

CODDLE Study: *Bacillus clausii* as an adjunctive treatment of acute community-acquired diarrhoea in Filipino children

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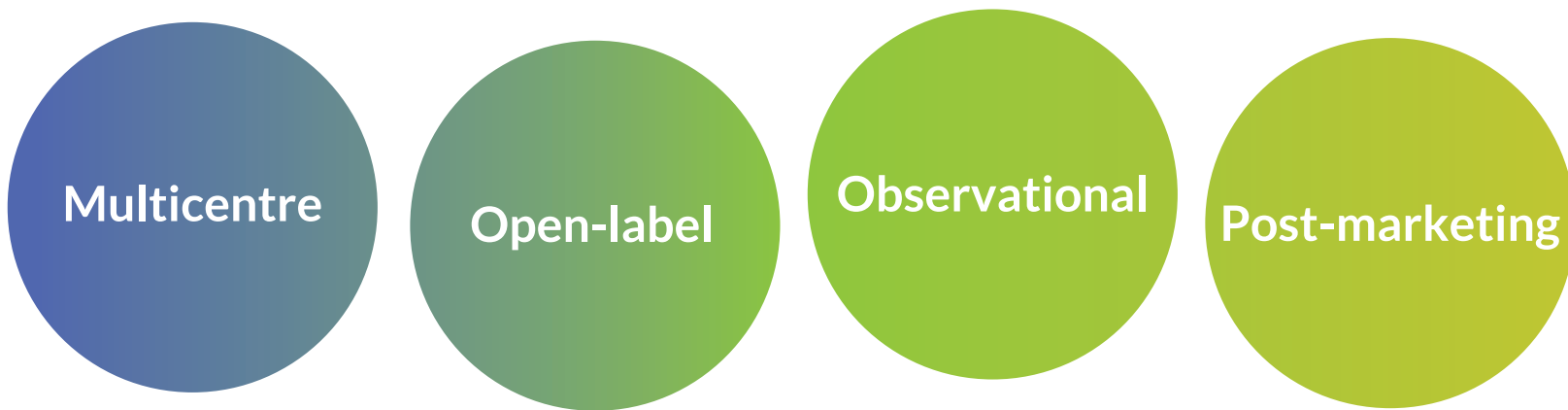
INTRODUCTION

- Diarrhoea ranks among the top 10 causes of paediatric mortality in the Philippines, causing 10,000 child deaths per year.¹
- *Bacillus clausii* (*B. clausii*) strains O/C, SIN, N/R and T have been used as an adjunct to oral rehydration therapy (ORT) for managing diarrhoea for several decades.²
- The efficacy of *B. clausii* as an adjunct to ORT in children with acute diarrhoea has been shown.³⁻⁵

OBJECTIVE

- To assess the efficacy and safety of *B. clausii* as an adjunct therapy to ORT in Filipino children with acute community-acquired diarrhoea or viral origin or antibiotic-associated diarrhoea (AAD).

METHODS



- The study analysed *B. clausii* in the treatment of acute community-acquired diarrhoea among Filipino children (CODDLE).

Inclusion criteria

Age: 1 month - 19 years	Diarrhoea < 48 hrs
Acute diarrhoea (viral origin or AAD)	≥ 3 watery stools 24 hrs prior

