SUPPLEMENTARY APPENDIX

Contents

SUPPLEMENTARY MATERIALS AND METHODS

Histology, Bacterial culture and antibiotic susceptibility test

During each endoscopic examination, a total of six biopsy specimens were obtained (three from the antrum and three from the body). Two of the three pairs of specimens were processed with hematoxylin and eosin and Giemsa staining. Histological parameters were graded by the pathologist blinded to the treatment protocol according to the updated Sydney system.[1]

Another pair of samples were homogenized and streaked onto an agar plate with selective medium.[2] The plates were incubated at 37°C under micro-aerophilic conditions (5% O_2, 10% CO_2, 85% N_2) for 3-7 days. *H. pylori* was identified by its characteristic biotyping. The primary isolates were subcultured and the colonies were harvested in 2-2.5 mL of BHI broth. The final inoculum was adjusted to give an opacity equivalent to a McFarland turbidity standard of 3 (approximately 10^9 cfu/mL). A 0.2-mL aliquot of suspension was swabbed on the agar plate with nonselective medium. The E-test strips (AB Biodisk, Solna, Sweden) were used for susceptibility testing.

^{13}C-urea breath test

The procedure of ^{13}C-urea breath test was modified from a previously described method.[2] A baseline sample of expired breath in a 20 mL vacutainer from each patient

was obtained before the administration of 100 mg of ^{13}C-urea (99% pure; Isotech, Irvine, CA) in 50 ml of distilled water. Thirty minutes after the ingestion of ^{13}C-urea, the expired breath was collected. All samples were taken in duplicated and analyzed by an automated breath ^{13}C analyzer (Analytical Precision Limited, Cheshire, England). A result of more than 5 units was considered a positive breath test.

Genotyping of CYP2C19 and IL-1β-511

Human genomic DNA was extracted from peripheral leukocytes of blood samples using methods described previously.[3] The DNA samples were stored at -80^{o}C until use. Genetic polymorphism of the *CYP2C19*2* (*CYP2C19 m1*) and *CYP2C19*3* (*CYP2C19 m2*) alleles and *IL-1β-511 C/C, C/T, T/T* alleles were identified by polymerase chain reaction-based restriction fragment length polymorphism (PCR-RFLP) as described previously.[4-6] Patients were identified as EM (homozygous extensive metabolizers; *CYP2C19 *1/*1*); IM (heterozygous extensive metabolizers; *CYP2C19 *1/*2* or **1/*3*) or PM (poor metabolizers; *CYP2C19 *2/*2, *2/*3* or **3/*3*) according to CYP2C19 genotypes.

