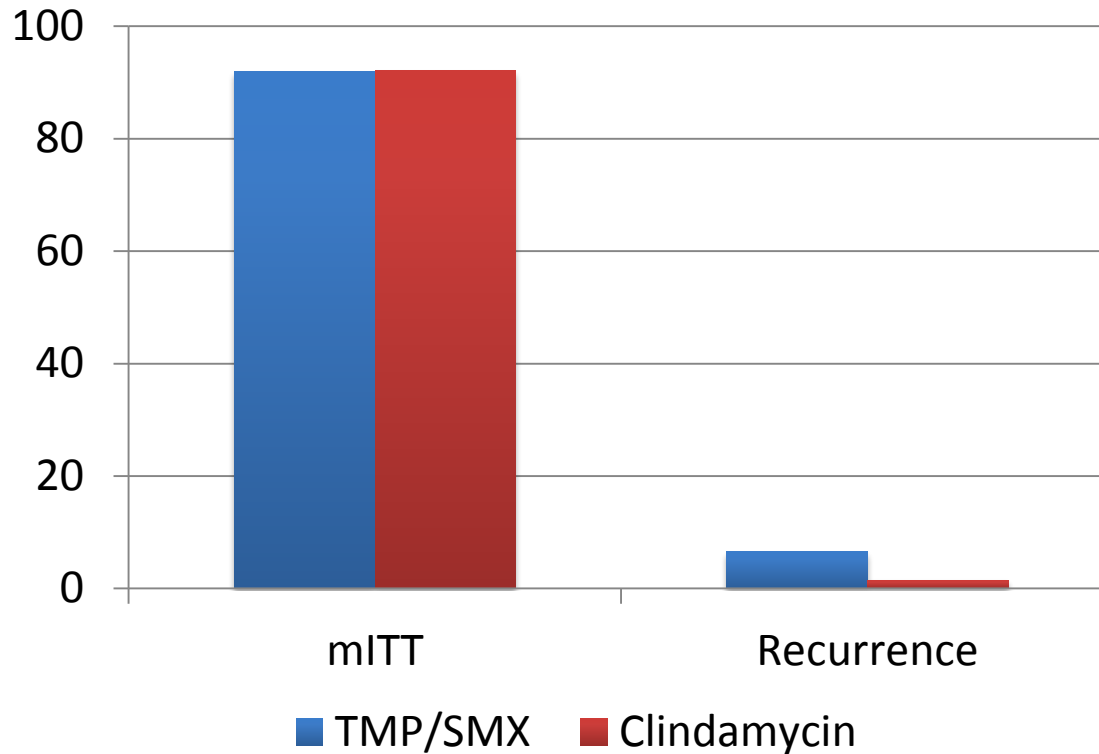
TMP/SMX 320/1600mg 2x/d for 7 days

Vs

Clindamycin 300mg 4x/d for 7 days

TMP/SMX vs clindamycin

401 patients – 198 TMP/SMX; 203 clindamycin



- Same cure at 7-14 days
- Higher recurrence in TMP/SMX group

TMP/SMX

- Several trials now demonstrating efficacy in SSTI – including with GAS
- Included as alternative to IM BPG in CARPA and TG: Antibiotic
- Could it be used at a broad population level?