Study design

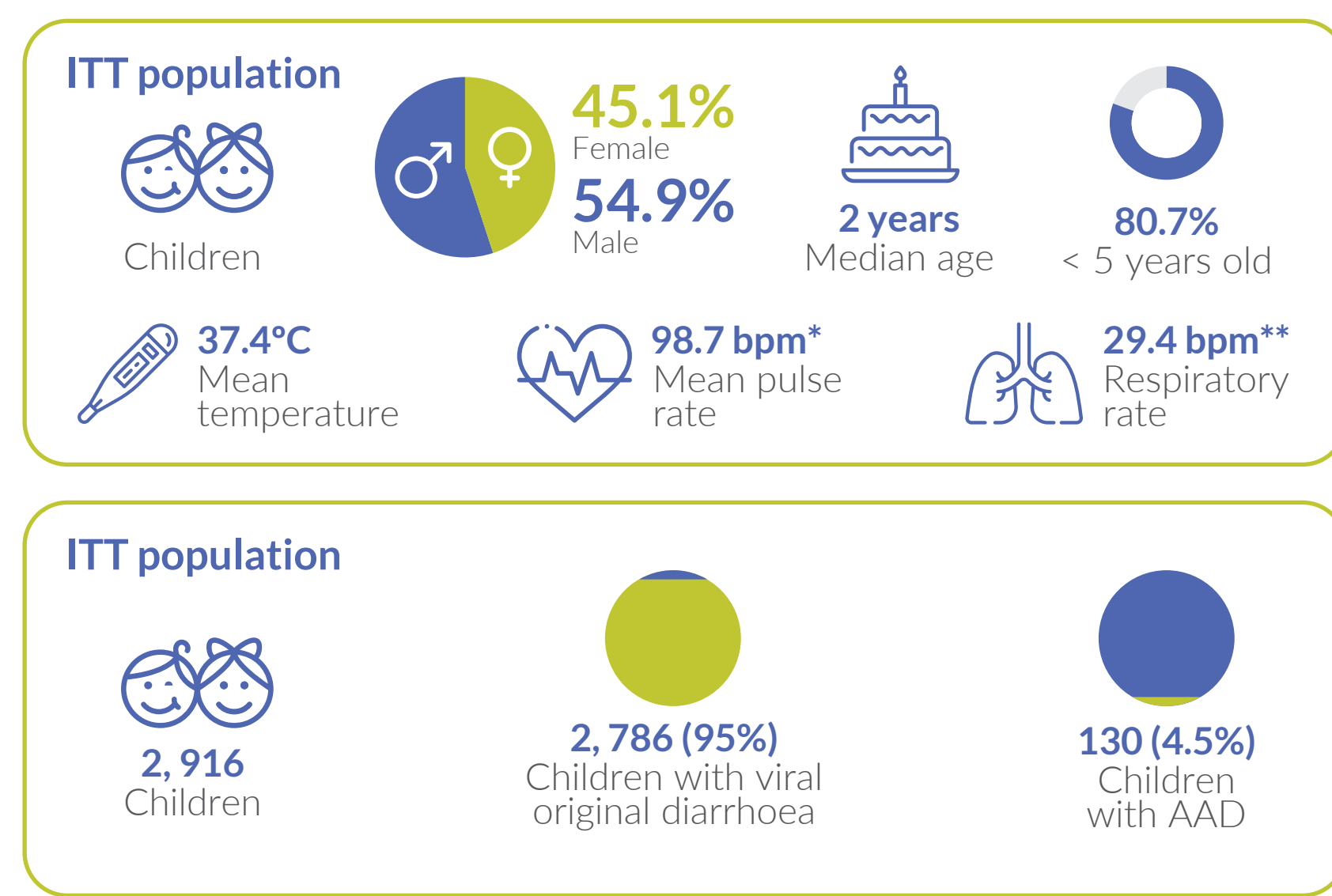


* Chi-square test of independence, repeated measures analysis of variance (ANOVA), and the McNemar test were used for data analysis. ** GI: gastrointestinal.

Study populations

- Intention-to-treat (ITT) population included all children aged 1 month - 19 years who received ≥ 1 daily dose of *B. clausii*.
- The per-protocol (PP) population included all children who satisfied the inclusion criteria and received full *B. clausii* treatment with at least 1 post-baseline efficacy measurement.

