



# The impact of point of care C-Reactive Protein testing on antibiotic prescriptions and future studies in routine care

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# Background

- Antimicrobial resistance in Southeast Asia is a '*burgeoning and often neglected problem*' (WHO)
- Overuse and misuse of antibiotics can lead to AMR (ECDC, Laxminarayan et al.)
- Antibiotic prescriptions increase the risk of bacterial resistance for up to 1 year (Costelloe et al.)
- Majority of antibiotics prescribed in the community (ECDC)
- Challenging to clinically differentiate between bacterial and self-limiting infections

WHO (2014). "Antimicrobial Resistance. Global Report on Surveillance."

ECDC (2014). "Surveillance of antimicrobial consumption in Europe 2012."

Laxminarayan, R., et al. (2013). "Antibiotic resistance - the need for global solutions." The Lancet Infectious Diseases **13**(12): 1057-1098.

Costelloe, C., et al. (2010). "Effect of antibiotic prescribing in primary care on antimicrobial resistance in individual patients: systematic review and meta-analysis." BMJ **340**.

# C- reactive protein

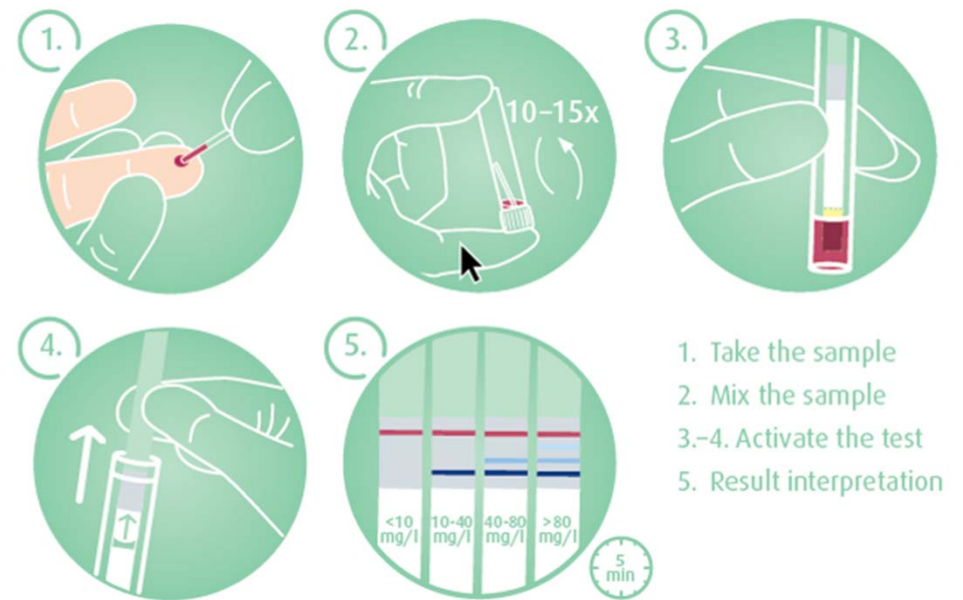
- C- reactive protein (CRP) is a biomarker of inflammation
- High sensitivity and moderate specificity for distinguishing viral from bacterial causes of fever in SE Asia (Lubell et al.)
- CRP is used to guide antibiotics for LRTI in Europe
- Vietnamese study found CRP use reduced antibiotics for non-severe acute respiratory tract infections (Do et al.)

Lubell, Y., et al. (2015). "Performance of C-reactive protein and procalcitonin to distinguish viral from bacterial and malarial causes of fever in Southeast Asia." BMC Infectious Diseases **15**: 511.