ANTIMICROBIAL RESISTANCE

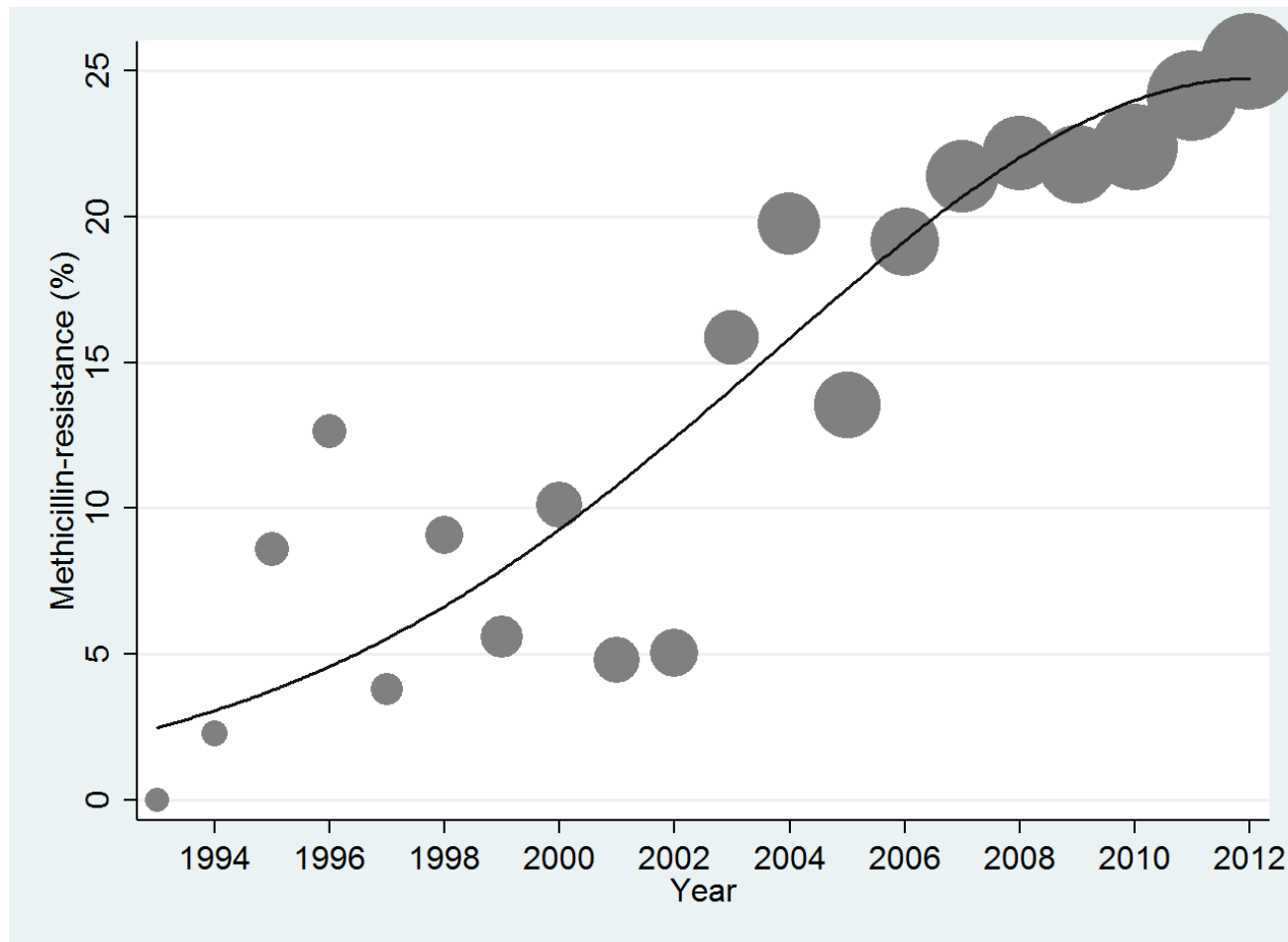
Antimicrobial resistance is not an issue with GAS at this stage...

