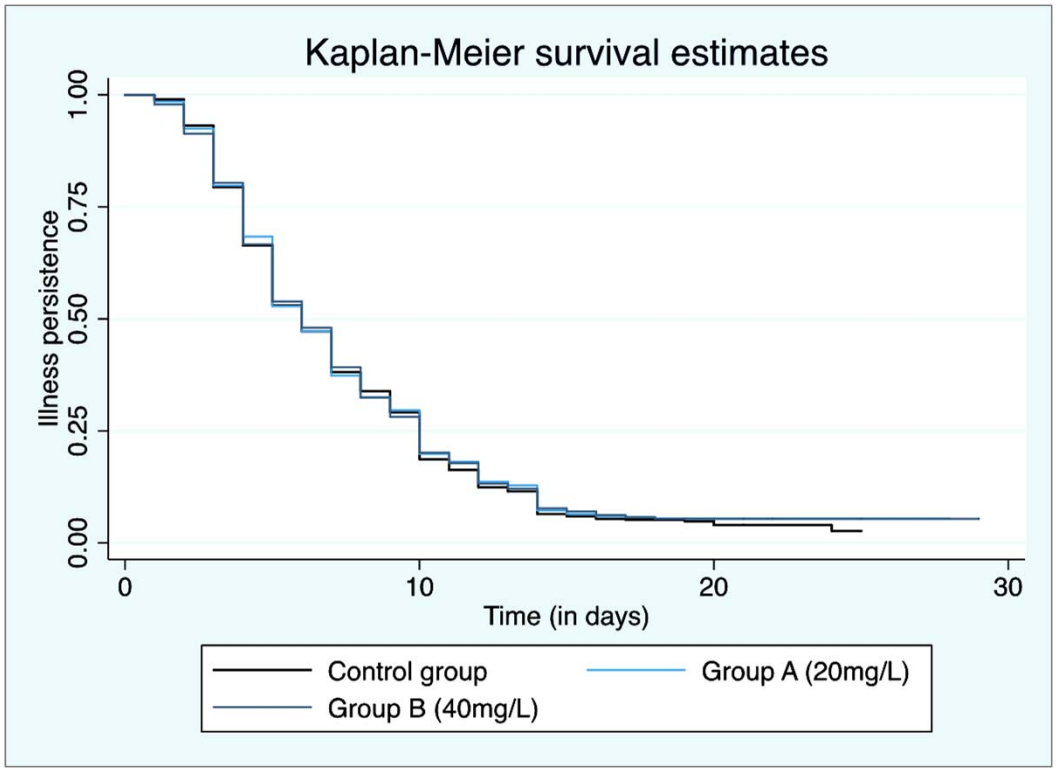
C-Reactive Protein point of care test for the management of febrile patients in primary care in Southeast Asia

Dr Rachel Greer & Dr Thomas Althaus

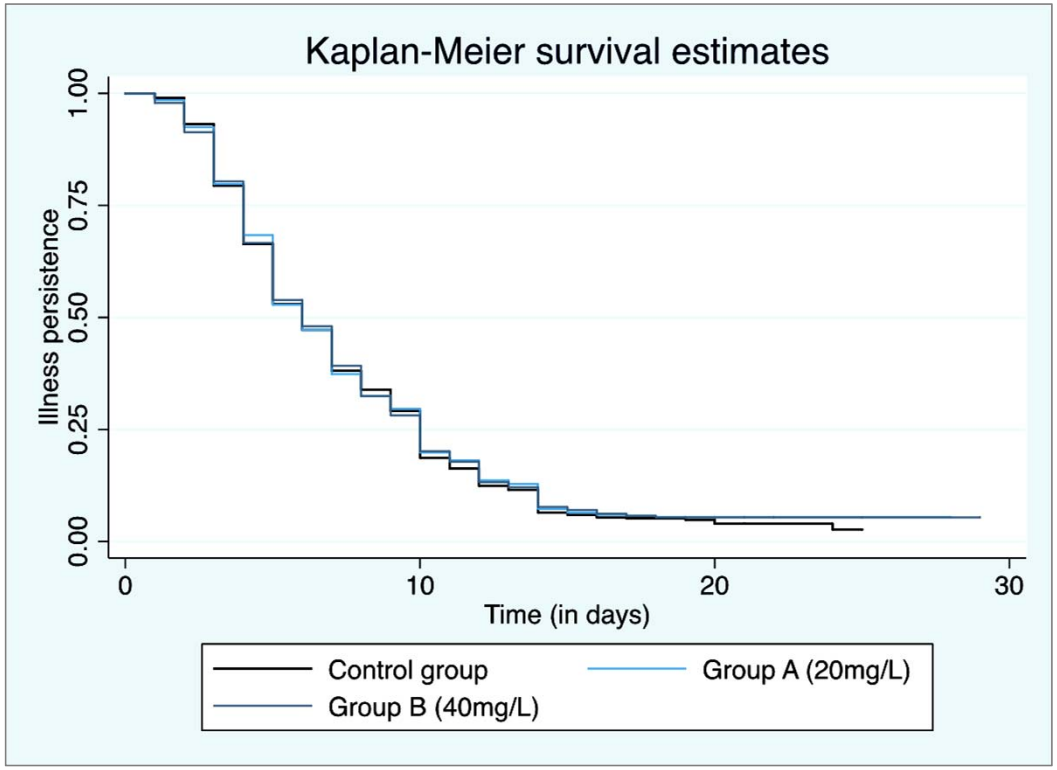
JITMM, Bangkok, Thailand
6th December 2017