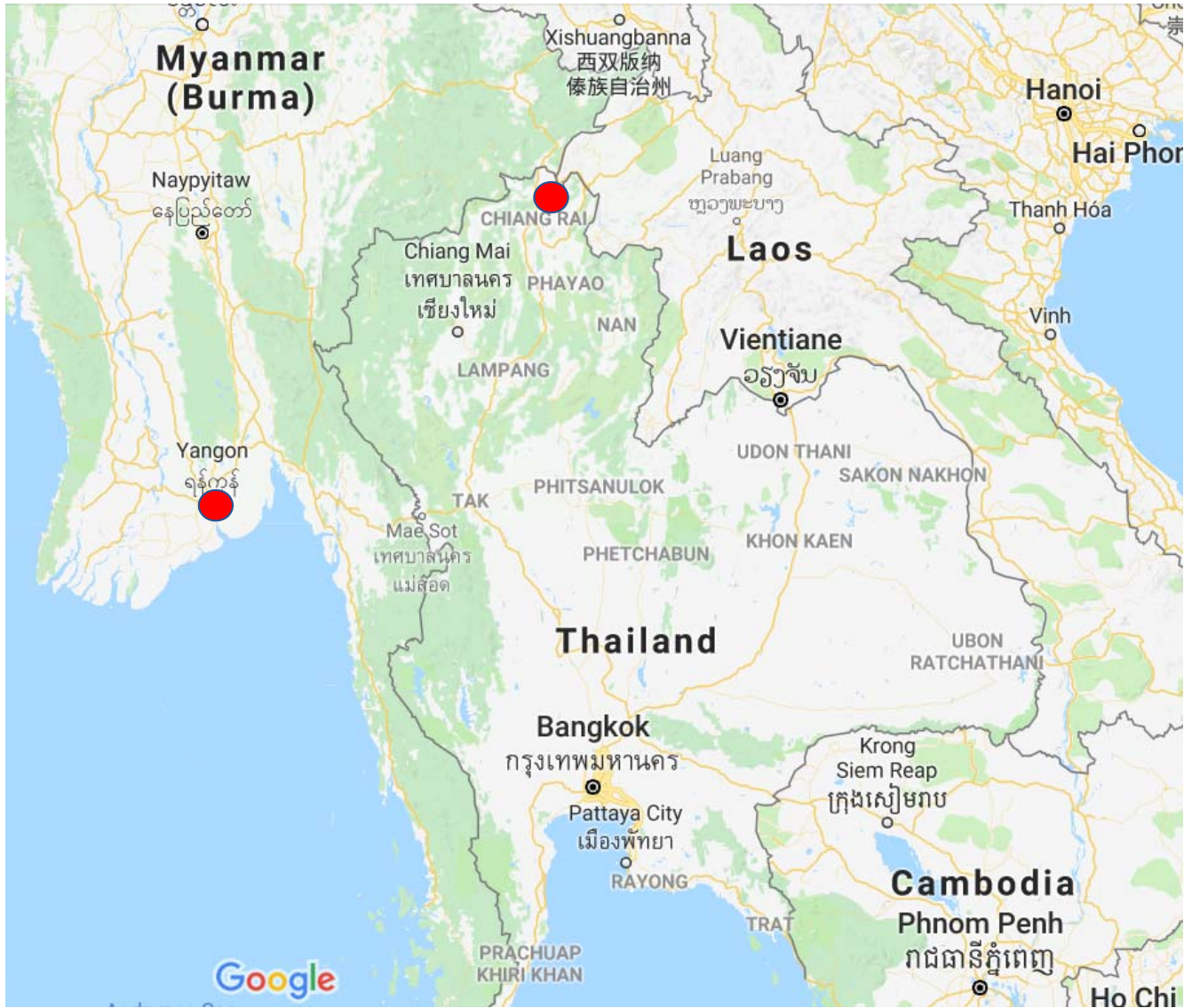
Do, N. T. T., et al. (2016). "Point-of-care C-reactive protein testing to reduce inappropriate use of antibiotics for non-severe acute respiratory infections in Vietnamese primary health care: a randomised controlled trial." The Lancet. Global Health **4**(9): e633-e641.