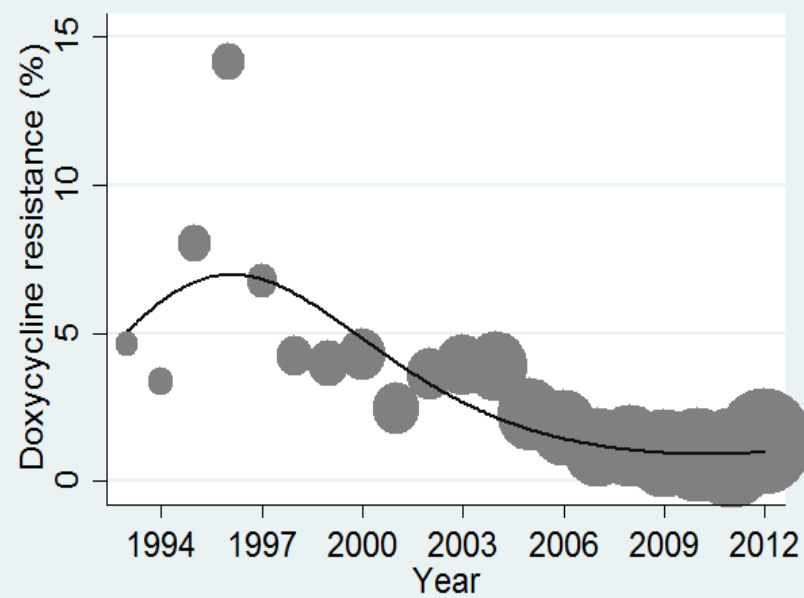
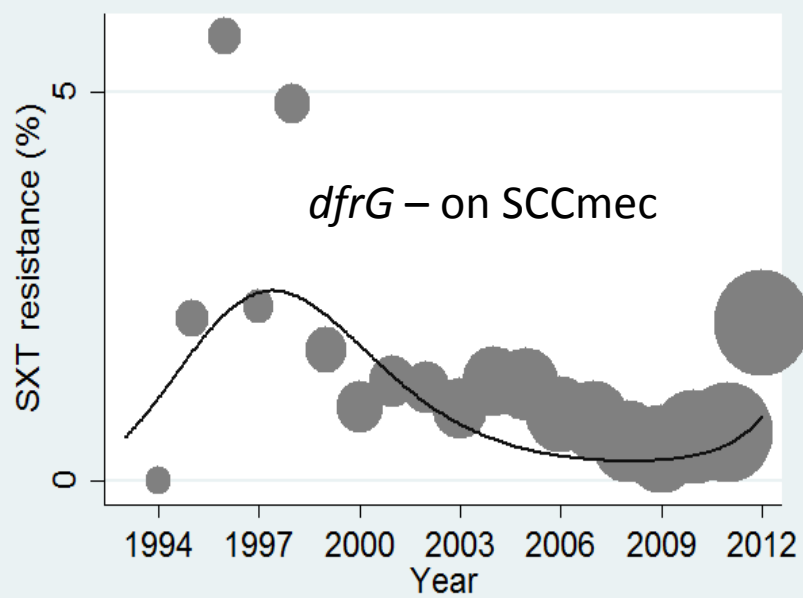
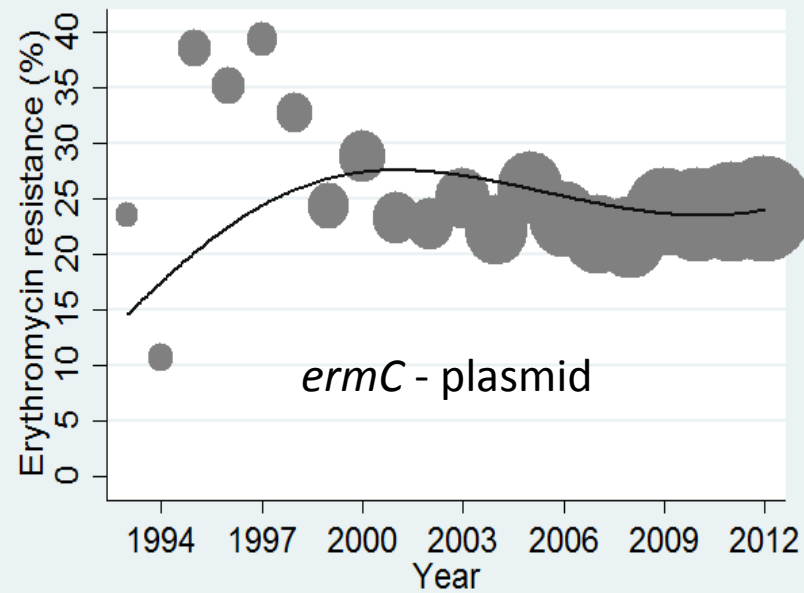
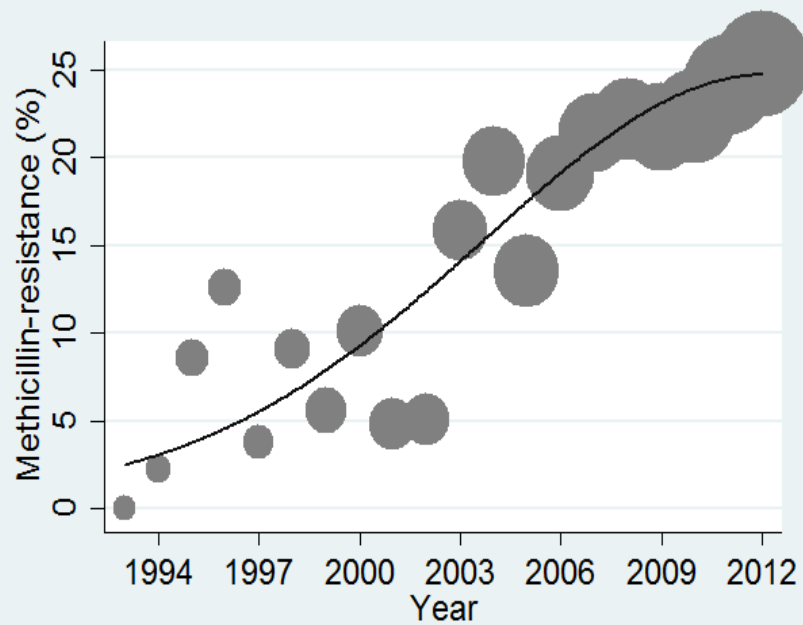
But it's not just about impetigo and scabies...