Impact of CRP testing on clinical recovery

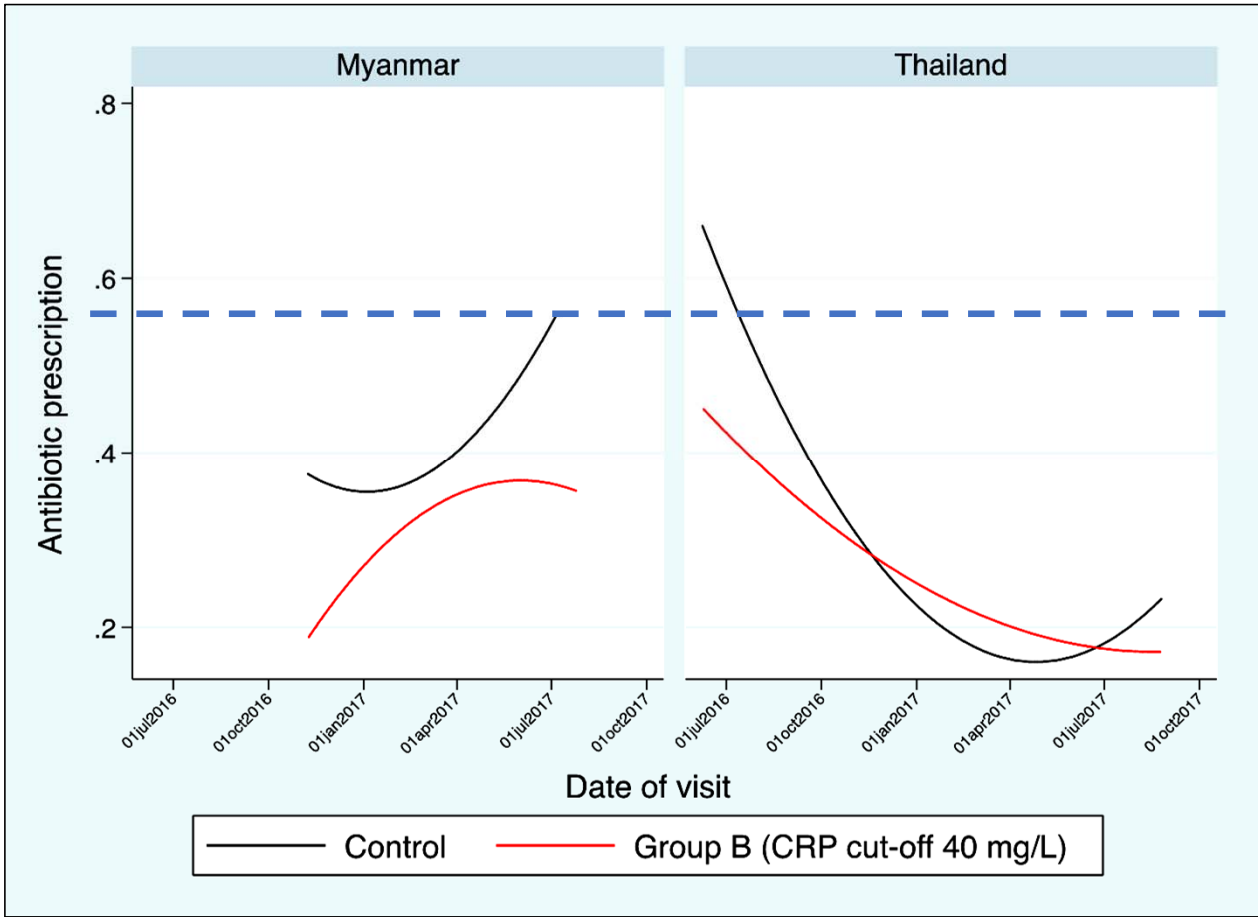


Impact of CRP testing on clinical recovery

Illness resolution at Day 5	Control group	CRP group	*P-value*
All CRP groups combined	491 (60.8)	983 (61.3)	0.960
CRP Group A (20mg/L)		495 (61.6)	0.752
CRP Group B (40mg/L)		488 (61.0)	0.821
Illness resolution at Day 14	**Control group**	**CRP group**	***P-value***
All CRP groups combined	738 (91.5)	1,451 (90.5)	0.183
CRP Group A (20mg/L)		718 (89.4)	0.312
CRP Group B (40mg/L)		733 (91.6)	0.181



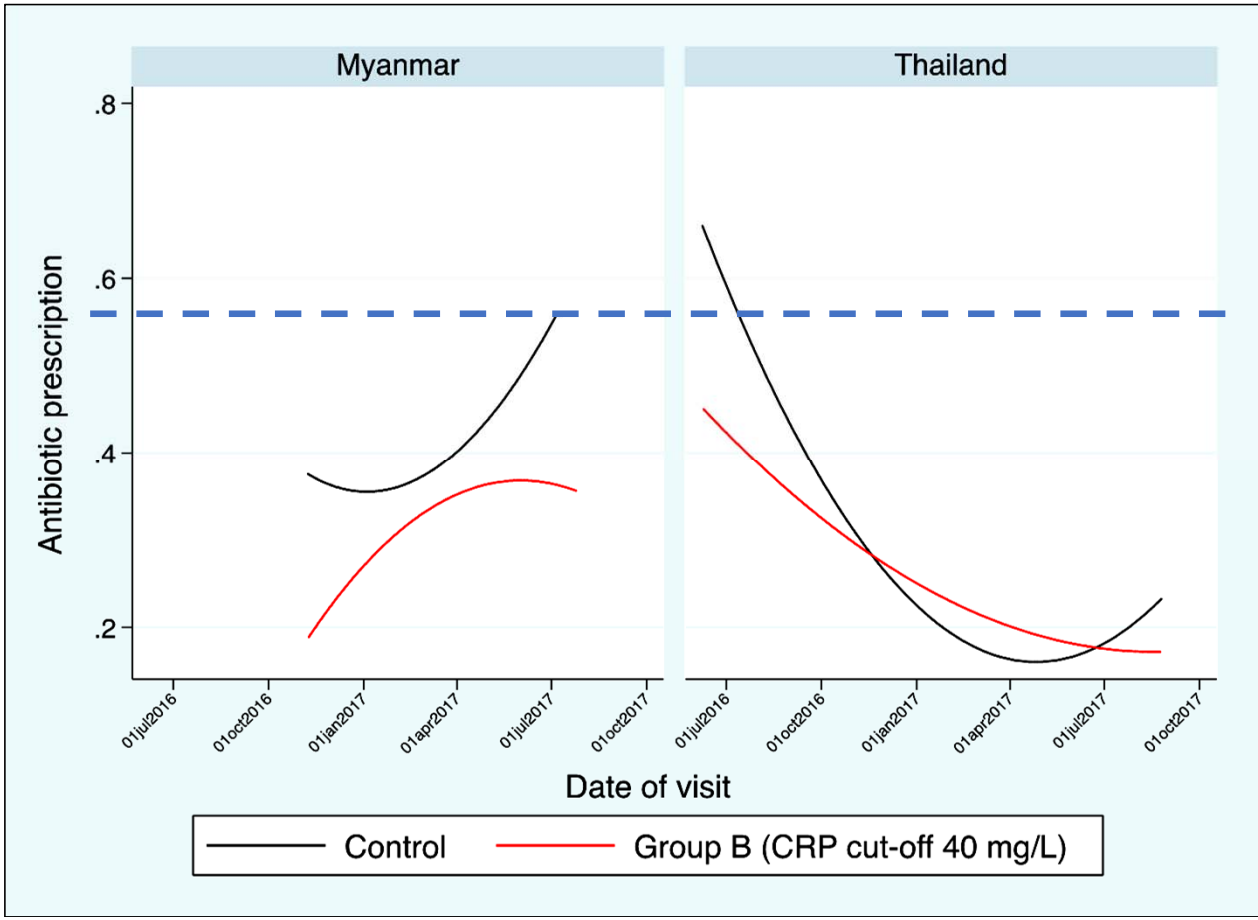
Trend antibiotic prescription over time – Group B (CRP 40 mg/L) *versus* Control