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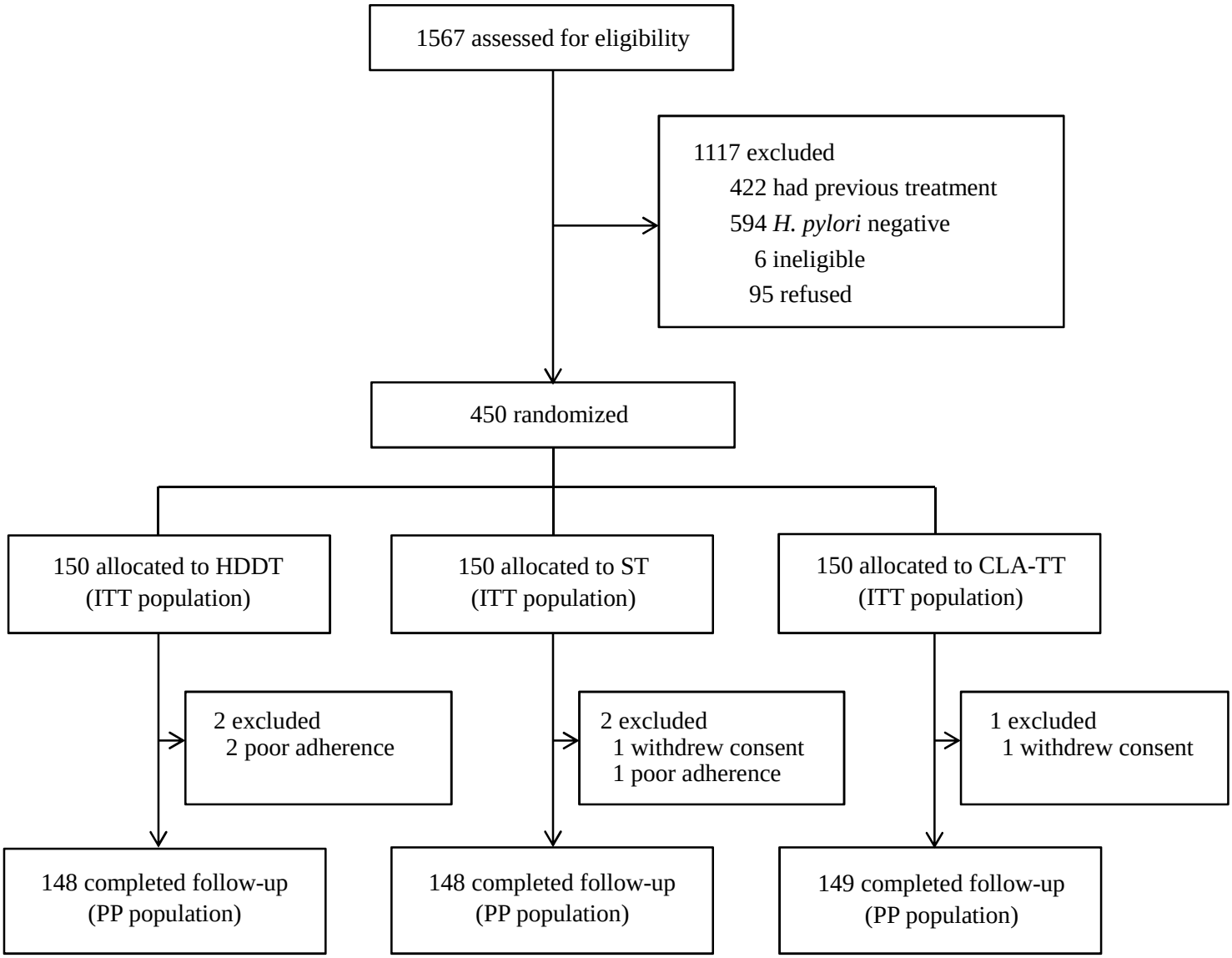