# CRP point of care tests

- Finger prick sample
- Take less than 5 minutes
- Cost < 1USD



Actim CRP test instructions



# Study context

## Hlaing Thar Ya, Yangon

- 3 clinics & 1 OPD in a district general hospital
- 3-4 doctors

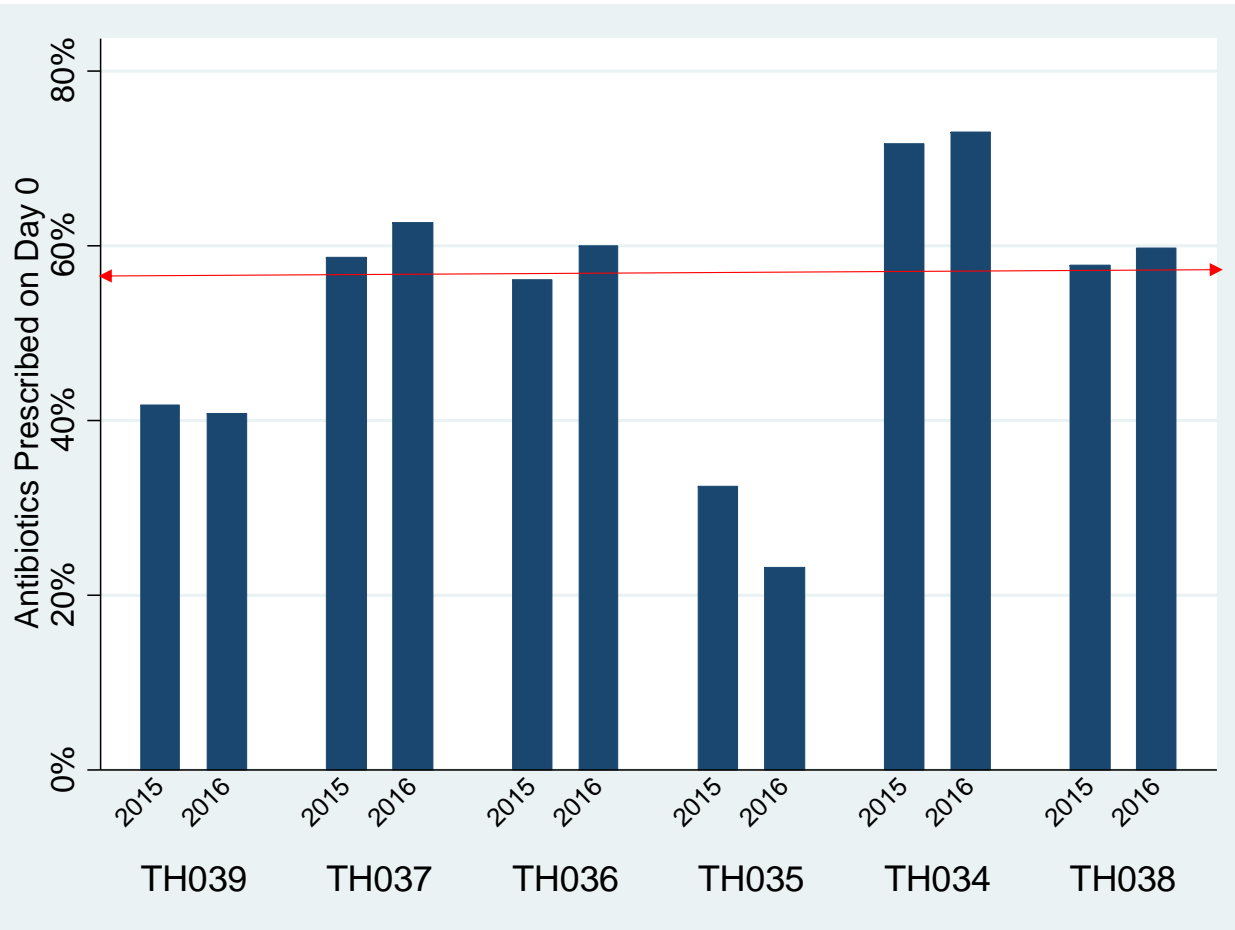


## Chiangrai

- 6 primary care units (PCUs)