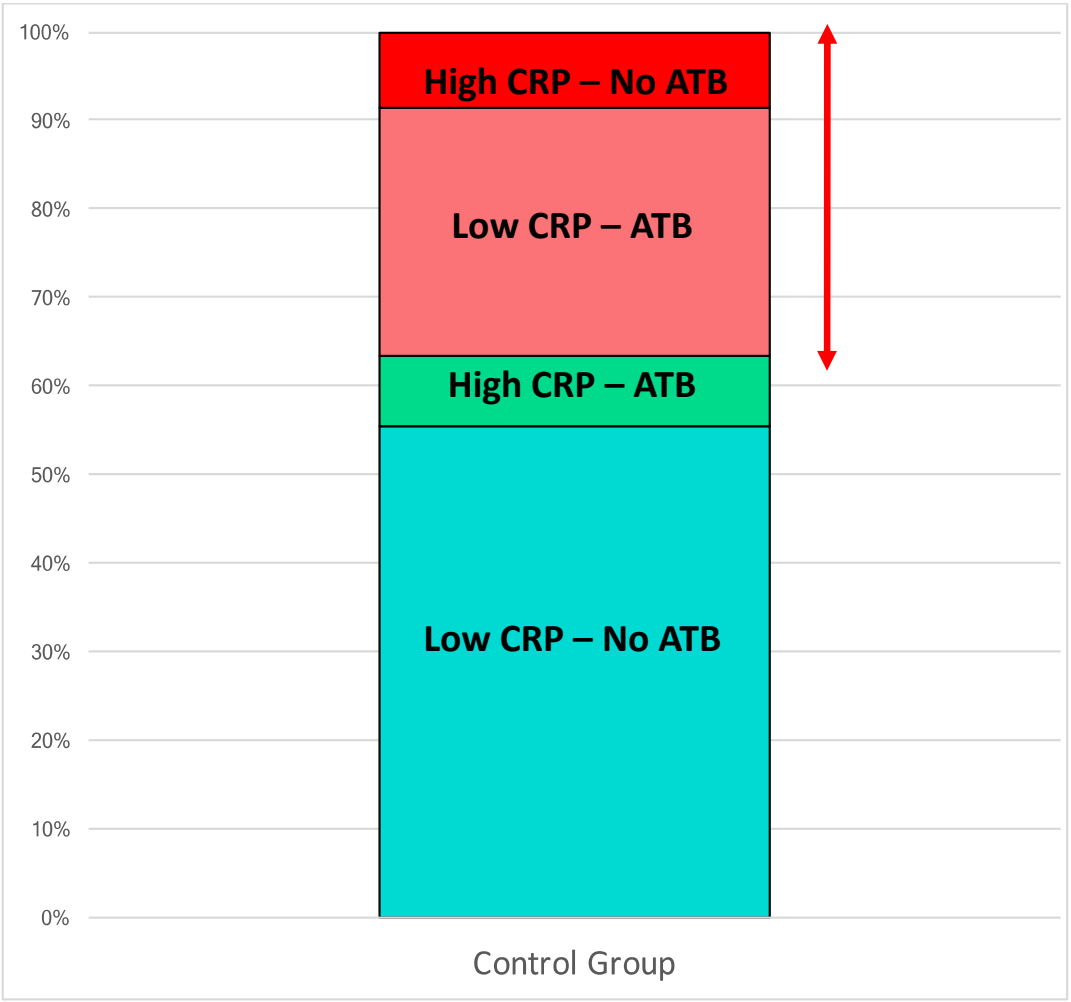
Trend antibiotic prescription over time – Group B (CRP 40 mg/L) *versus* Control