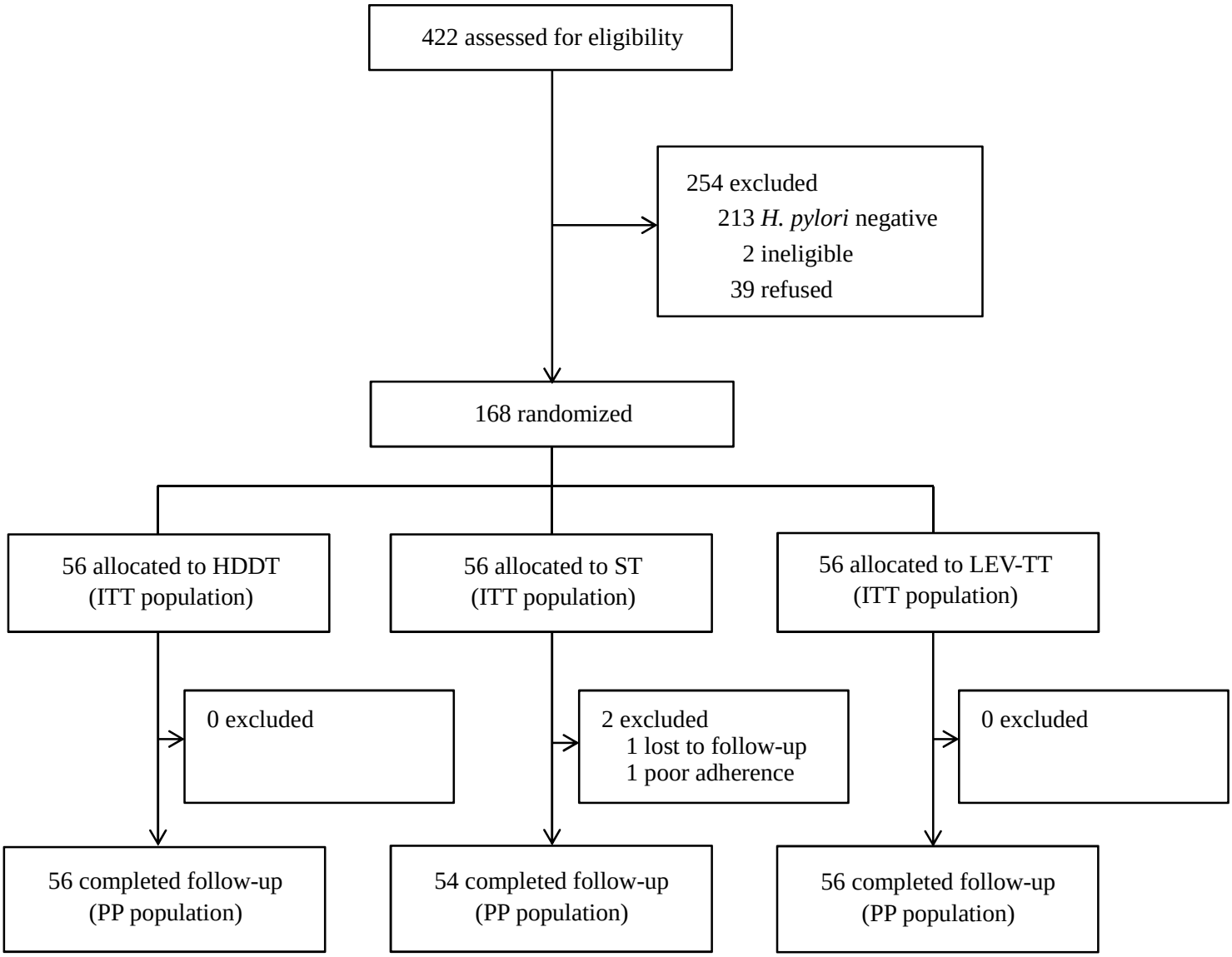
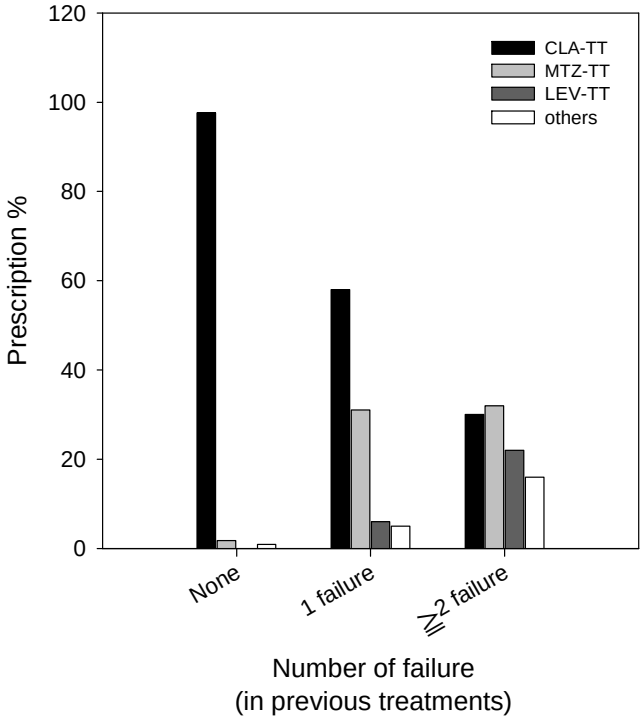
Supplementary Figure 1A.