Overall high burden of SSTI

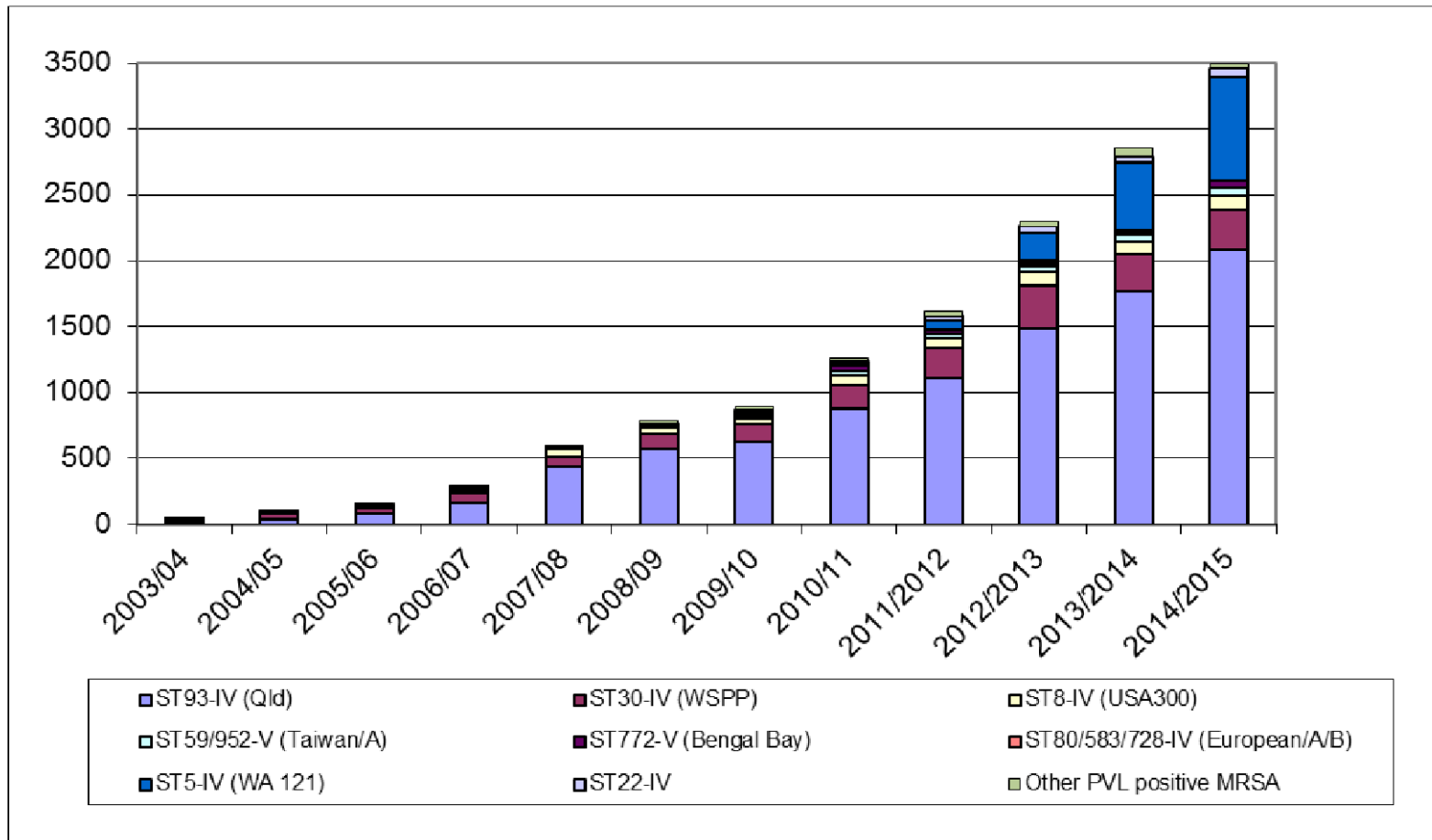
- Central Australia: **2%** annual incidence of hospitalization due to SSTI in Indigenous population¹
- Two remote communities: **5%** annual incidence of complicated SSTI²