Possible effects of the study

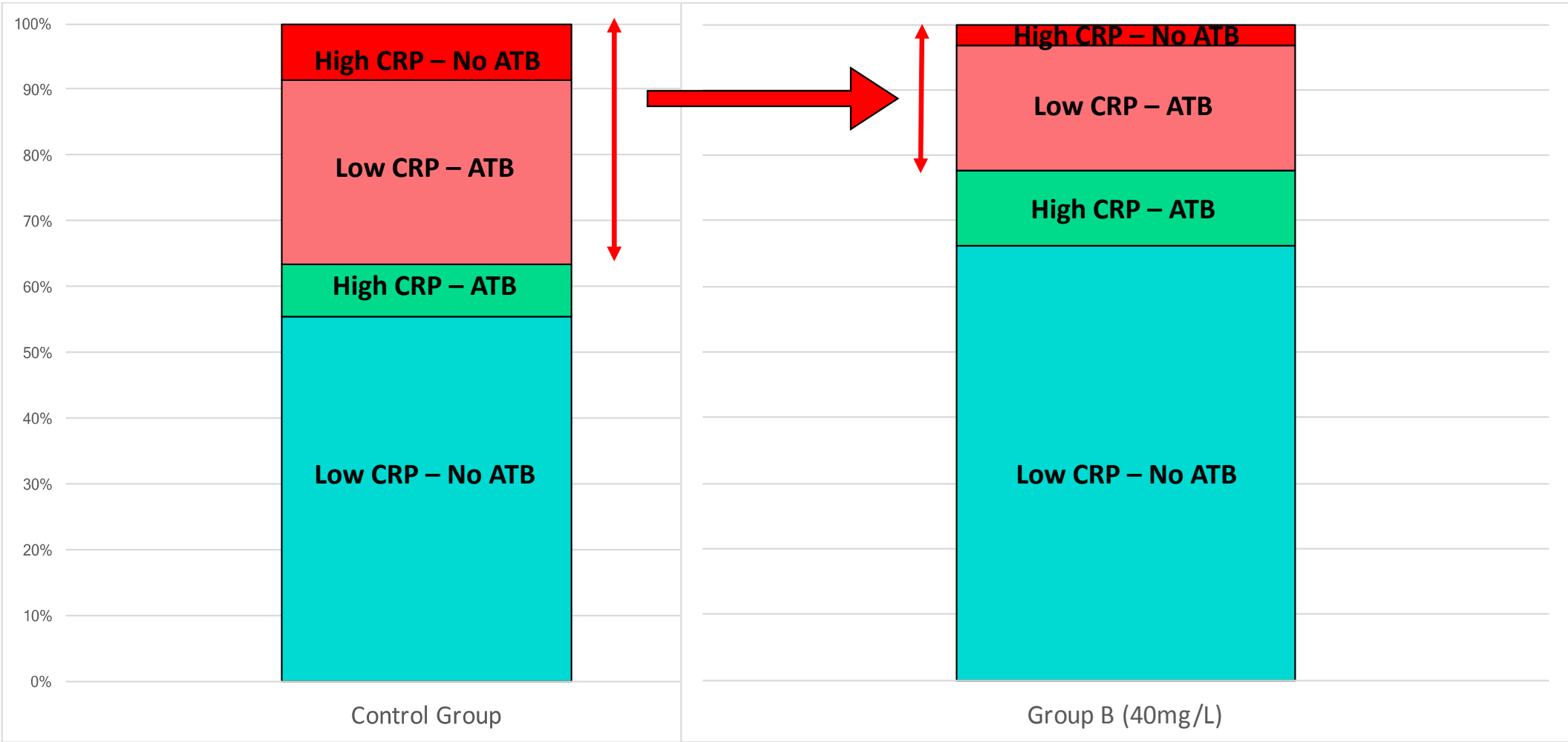
- Better awareness of overall need to improve prescribing
- Contamination – health workers learn that most patients have low CRP and therefore more willing to prescribe less in controls
- Hawthorne effect