Subjects



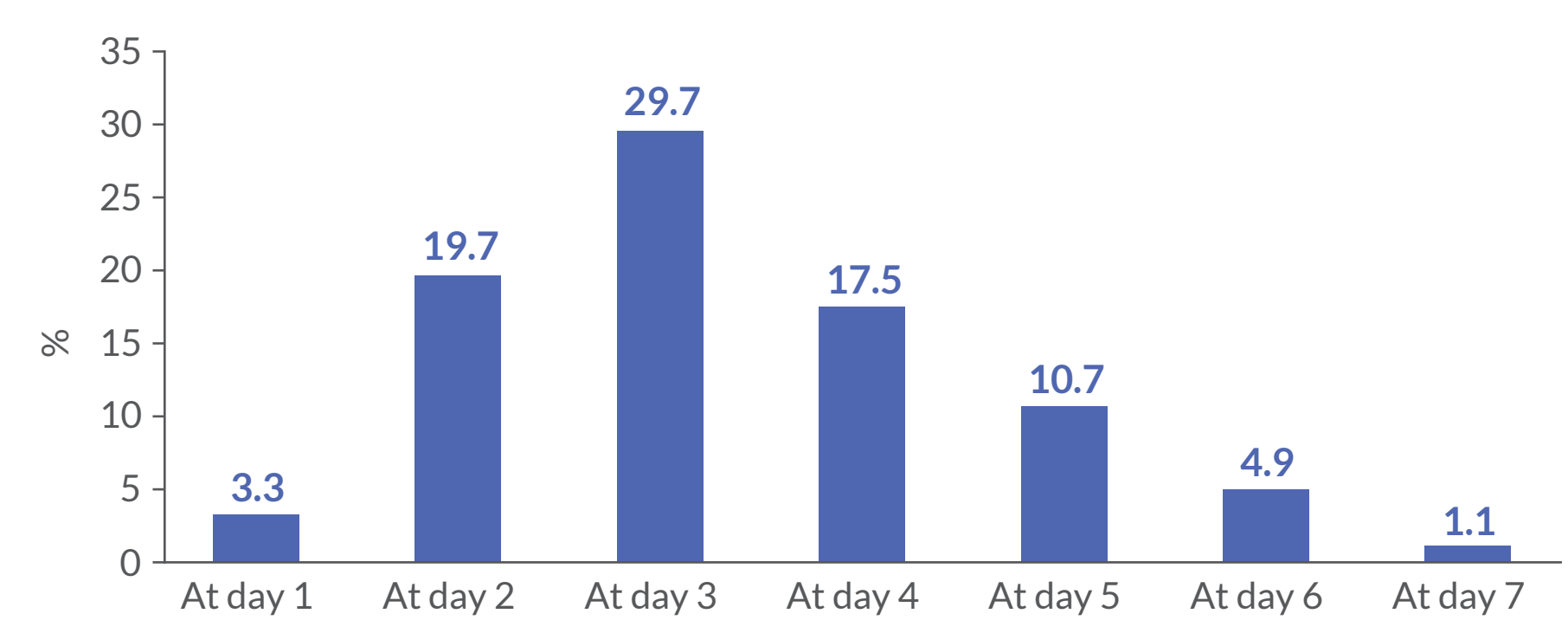
* = beats per minute. ** = breaths per minute. AAD: Antibiotic-Associated Diarrhoea.

PRIMARY EFFICACY OUTCOMES

Primary analysis

- *B. clausii* treatment was most effective at day 3: a total of 1,535/2,916 children (52.7%) had resolved diarrhoea (Figure 2).
- By treatment day 7: 2,534/2,916 children (86.9%) had resolved diarrhoea (Figure 2).

Figure 2: Percentage of children per day whose diarrhoea had resolved



Subgroup analysis

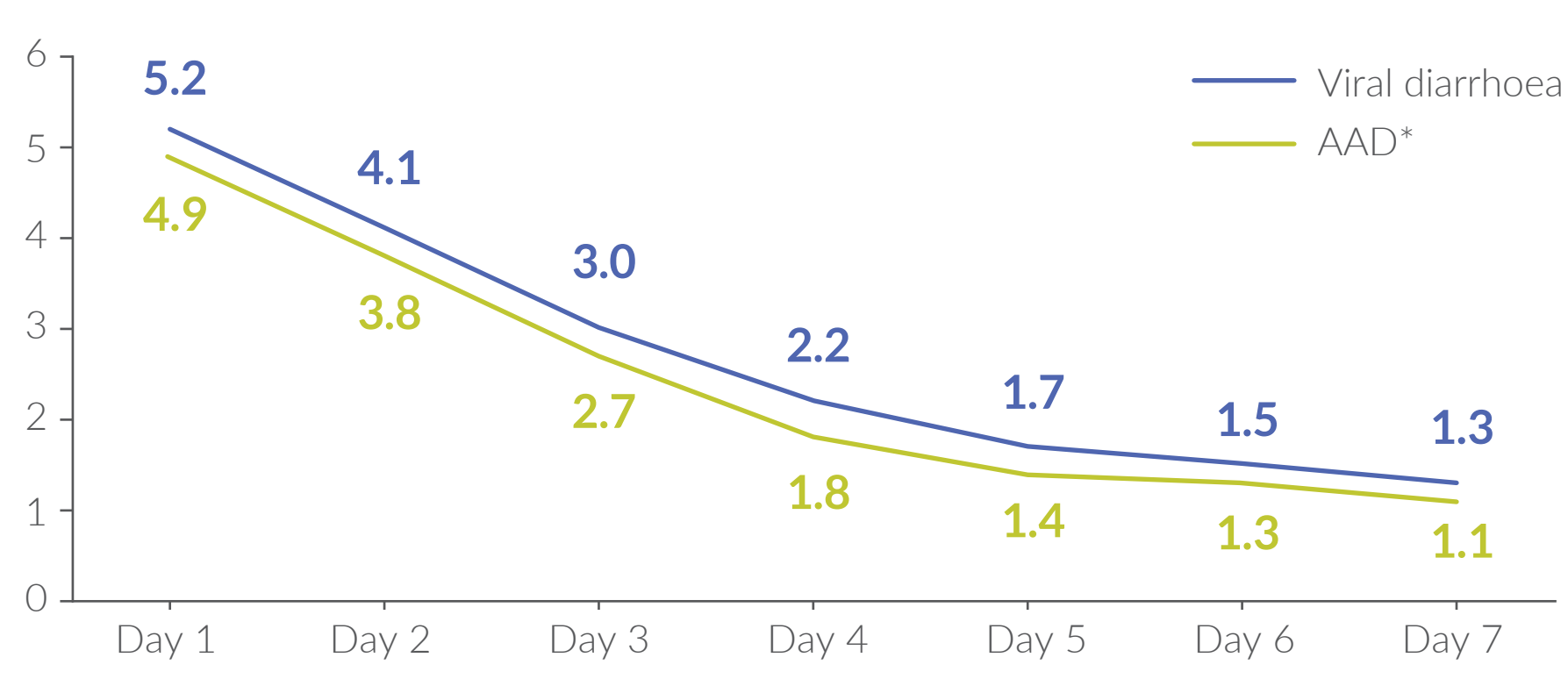
Mean ± SD duration of diarrhoea	
Viral origin	AAD
3.4 ± 1.3 days	3.3 ± 1.3 days
Population with diarrhoea resolved	
Viral origin	AAD
29.5%	32.3%
p=0.297 (NS)	
Mean ± SD duration of diarrhoea	
+ Pre/probiotics received prior	- Pre/probiotics received prior
3.2 ± 0.9 days	3.4 ± 1.3 days
p=0.742 (NS)	