- 2-5 nurses & public health officers

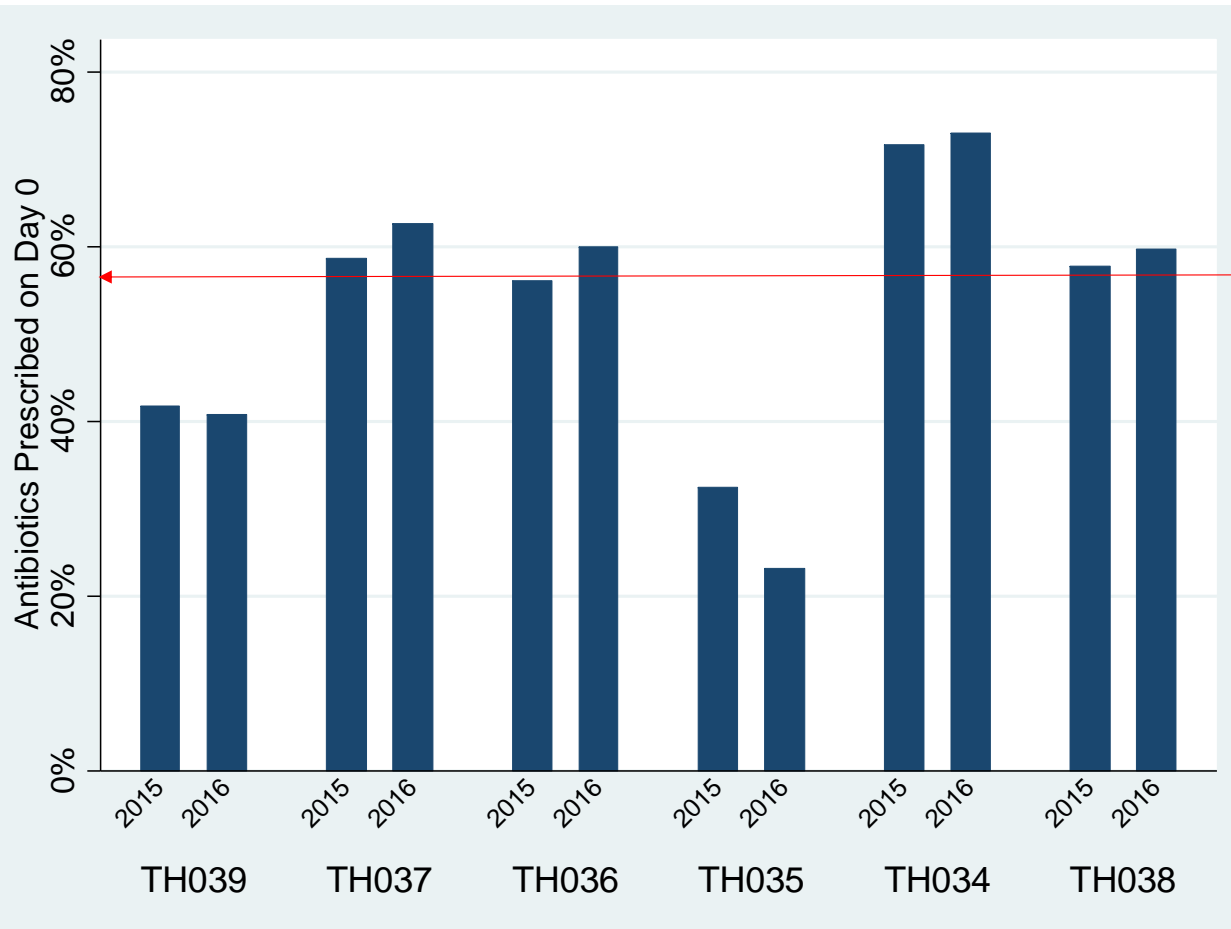
# Baseline surveys - Thailand

Retrospective survey, n=6,993 patients with a history of fever or temperature >37.5°C



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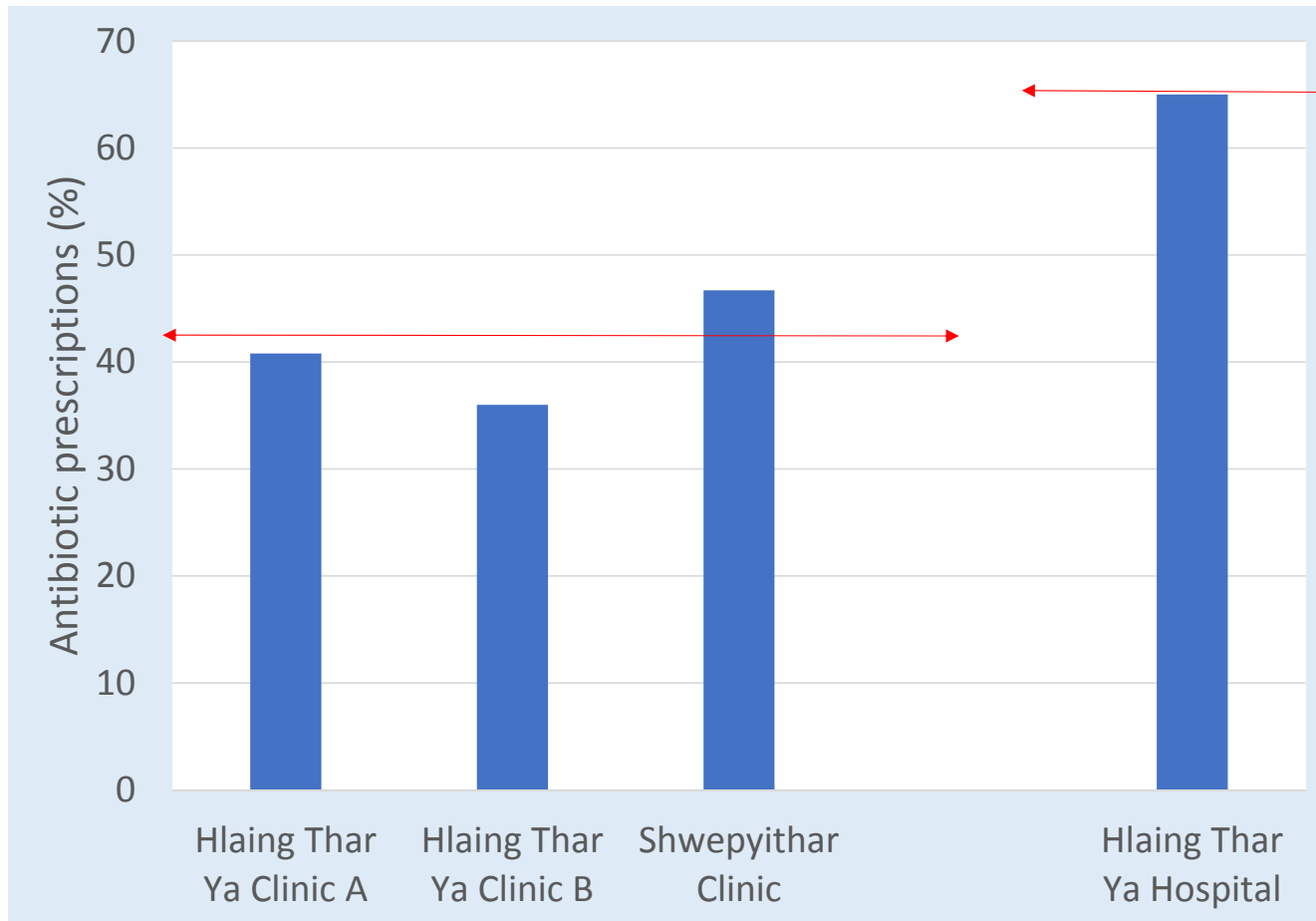
Prospective survey, n=83 patients