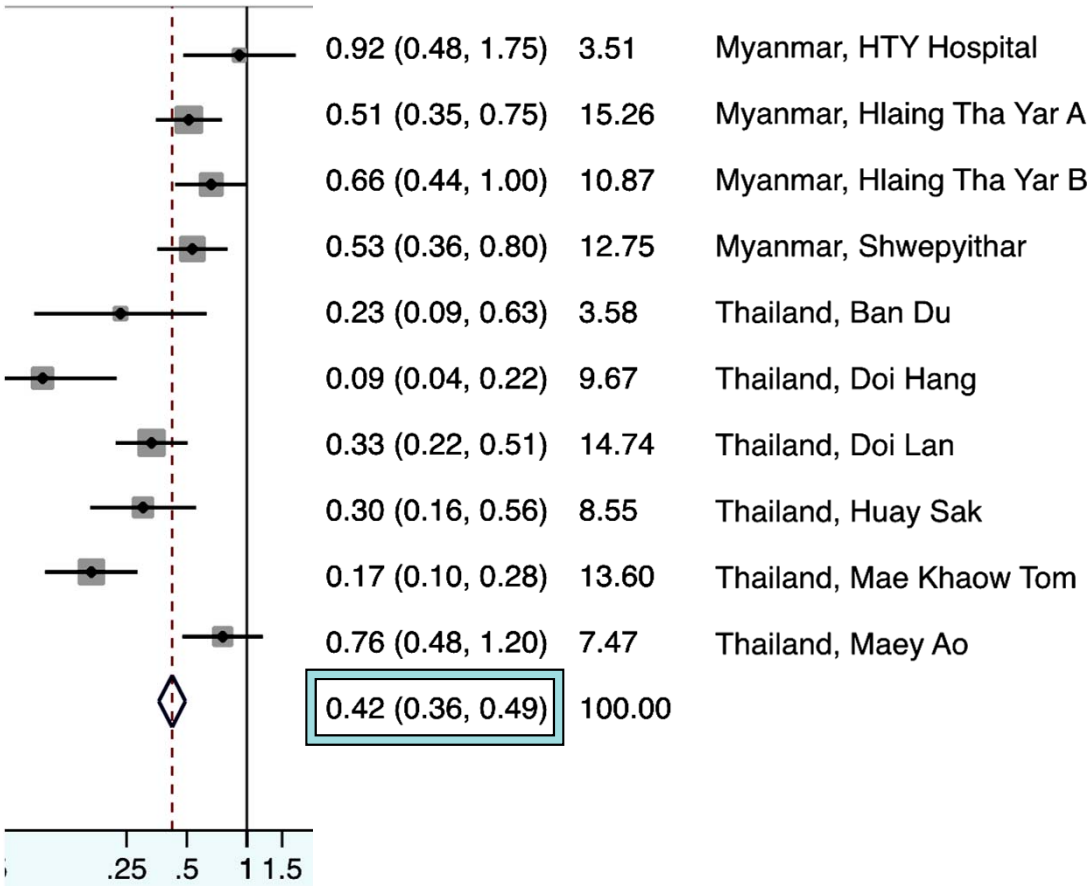
Reducing & Targeting



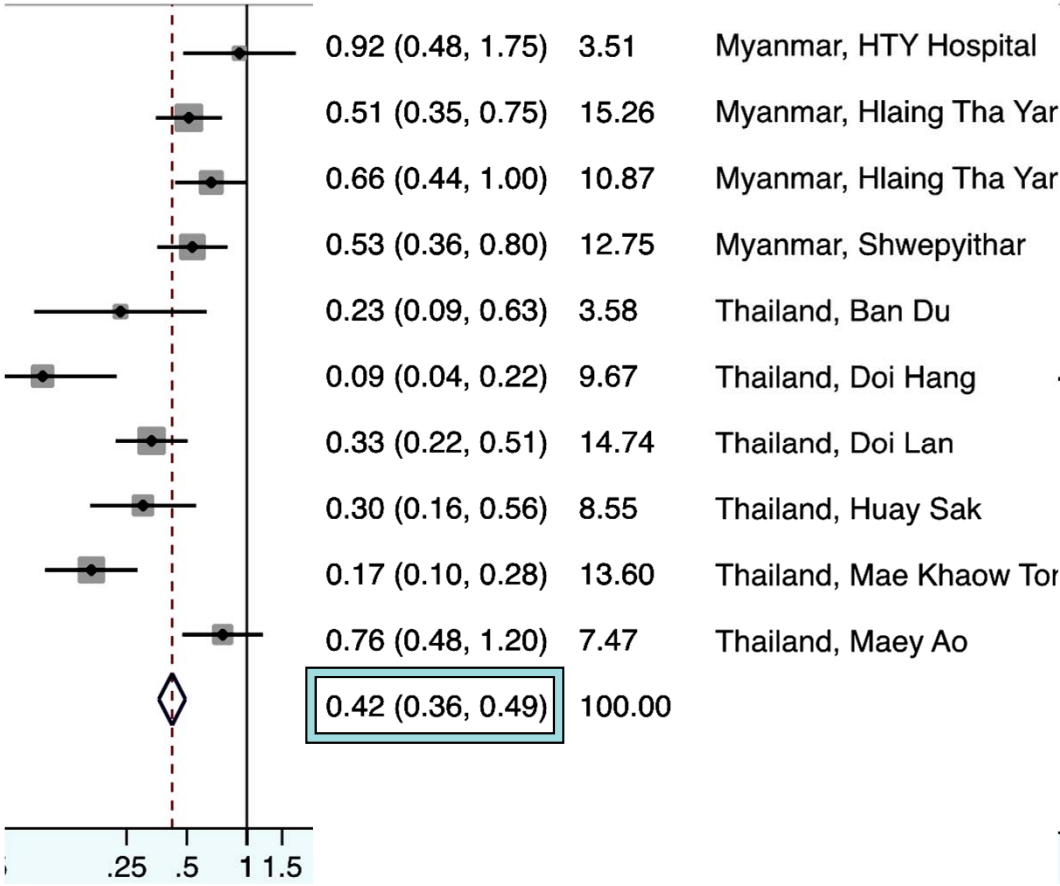
Reducing & Targeting



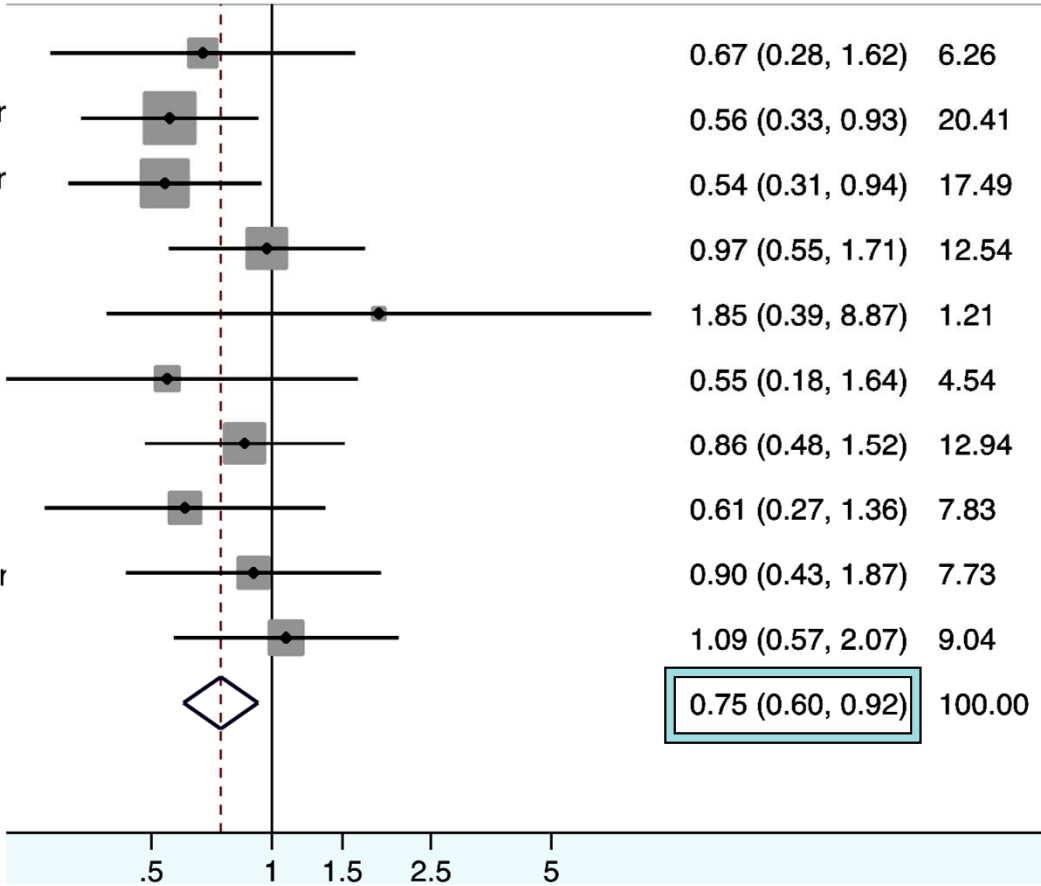
Comparison between group **B** and *Baseline*



Comparison between group **B** and *Baseline*



Comparison between group **B** and *controls*



Preliminary conclusions

- CRP testing lead to a significant reduction of antibiotic prescription compared with the Baseline with an adjusted OR 0.42 [0.36-0.49]

Preliminary conclusions

- CRP testing lead to a significant reduction of antibiotic prescription compared with the Baseline with an adjusted OR 0.42 [0.36-0.49]

- Using higher threshold was associated with higher reduction in prescribing than the Controls with an adjusted OR 0.75 [0.60-0.92]

Preliminary conclusions

- CRP testing lead to a significant reduction of antibiotic prescription compared with the Baseline with an adjusted OR 0.42 [0.36-0.49]