SECONDARY EFFICACY OUTCOMES

Number of stools per day

- *B. clausii* treatment significantly reduced the mean ± SD number of stools per day, from 5.2 ± 2.0 to 1.25 ± 0.63 stools from baseline to after 7 days of treatment (p<0.0001) (Figure 3).
- With no difference in the number of stools per treatment day between viral diarrhoea and AAD subgroups.

Figure 3: Mean number of stools per day of treatment



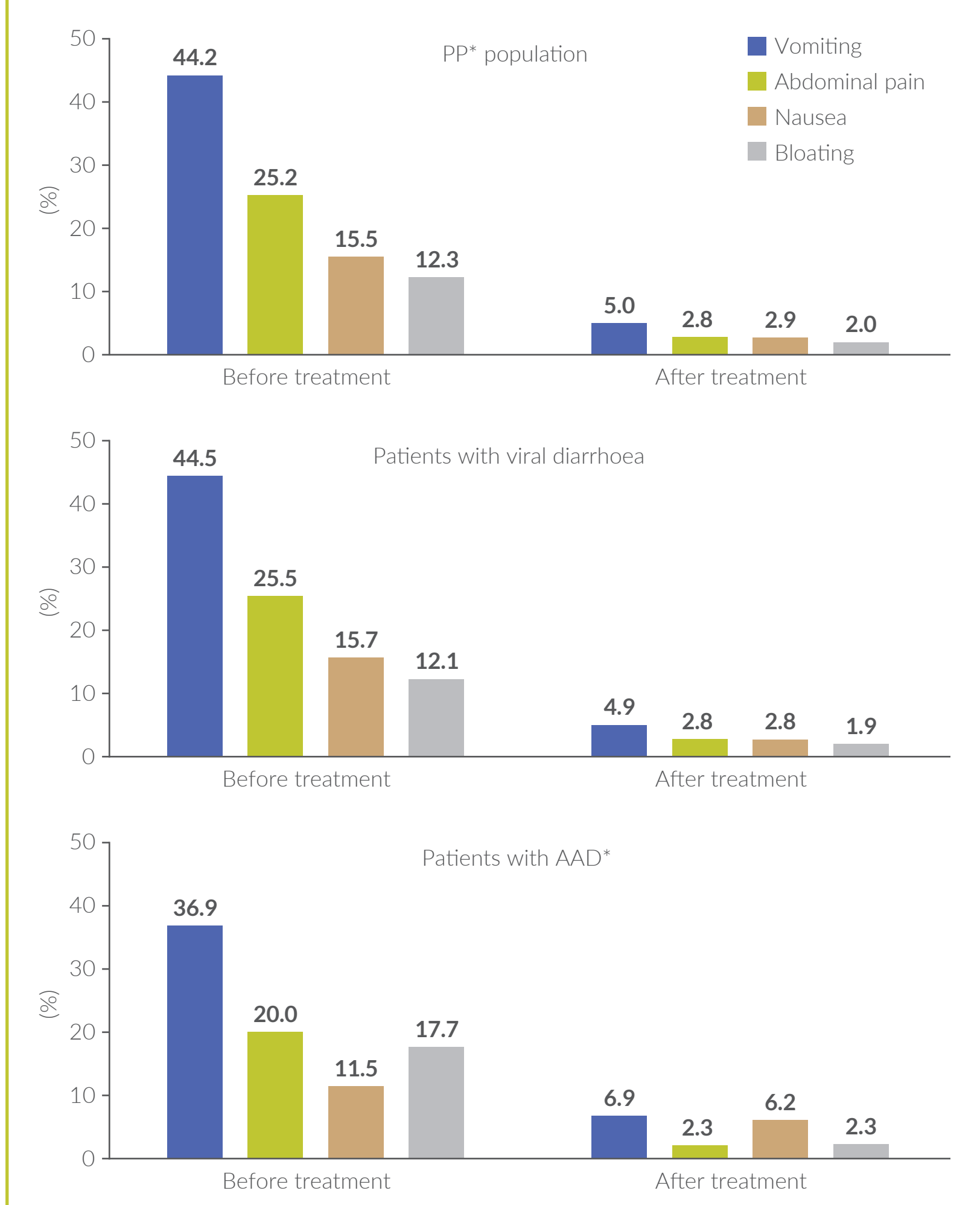
* AAD: Antibiotic-Associated Diarrhoea. / Repeated Measures Analysis of Variance: viral diarrhoea vs AAD: p=0.9380.