Supplementary Figure 1B.



Supplementary Figure 1. Consort flow charts for (A) first-line treatment and (B) rescue treatment. HDDT: high-dose dual therapy; ST: sequential therapy; CLA-TT: Clarithromycin-containing triple therapy; LEV-TT: Levofloxacin-containing triple therapy; ITT: intention-to-treat; PP: per-protocol.



Supplementary Figure 2. Anti-*H. pylori* regimens that had been prescribed in the rescue population according to the number of treatment failure. CLA-TT: Clarithromycin-based triple therapy; MTZ-TT: Metronidazole-based triple therapy; LEV-TT: Levofloxacin-based triple therapy.

Supplementary Table 1. Univariate analysis of other factors (in addition to factors reported in Table 4 and Table 5) that may influence *H. pylori* eradication in first-line and rescue regimens

First-line regimens	**ODT group**	**ST group**	**CLA-TT group**
BMI, kg/m^2			
Not eradicated	25.4±3.5(7)	24.2±4.3(22)	23.7±3.6(29)
eradicated	23.7±3.5(143)	24.1±3.5(128)	23.7±3.6(121)
P-value	0.197	0.860	0.975
IL-1β-511 genotype			
C/C	95.2 (40/42)	81.6 (31/38)	80.6 (29/36)
C/T	97.4 (75/77)	91.4 (74/81)	79.8 (75/94)
T/T	96.4 (27/28)	79.3 (23/28)	89.5 (17/19)
P-value	0.839	0.165	0.652
Bacterial density			
Mild	93.3 (42/45)	88.1 (37/42)	70.5 (31/44)
Moderate	98.0 (48/49)	88.0 (44/50)	85.0 (51/60)
Severe	98.1 (53/54)	83.9 (47/56)	86.7 (39/45)
P-value	0.444	0.829	0.092
Sex			

Male	97.1 (67/69)	89.7 (52/58)	79.7 (47/59)
Female	96.2 (76/79)	84.4 (76/90)	82.2 (74/90)
P-value	1	0.487	0.831
Regular Alcohol use			
Yes	95.5 (21/22)	95.2 (12/13)	90.0 (18/20)
No	96.8 (120/124)	86.5 (115/133)	79.5 (101/127)
P-value	1	0.7	0.367
Smoking			
Yes	97.1 (33/34)	90.3 (28/31)	86.1 (31/36)
No	96.0 (95/99)	86.4 (89/103)	79.4 (81/102)
P-value	1	0.761	0.463
Good adherence			
Yes	96.5 (136/141)	88.4 (122/138)	82.8 (120/145)
No	100.0 (6/6)	100.0 (2/2)	50.0 (1/2)
P-value	1	1	0.323
Peptic ulcer disease			
Yes	95.1 (98/103)	85.7(84/98)	82.0 (82/100)
No	95.1 (45/47)	84.6 (44/52)	78.0 (39/50)
P-value	1	1	0.661

Rescue regimens	**ODT group**	**ST group**	**LEV-TT group**
BMI, kg/m^2			
Not eradicated	25.2±4.3(6)	23.9±4.0(27)	24.7±4.8(12)
eradicated	24.0±3.3(50)	23.6±5.0(29)	23.9±3.7(44)
P-value	0.440	0.866	0.458
IL-1β-511 genotype			
C/C	94.4 (17/18)	58.3 (7/12)	76.9 (10/13)
C/T	84.6 (22/26)	51.6 (16/31)	82.1 (23/28)
T/T	91.7 (11/12)	54.5 (6/11)	73.3 (11/15)
P-value	0.559	0.933	0.912
Bacterial density			
Mild	84.0 (21/25)	43.5 (10/23)	87.0 (20/23)
Moderate	93.3 (14/15)	66.7 (8/12)	81.0 (17/21)
Severe	93.8 (15/16)	61.1 (11/18)	58.3 (7/12)
P-value	0.637	0.356	0.163
Sex			
Male	91.3 (21/23)	60.0 (12/20)	95.2 (20/21)
Female	87.9 (29/33)	50.0 (17/34)	68.6 (24/35)

P-value	1	0.576	0.040
Regular Alcohol use			
Yes	75.0 (6/8)	80.0 (4/5)	83.8 (5/6)
No	91.7 (44/48)	50.0 (24/48)	78.0 (39/50)
P-value	0.2	0.355	1
Smoking			
Yes	90.9 (10/11)	75.0 (9/12)	85.7 (12/14)
No	88.4 (38/43)	47.6 (20/42)	76.2 (32/42)
P-value	1	0.113	0.709
Good adherence			
Yes	88.5 (46/52)	56.9 (29/51)	77.4 (41/53)
No	100.0 (2/2)	0.0 (0/2)	-
P-value	1	0.2	-
Age, years			
Not eradicated	57.0±9.9(6)	56.4±11.8(27)	53.3±14.1(12)
eradicated	52.7±12.6(50)	55.2±13.0(29)	49.7±12.8(44)
P-value	0.425	0.720	0.402

Data are % (n/N); ODT: optimized dual therapy; ST: sequential therapy; CLA-TT: clarithromycin-based triple therapy; LEV-TT: levofloxacin-based triple therapy; BMI: body mass index; good adherence: took at least 80% of drugs.