- Using higher threshold was associated with higher reduction in prescribing than the Controls with an adjusted OR 0.75 [0.60-0.92]

- The high threshold of 40mg/L did not impact the clinical outcome

Microbiology Research

2,410 febrile children & adults

Group **A**, 20mg/L

Group **B**, 40mg/L

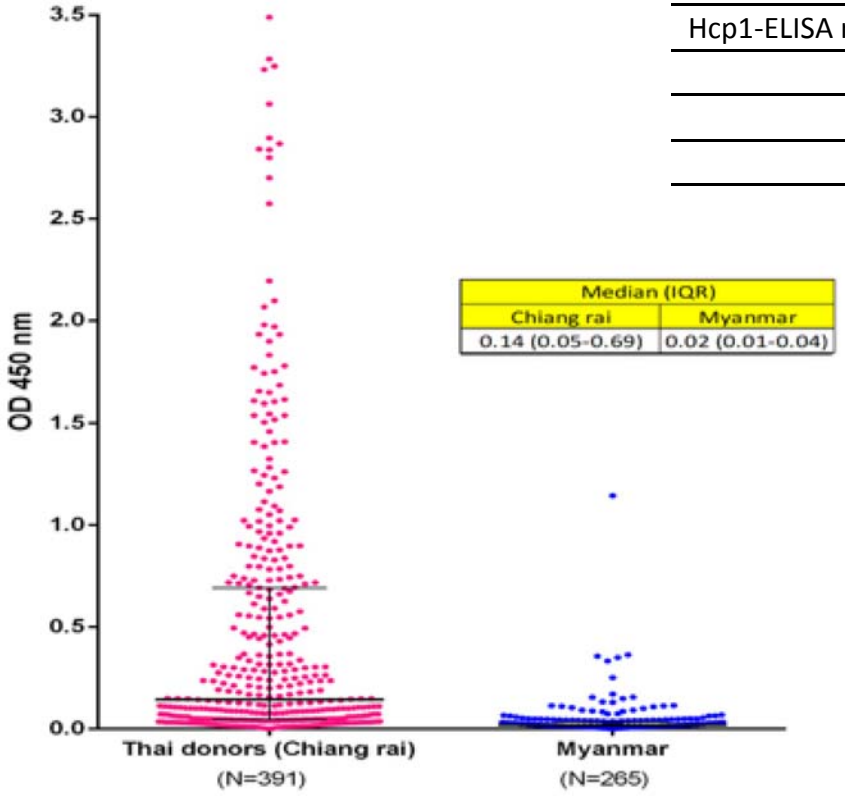
Group **C**, controls (n=807)

Blood, Respiratory & Urine samples

- ✓ **Key pathogens in the community**
- ✓ **Performance of CRP**
- ✓ **Innovative biomarkers & techniques**

1. Singleplex PCR
2. Multiplex Taqman Array Card (TAC)
3. ELISA
4. Proteomics…

Microbiology Research - preliminary findings on Melioidosis

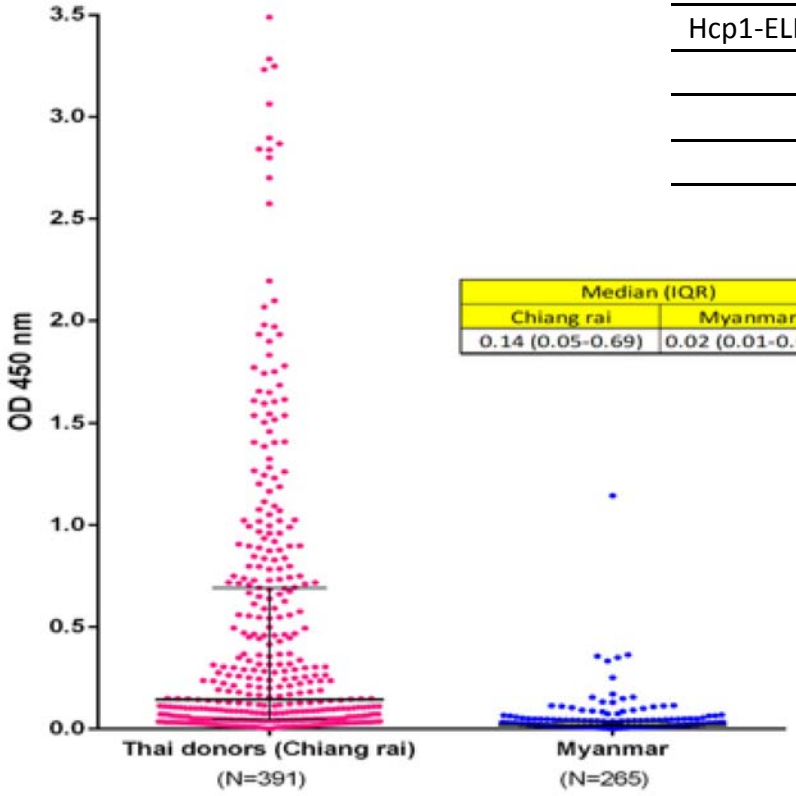


Hcp1-ELISA results (cut off OD >1.16)	Sera from Chiang rai	Sera from Myanmar	Total
Positive	51 (13%)	0	51
Negative	340 (87%)	265 (100%)	605
Total	391	265	656

Faculty of Tropical Medicine
MAHIDOL UNIVERSITY Wisdom of the Land

Pr. Narisara Chantratita
Phornpan (Deep)

Microbiology Research - preliminary findings on Melioidosis



Hcp1-ELISA results (cut off OD >1.16)	Sera from Chiang rai	Sera from Myanmar	Total
Positive	51 (13%)	0	51
Negative	340 (87%)	265 (100%)	605
Total	391	265	656

- ✓ Clinical presentation?
- ✓ CRP-levels?
- ✓ Hcp1-threshold in the region?