Age category	No antibiotic prescribed	Antibiotic prescribed	Total patients
Children	40.2%	59.2%	49
Adults	50.0%	50.0%	34
<b>Total</b>	<b>44.6%</b>	<b>55.4%</b>	<b>83</b>



# Baseline surveys - Myanmar

Retrospective survey, n=32,345 **ALL** outpatients



# The impact of C-reactive protein testing on antibiotic prescription in febrile patients attending primary care in low-resource settings

- Individually randomised controlled trial
- $\geq 1$  year old
- Fever or history of fever
  
- June 2016-August 2017

Screening

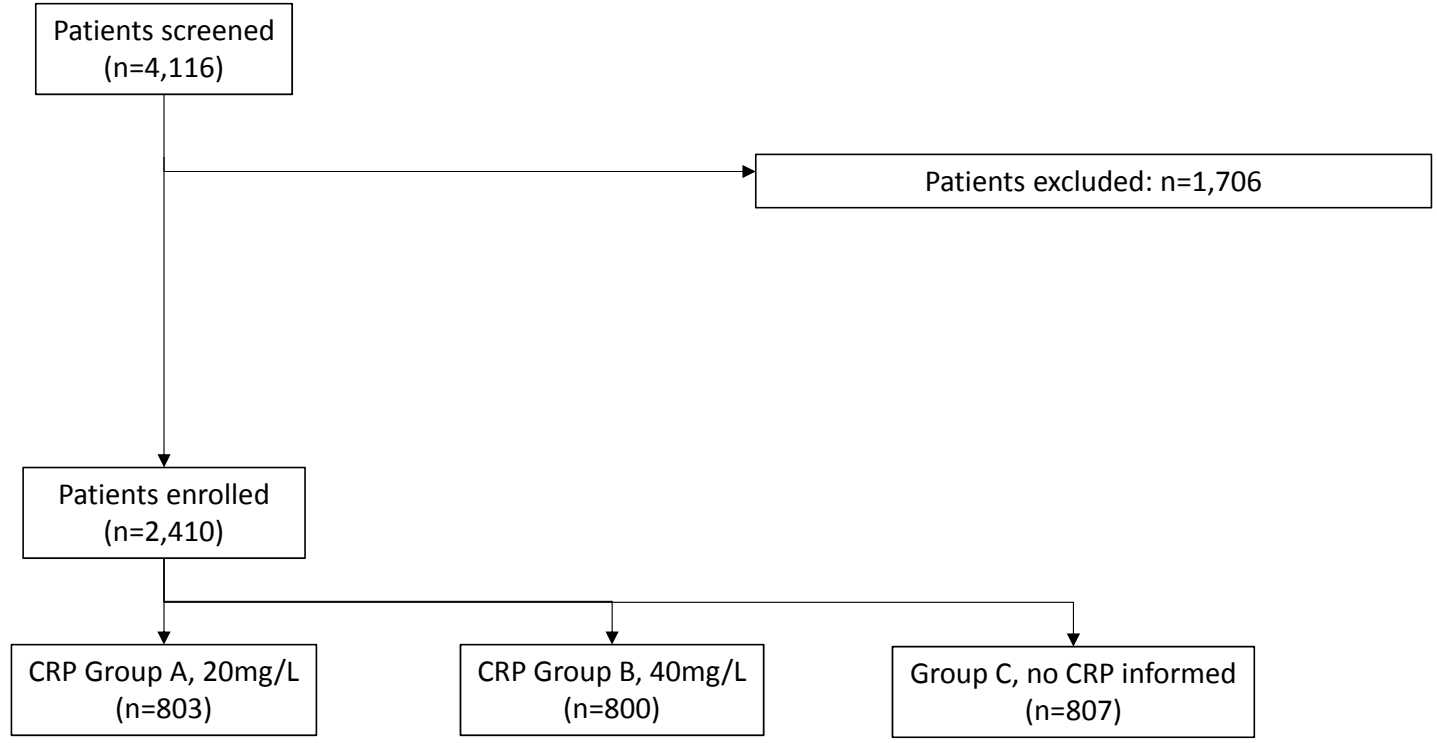
Patients screened  
(n=4,116)