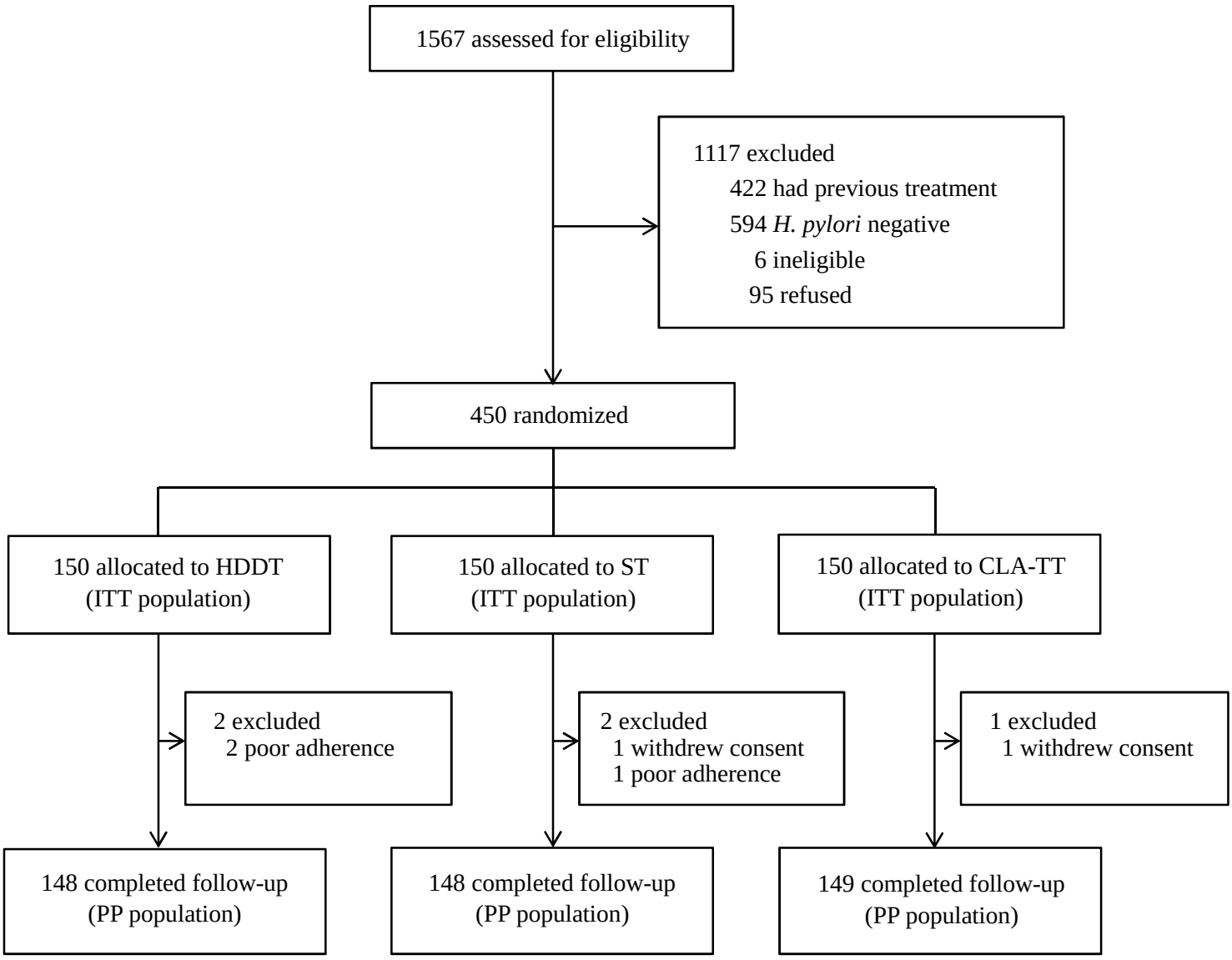
Supplementary Table 2. Prevalence of antibiotic none-resistance and co-resistance in the first-line and rescue regimens

None-resistance or co-resistance	First-line (N=450)	Rescue (N=167)	P-value
None	49.8 (224)	9.0 (15)	<0.001
CLA/MTZ	8.0 (36)	43.7 (73)	<0.001
CLA/LEV	5.8 (26)	19.2 (32)	<0.001
MTZ/LEV	6.9 (31)	14.4 (24)	0.005
AMO/CLA	0.0 (0)	3.0 (5)	0.001
CLA/MTZ/LEV	2.9 (13)	13.2 (22)	<0.001
AMO/CLA/MTZ	0.0 (0)	2.4 (4)	0.005
AMO/CLA/MTZ/LEV	0.0 (0)	1.8 (3)	0.020