Faculty of Tropical Medicine
MAHIDOL UNIVERSITY Wisdom of the Land

Pr. Narisara Chantratita
Phornpan (Deep)

Social research: Case Report Form (CRF)

Social research: Case Report Form (CRF)

Attitude towards care overall

97% of the patients were satisfied with their care overall in both the control and intervention groups

Social research: Case Report Form (CRF)

Attitude towards care overall

97% of the patients were satisfied with their care overall in both the control and intervention groups

Attitudes toward CRP testing

81.8% of patients reported that CRP POCT made them feel more confident that antibiotics were needed or not needed for their illness

Social Research: preliminary findings (CRF)

Prior attending primary care

Patient's perspective

Healthcare type	Overall n=2,410	Myanmar n=1,228	Thailand n=1,182
Overall, n (%)	**1,372 (56.9)**	**918 (74.8)**	**454 (38.4)**
Same clinic	131 (9.6)	65 (7.1)	66 (14.5)
Another clinic	312 (22.7)	222 (24.2)	90 (19.8)
Pharmacy	755 (55)	615 (67)	140 (30.8)
Hospital	39 (2.8)	8 (0.9)	31 (6.8)
Community HW	6 (0.4)	2 (0.2)	4 (0.9)
Natural healer	129 (9.4)	7 (0.8)	122 (26.9)
Other	33 (2.4)	29 (3.2)	4 (0.9)

Social Research: preliminary findings (CRF)

Prior attending primary care

Patient's perspective

Healthcare type	Overall n=2,410	Myanmar n=1,228	Thailand n=1,182
Overall, n (%)	**1,372 (56.9)**	**918 (74.8)**	**454 (38.4)**
Same clinic	131 (9.6)	65 (7.1)	66 (14.5)
Another clinic	312 (22.7)	222 (24.2)	90 (19.8)
Pharmacy	755 (55)	615 (67)	140 (30.8)
Hospital	39 (2.8)	8 (0.9)	31 (6.8)
Community HW	6 (0.4)	2 (0.2)	4 (0.9)
Natural healer	129 (9.4)	7 (0.8)	122 (26.9)
Other	33 (2.4)	29 (3.2)	4 (0.9)

Social Research: preliminary findings (CRF)

Prior attending primary care

Patient's perspective

Healthcare type	Overall n=2,410	Myanmar n=1,228	Thailand n=1,182
Overall, n (%)	**1,372 (56.9)**	**918 (74.8)**	**454 (38.4)**
Same clinic	131 (9.6)	65 (7.1)	66 (14.5)
Another clinic	312 (22.7)	222 (24.2)	90 (19.8)
Pharmacy	755 (55)	615 (67)	140 (30.8)
Hospital	39 (2.8)	8 (0.9)	31 (6.8)
Community HW	6 (0.4)	2 (0.2)	4 (0.9)
Natural healer	129 (9.4)	7 (0.8)	122 (26.9)
Other	33 (2.4)	29 (3.2)	4 (0.9)

Drug type	Overall n=2,410	Myanmar n=1,228	Thailand n=1,182
Overall, n (%)	**1,372 (56.9)**	**918 (74.8)**	**454 (38.4)**
Antibiotic	126 (9.2)	61 (6.6)	65 (14.3)
Paracetamol	1,015 (74)	620 (67.5)	395 (87)
Anti-inflammatory	42 (3.1)	28 (3.1)	14 (3.1)
Antitussive Anti-histaminic	134 (9.8)	30 (3.3)	104 (22.9)
Other	219 (16)	152 (16.6)	67 (14.8)

Social Research: preliminary findings (CRF)

Prior attending primary care

Patient's perspective

Healthcare type	Overall n=2,410	Myanmar n=1,228	Thailand n=1,182
Overall, n (%)	**1,372 (56.9)**	**918 (74.8)**	**454 (38.4)**
Same clinic	131 (9.6)	65 (7.1)	66 (14.5)
Another clinic	312 (22.7)	222 (24.2)	90 (19.8)
Pharmacy	755 (55)	615 (67)	140 (30.8)
Hospital	39 (2.8)	8 (0.9)	31 (6.8)
Community HW	6 (0.4)	2 (0.2)	4 (0.9)
Natural healer	129 (9.4)	7 (0.8)	122 (26.9)
Other	33 (2.4)	29 (3.2)	4 (0.9)

Drug type	Overall n=2,410	Myanmar n=1,228	Thailand n=1,182
Overall, n (%)	**1,372 (56.9)**	**918 (74.8)**	**454 (38.4)**
Antibiotic	126 (9.2)	61 (6.6)	65 (14.3)
Paracetamol	1,015 (74)	620 (67.5)	395 (87)
Anti-inflammatory	42 (3.1)	28 (3.1)	14 (3.1)
Antitussive Anti-histaminic	134 (9.8)	30 (3.3)	104 (22.9)
Other	219 (16)	152 (16.6)	67 (14.8)

Social Research: preliminary findings (KAP)

What is the impact of the CRP study?

Health worker's perspective

Antibiotic prescription	Overall	Pre-intervention
1-24% (few)	32.7	19.2
25-49% (minority)	32.7	23.1
50% (half)	12.7	23.1
51-75% (majority)	16.3	26.9
76-99% (most)	5.5	7.7

Social Research: preliminary findings (KAP)

What is the impact of the CRP study?

Health worker's perspective

Antibiotic prescription	Overall	Pre-intervention
1-24% (few)	32.7	19.2
25-49% (minority)	32.7	23.1
50% (half)	12.7	23.1
51-75% (majority)	16.3	26.9
76-99% (most)	5.5	7.7