- Patients excluded: n=1,706\*
- Not meeting inclusion criteria: n=22
  - Declined to participate: n=133
  - Suspicion tuberculosis: n=438
  - Not able to comply to follow-up: n=432
  - Symptoms >14 days: n=309
  - Skin/Dental abscess: n=242
  - Urinary tract infection: n=129
  - Bleeding: n=106
  - Trauma: n=101
  - Referral to hospital: n=100
  - Neoplastic disease: n=15
  - Malaria: n=7

\*can meet more than one criteria

Screening

Allocation



Screening

Patients screened  
(n=4,116)

Patients excluded: n=1,706

Allocation

Patients enrolled  
(n=2,410)

CRP Group A, 20mg/L  
(n=803)

CRP Group B, 40mg/L  
(n=800)

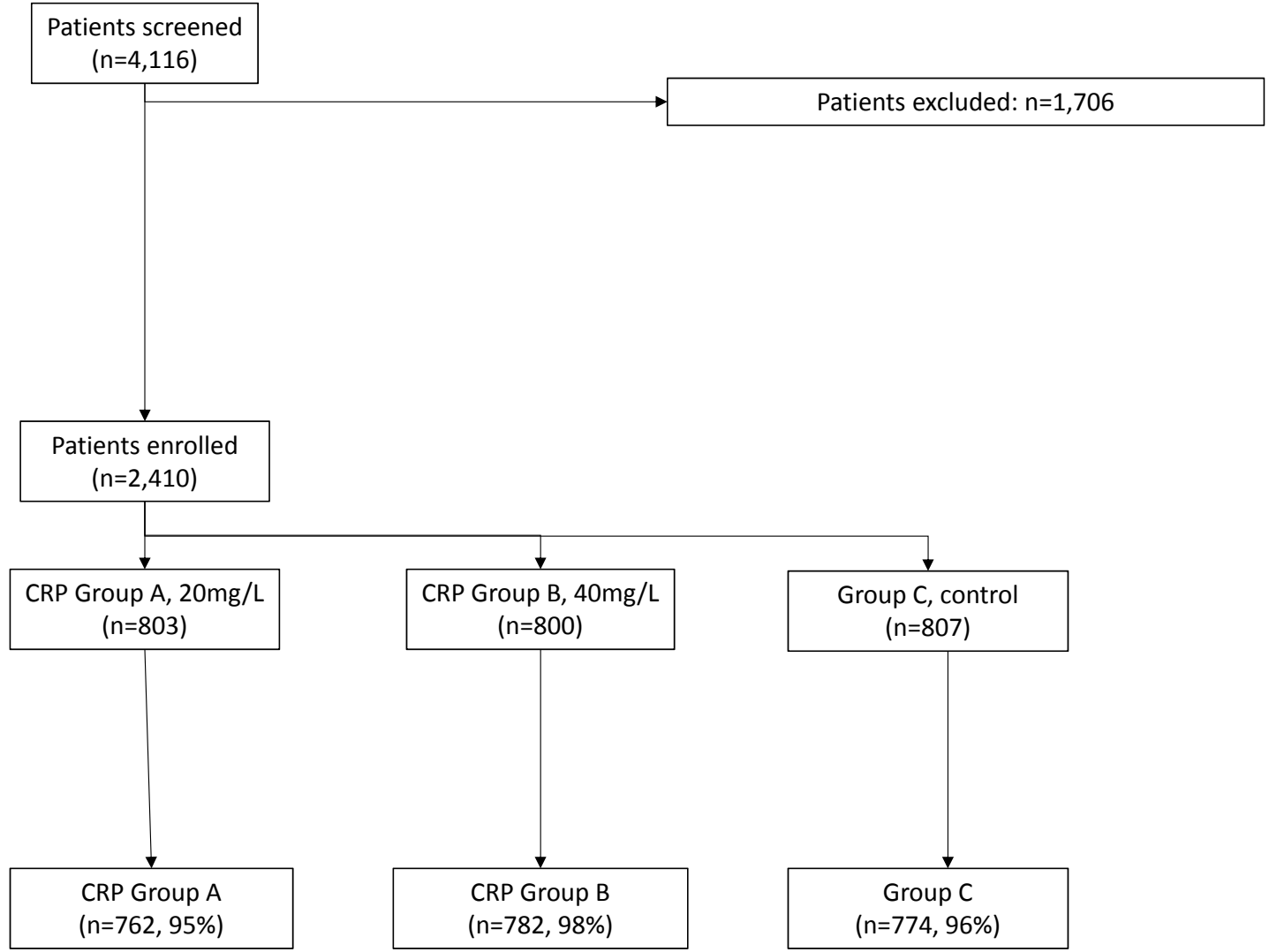
Group C, control  
(n=807)