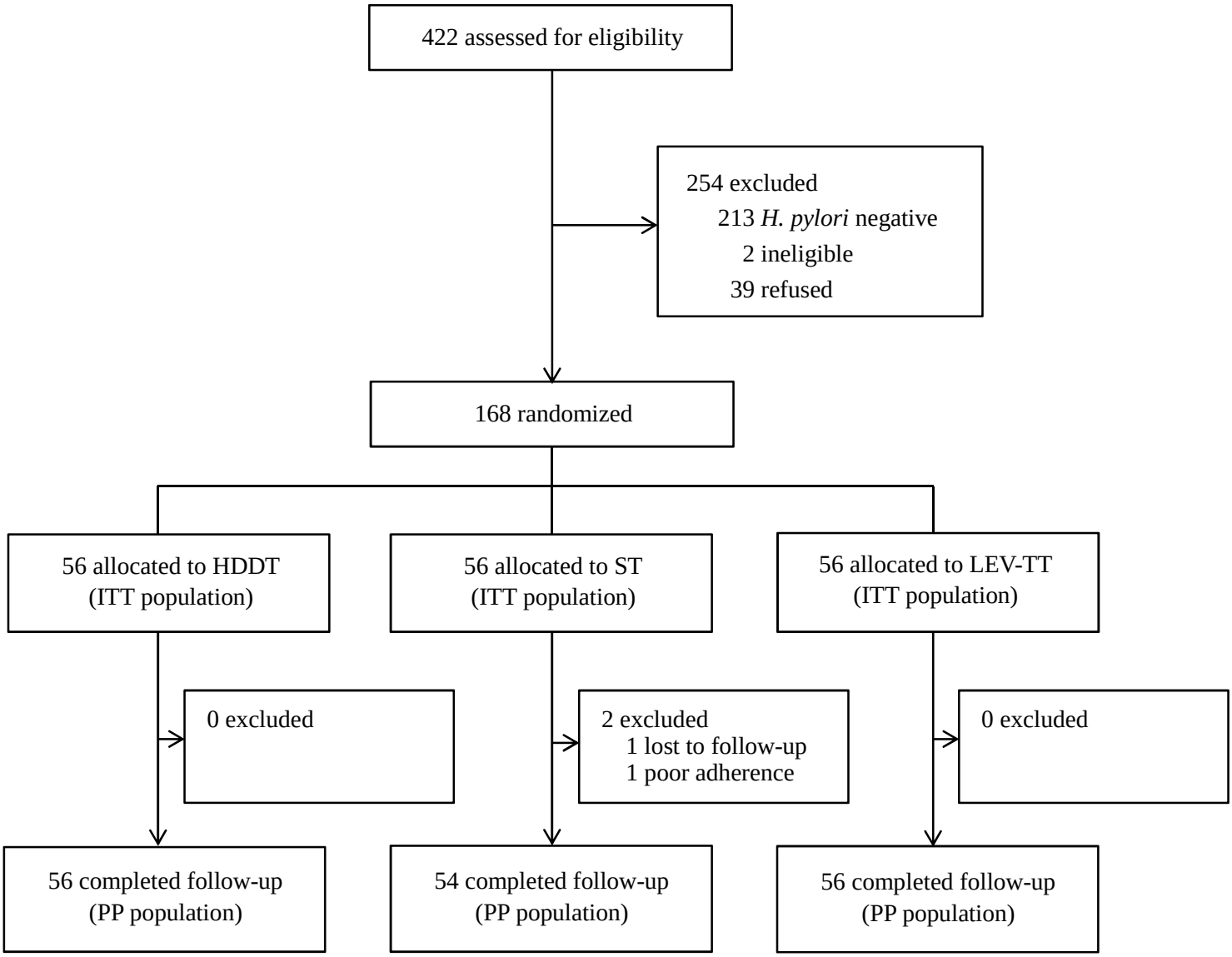
Data are % (n); AMO: amoxicillin; CLA: clarithromycin; MTZ: metronidazole; LEV: levofloxacin.

CONSORT Flow Diagram

Supplementary Figure 1 A



Supplementary Figure 1 B



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