>50% patients for whom an antibiotic would be prescribed

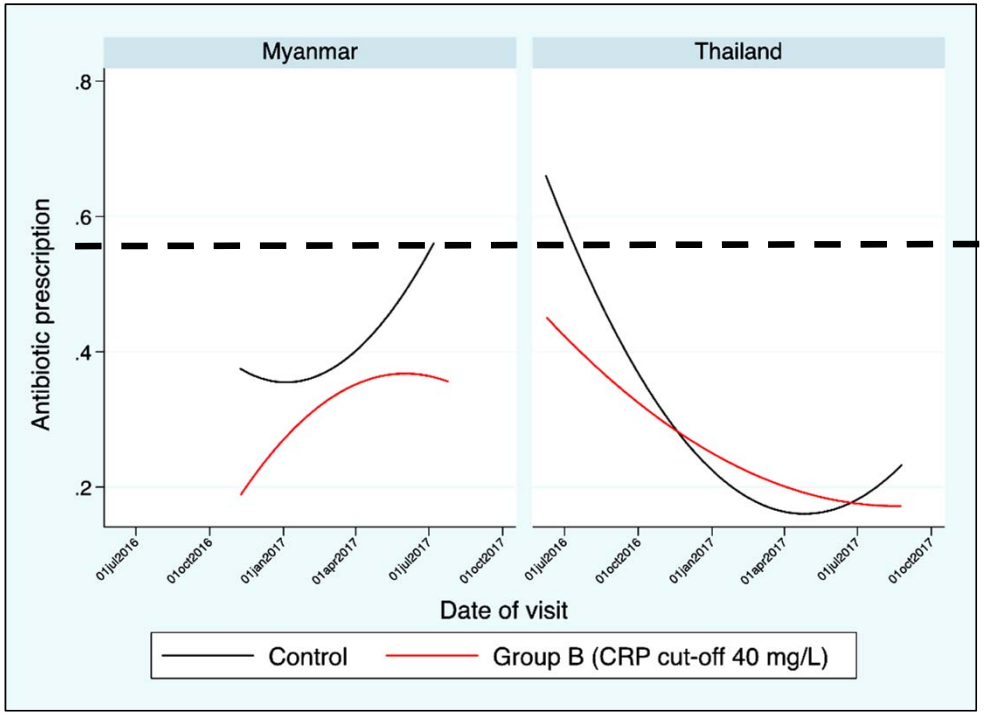
Social Research: preliminary findings (KAP)

What is the impact of the CRP study?

Health worker's perspective

Antibiotic prescription	Overall	Pre-intervention
1-24% (few)	32.7	19.2
25-49% (minority)	32.7	23.1
50% (half)	12.7	23.1
51-75% (majority)	16.3	26.9
76-99% (most)	5.5	7.7

> 50% of HW would be likely to prescribe an antibiotic to febrile patients

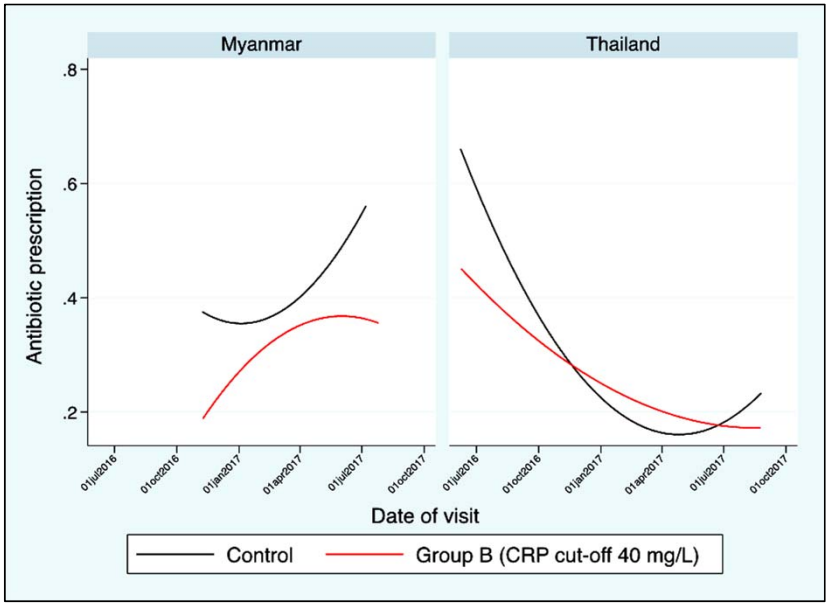


Social Research: preliminary findings (KAP)

What is the impact of the CRP study?

Health worker's perspective

Antibiotic prescription	Overall	Pre-intervention	Intervention
1-24% (few)	32.7	19.2	44.8
25-49% (minority)	32.7	23.1	41.4
50% (half)	12.7	23.1	3.5
51-75% (majority)	16.3	26.9	6.9
76-99% (most)	5.5	7.7	3.5



< 15% of HW would be likely to prescribe an antibiotic to febrile patients

Next steps: ICAT study

First large scale implementation of CRP testing in routine care in LMIC, expected start in 2018

Objectives:

- Assess the impact of CRP point of care testing on antibiotic prescriptions in a **routine** primary healthcare environment
- Evaluate the usability and acceptability of CRP testing for healthcare workers
- Assess the cost effectiveness of CRP testing

Design:

- Stepped wedge cluster randomised trial in ~60 facilities in Chiang Rai, ~80-100k patients
- **No research staff on site**, all data collected via routine records.

Summary points:

- Pragmatic design – minimal training, no strict algorithm

  → CRP testing still associated with halving in prescribing compared with baseline and significant difference to control group

Summary points:

- Pragmatic design – minimal training, no strict algorithm
- Benefit was not only reduction but better targeting of antibiotics

Summary points:

- Pragmatic design – minimal training, no strict algorithm
- Benefit was not only reduction but better targeting of antibiotics
- Reducing antibiotic prescription only through policy antibiotic supervision might not be safe

Summary points:

- Pragmatic design – minimal training, no strict algorithm
- Benefit was not only reduction but better targeting of antibiotics
- Reducing antibiotic prescription only through antibiotic supervision might not be safe
- Low cost & accurate CRP tests are commercially available

  → While higher reductions will be achieved with newer tests under evaluation, the incremental gains would have to justify the costs AND delays in postponing taking much needed action

Acknowledgements

MORU & MOCRU colleagues including members of administrative team, Clinical Trial Support Group, Microbiology, site study staff

- Frank Smithuis
- Myo Maung Maung Swe
- Ni Ni Tun
- James Heaton
- Josh Cohen
- Kyaw Soe
- Paul Newton
- Paul Turner
- Clare Ling
- Elizabeth Ashley
- Pieter Smit
- Arjen Dondorp
- Mavuto Mukaka & Sue Lee
- Lisa White
- Direk Limmathurotsakul
- Premjit Amornchai
- Janjira Thaipadungpanit
- Narisara Chantratita
- Stuart Blacksell
- Phaikyeong Cheah
- Nick Day
- Nick White
- Sabine Dittrich
- Do Thi Thuy Nga
- Heiman Wertheim
- Dr Supalert & Dr Daranee
- Rachel Greer
- Tri Wangrangsimakul
- Marco Haenssgen
- Nutcha Charoenboon

Thank you!!!

Thomas.a@tropmedres.ac
Yoel@tropmedres.ac
Rachel@tropmedres.ac