Gastrointestinal symptoms

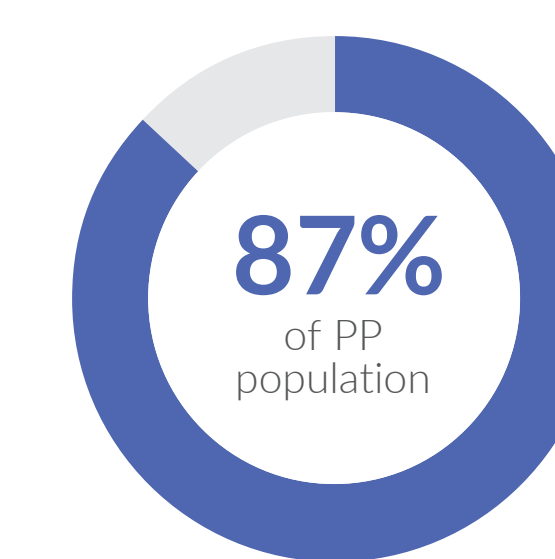
- The incidence of gastrointestinal symptoms significantly decreased from baseline to study end (p<0.0001) in the overall population, viral diarrhoea and AAD subgroups (Figure 4).

Figure 4: Percentage of children experiencing gastrointestinal symptoms before and after treatment.



* PP, per-protocol; **AAD, Antibiotic-Associated Diarrhoea. Before versus after treatment (in overall PP population): p<0.0001 (McNemar test). Before versus after treatment (viral diarrhoea): p<0.0001 (McNemar test). Before versus after treatment (AAD): p<0.0001 (except for nausea: p=0.833) (Chi-square test). Viral diarrhoea versus AAD: p<0.05 (Chi-square test).

Gastrointestinal symptoms



Very Good to Excellent acceptance of study drug according to caregivers

SAFETY

- Three mild-moderate adverse events (AEs) were observed in population ITT.
- Two AEs (vomiting and stool colour change) were of unknown and likely relation to the study drug, respectively.

SUMMARY AND CONCLUSIONS

- This study showed that *B. clausii* (strains O/C, SIN, N/R and T) is an effective adjunct therapy for acute diarrhoea management in child outpatients.
- Limitations included the absence of a comparator arm and a wide age-range of patients.
- *B. clausii* treatment had an acceptable safety profile and was well tolerated.
- **Disclosures:** MOP is a Sanofi employee. JADC is a speaker for Sanofi, Abbott and Pediatrca. MJVG has no conflicts of interest.

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