Day 14  
Follow-up

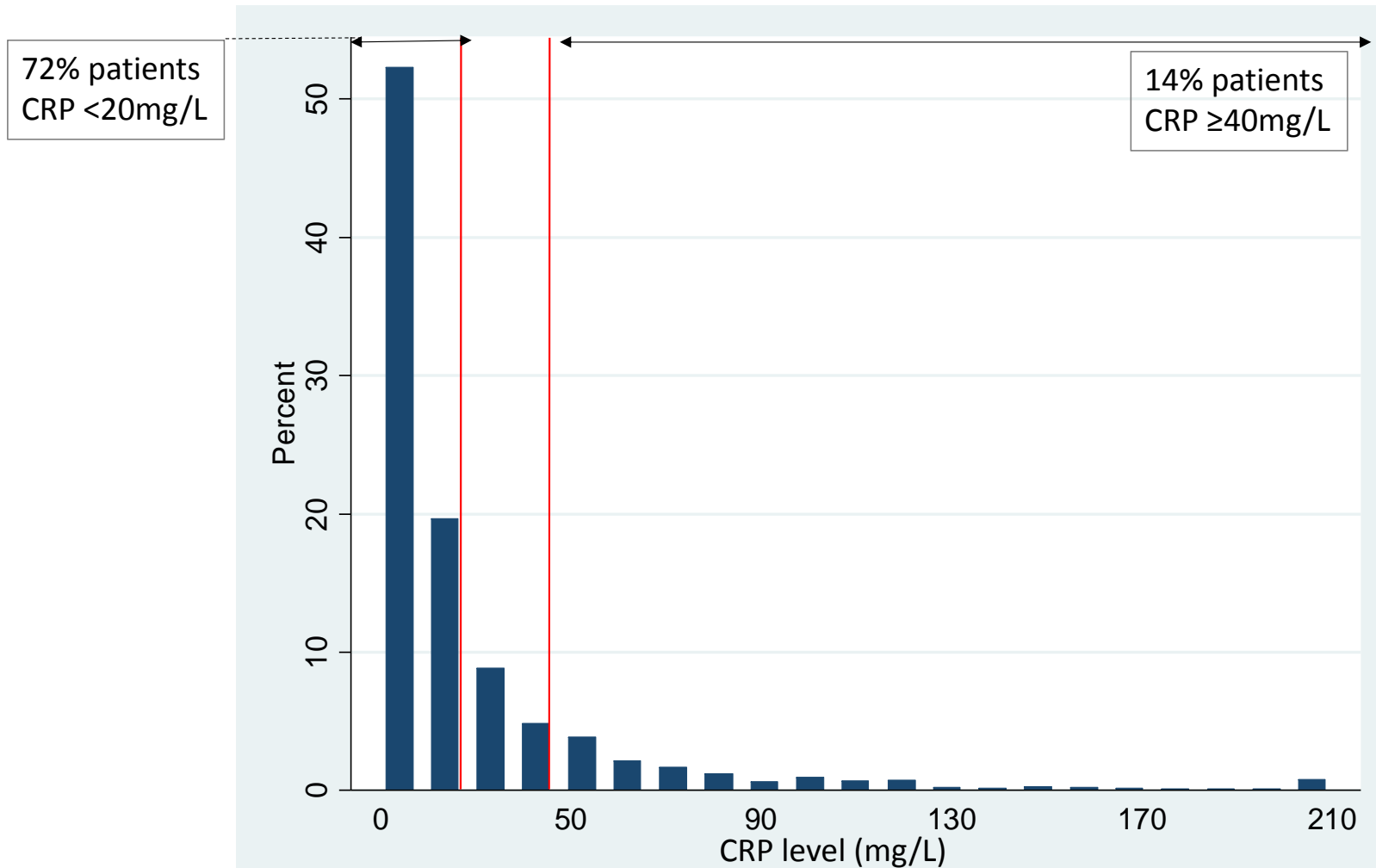
CRP Group A  
(n=762, 95%)