S. aureus in the community

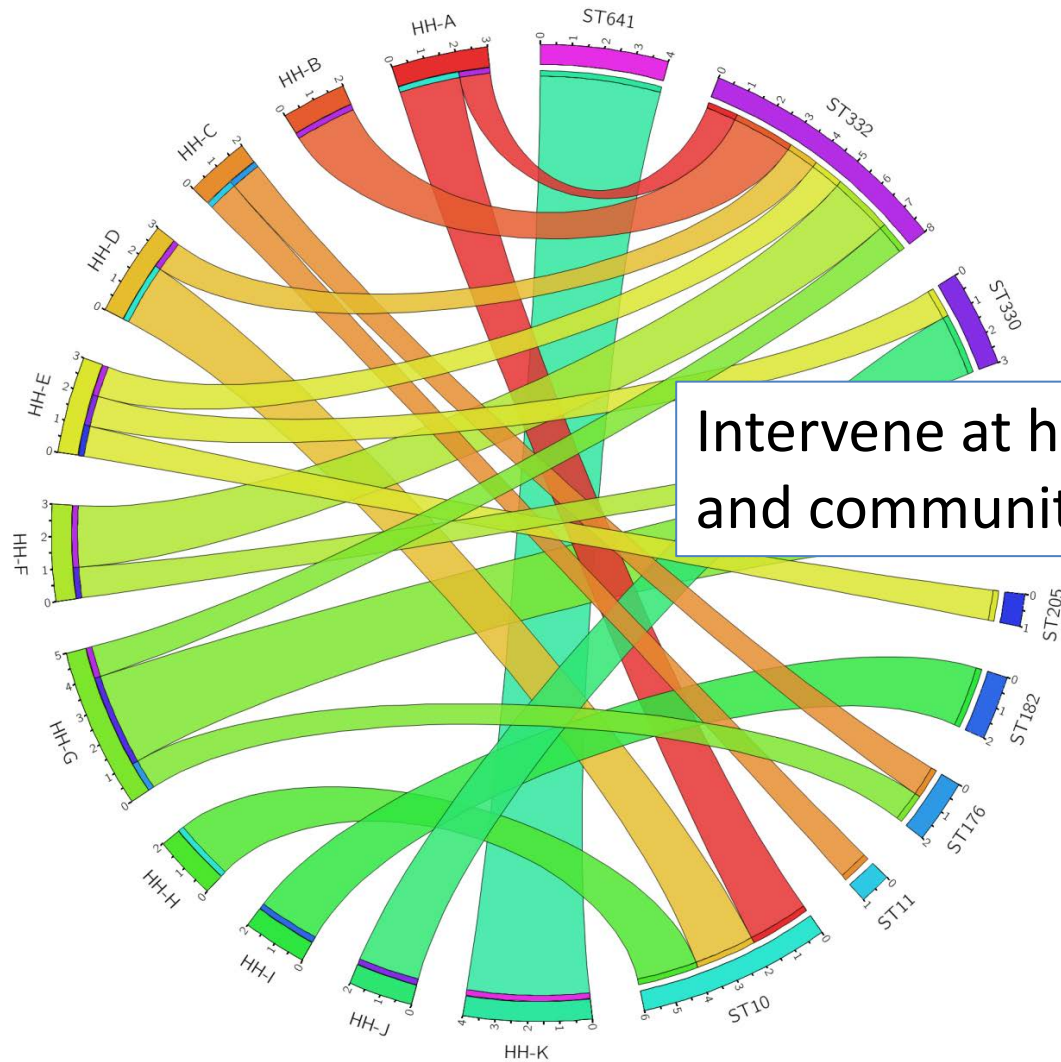




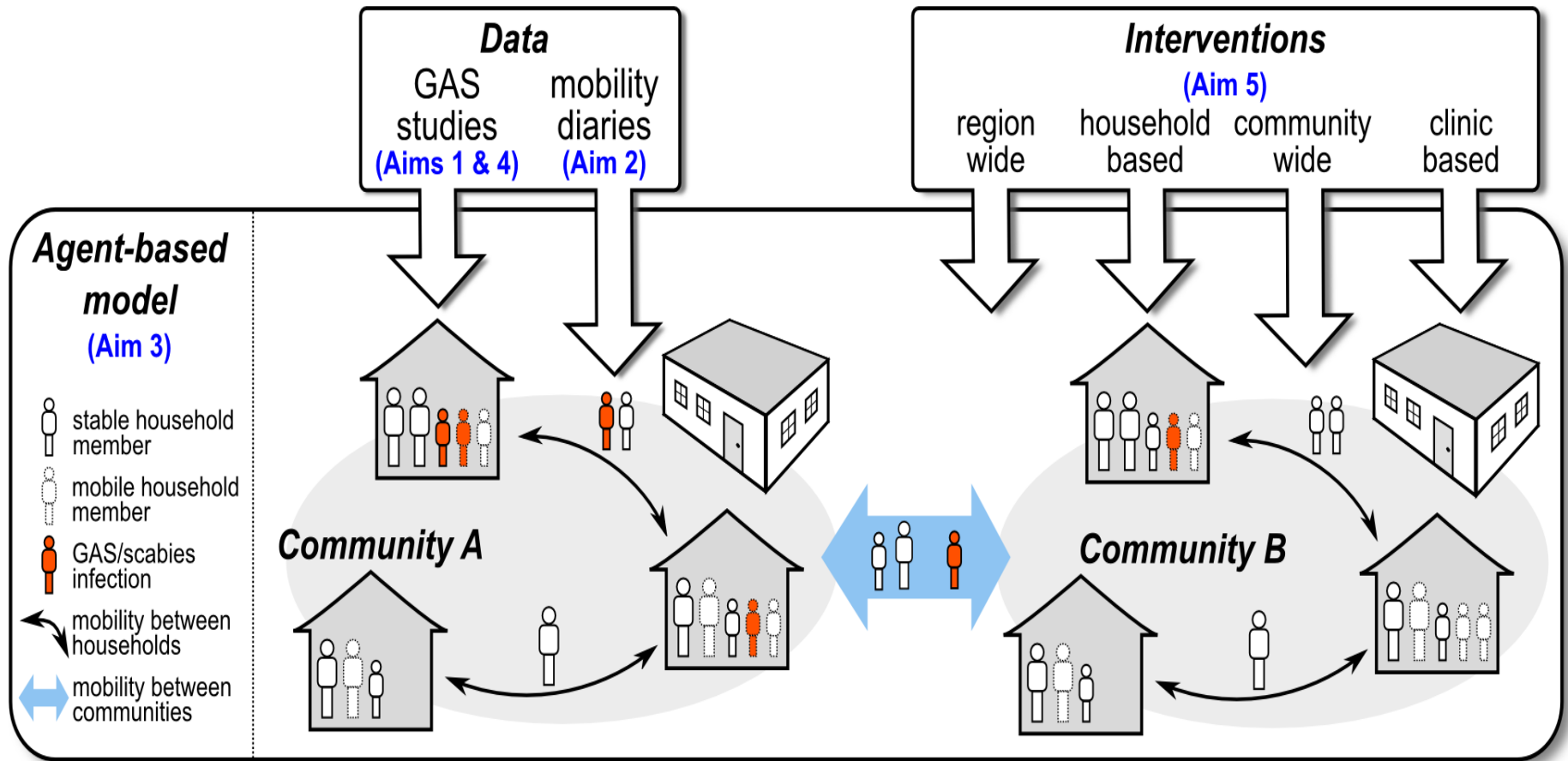
ST5 PVL+ SXT R



Understanding transmission

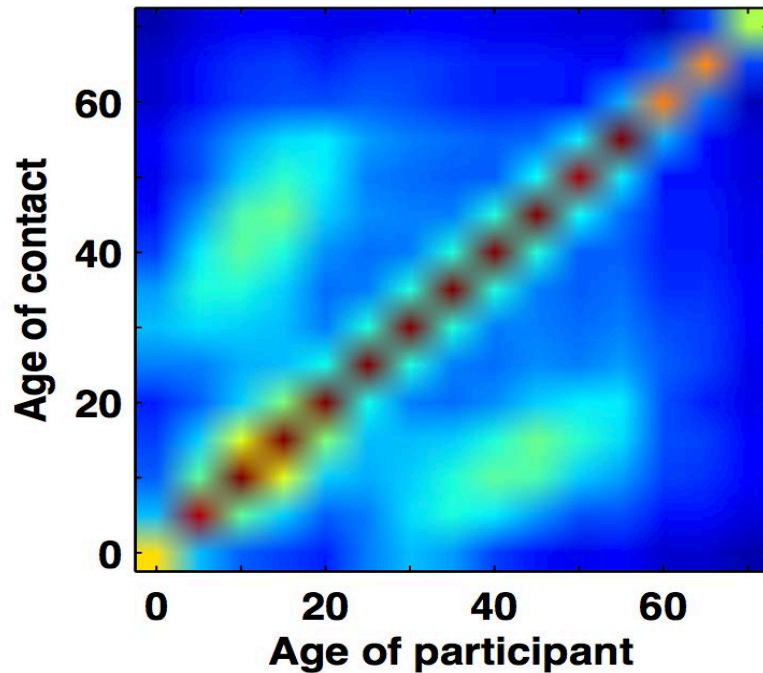


GAS modelling grant

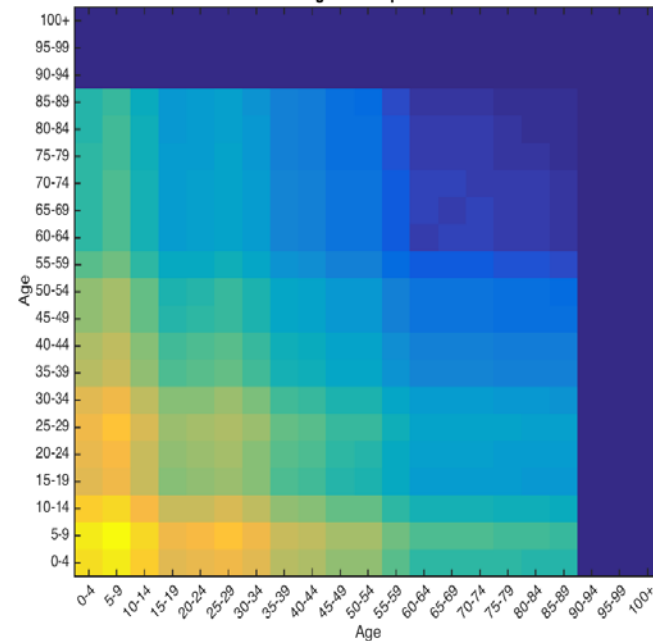


Household structures

Australian households



Indigenous Population



GAS modelling grant



- Compartmental models
 - Previous collected datasets
 - One Disease community surveys
- Population mobility
 - Census data
 - Social media / GPS
- Agent based models
- WGS to aid in parameterizing models

Conclusions

- We have interventions that work
 - BPG, cotrimoxazole, ivermectin MDA
- Some concerns
 - Resistance, applicability to our setting
 - Sustainability and translation
- Continuing to build evidence base and surveillance