CRP Group B  
(n=782, 98%)

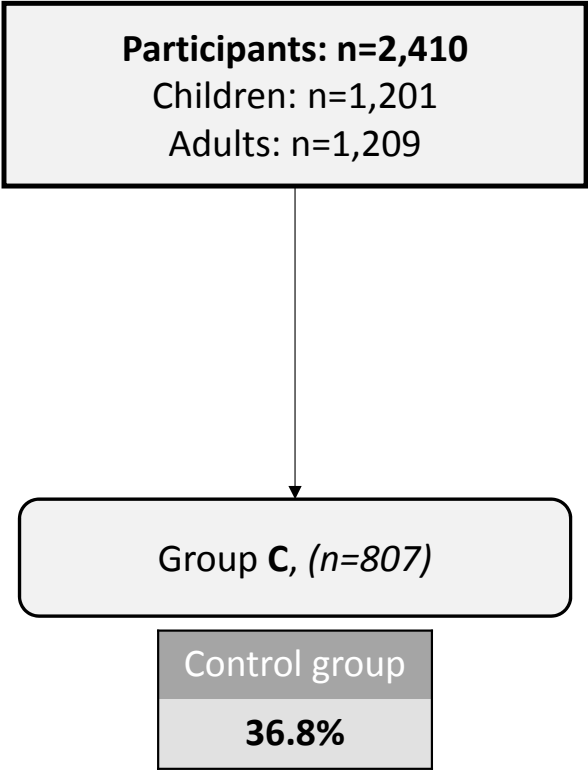
Group C  
(n=774, 96%)



# CRP distribution on Day 0



# Antibiotic prescription at Day 0



# Antibiotic prescription at Day 0

**Participants: n=2,410**  
Children: n=1,201  
Adults: n=1,209

Group C, (n=807)

Control group

**36.8%**

CRP group A, 20mg/L (n=803)

CRP group A	Adjusted OR, 95% CI
33.5%	0.86 [0.70-1.06]



# Antibiotic prescription at Day 0

**Participants: n=2,410**  
Children: n=1,201  
Adults: n=1,209

Group C, (n=807)

Control group  
**36.8%**

CRP group A, 20mg/L (n=803)

CRP group A	Adjusted OR, 95% CI
33.5%	0.86 [0.70-1.06]

CRP group B, 40mg/L (n=800)

CRP group B	Adjusted OR, 95% CI
30.6%	0.75 [0.60-0.92]

# Antibiotic prescription at Day 0



CRP group **B**, 40mg/L

Control group	CRP group <b>B</b>	Adjusted OR, 95% CI
36.8%	<b>30.6%</b>	0.75 [0.60-0.92]

Myanmar children

Control group	CRP group <b>B</b>	Adjusted OR, 95% CI
37.7%	<b>31.6%</b>	0.76 [0.50-1.15]

Myanmar adults

Control group	CRP group <b>B</b>	Adjusted OR, 95% CI
45.1%	<b>32.7%</b>	0.58 [0.38-0.87]

Thai children

Control group	CRP group <b>B</b>	Adjusted OR, 95% CI
32.8%	<b>25.4%</b>	0.68 [0.43-1.08]

Thai adults

Control group	CRP group <b>B</b>	Adjusted OR, 95% CI
31.3%	<b>32.7%</b>	1.06 [0.69-1.63]

# Antibiotic prescription between Day 0 and 5

**Participants:  $n=2,410$**   
Children:  $n=1,201$   
Adults:  $n=1,209$

Controls *versus* CRP groups

CRP group A, 20mg/L ( $n=803$ )

Control group	CRP group A	Adjusted OR, 95% CI
39.4%	36.1%	0.86 [0.70-1.06]

CRP group B, 40mg/L ( $n=800$ )

Control group	CRP group B	Adjusted OR, 95% CI
39.4%	34.4%	0.80 [0.65-0.98]

Break for questions