INTRODUCTION
Typhoid fever is a communicable disease accounting for 22 million cases annually and is the cause of mortality in 216,000–600,000 people worldwide. Typhoid fever is an endemic disease in Indonesia [1].

METHODS
In this cross-sectional analytical study, secondary of prescription and administrative financial data were retrospectively obtained using the total sampling method. Data of 63 patients, comprising 43 and 20 patients treated with generic and patent ceftriaxone, respectively, were analyzed. The effectiveness of the treatment was measured in terms of the length of hospital stay of the patients. The total cost of the treatment was the total median of the costs of drugs, laboratory examinations, medical device usage, physician service, and hospitalization.

RESULTS
The effectiveness of both generic and patent ceftriaxone was 4 days of hospital stay. Cost-effectiveness ratio of generic ceftriaxone was Rp 575,937.25/day and that of patent ceftriaxone was Rp 888,601.75/day.

Conclusion: Generic ceftriaxone was more cost-effective than patent ceftriaxone.

Keywords: Cost-effectiveness analysis, Pharmacoeconomic, Typhoid fever, Ceftriaxone, Karya Bhakti Pratiwi Hospital.

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METHODS
In this cross-sectional analytical study, secondary of prescription and administrative financial data of patients were retrospectively obtained [4]. The study was conducted at the inpatient installation of Karya Bhakti Pratiwi Hospital, Bogor, from February to April 2017. The study included all children with typhoid fever who were administered generic or patent ceftriaxone in 2016 and who met the inclusion criteria. Data were obtained using the total sampling method. Variables measured included medication effectiveness, total medication cost, age, and sex.

Inclusion criteria were children with typhoid fever aged 1–19 years who were treated with generic or patent ceftriaxone. Exclusion criteria were patients with unclear, incomplete, or untracked medical records, those undergoing treatment with antibiotics other than ceftriaxone, and those with a change of treatment class or antibiotic type during the inpatient period.

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maximum and minimum simulations from total medication cost. Both sensitivity analyses were performed with a fixed effectiveness value.

RESULTS

Based on prescription data in 2016, 167 pediatric patients used generic or patent ceftriaxone as treatment for typhoid fever in 2016. After adjusting the inclusion and exclusion criteria, the study included 63 children. Patients' characteristics are summarized in Table 1.

CEA

Treatment effectiveness in this study was measured in terms of the length of hospital stay of patients. The results of effectiveness analysis parameter were presented as the median length of stay of the generic and patent ceftriaxone groups. Based on the analysis, the median length of hospital stay was 4 days. Mann-Whitney U-test revealed no significant difference between generic and patent ceftriaxone treatment effectiveness in terms of the length of hospital stay (p=0.548).

The results of cost analysis using the total cost of direct medical components for the two groups are presented in Table 2.

Drug cost was defined as the cost of ceftriaxone used during the hospitalization period. The median drug cost of generic and patent ceftriaxone was Rp 97,000 and Rp 1,070,880, respectively. Based on non-parametric Mann-Whitney U-test, the p-value obtained was 0.000. Drug costs of generic and patent ceftriaxone were significantly different (p<0.05).

Laboratory examinations were performed in the diagnostic stage, therapy progress observation, and final results of the treatment. Laboratory examinations for pediatric patients with typhoid fever usually include the Widal test, immunochromatography test, and polymerase chain reaction test (3.1 [EN] Please expand the abbreviation). Median laboratory examination cost during the use of ceftriaxone was calculated and compared between the generic and patent ceftriaxone groups. Based on the sample data obtained from Information System and Management of Hospital, median laboratory costs for the two groups were Rp 308,000 and Rp 365,000, respectively. Based on non-parametric Mann-Whitney U-test, the p-value obtained was 0.963 (p>0.05), indicating that laboratory examination cost was not significantly different between the two groups.

Median medical device use cost during the use of ceftriaxone was calculated and compared between the generic and patent ceftriaxone groups. Medical devices included needle, syringe, infusion equipment, NaCl 0.9% solution, alcohol swab, bandage, mask, and gloves. Based on cost data stated on Information System of Hospital in each patient, median medical device use cost in the generic and patent ceftriaxone groups was Rp 87,351 and Rp 133,529, respectively. Based on nonparametric Mann-Whitney U-test, the p-value obtained was 0.040 (p<0.05), indicating that medical device use cost was significantly different between the two groups.

Service cost included physician service cost during patients' stay in the hospital. Median service cost in generic and patent ceftriaxone groups was Rp 130,000 and Rp 260,000, respectively. Based on non-parametric

| Table 1: Patient characteristics |
|----------------------------------|
| **Patient characteristics**      | **Total n=63 (%)** | **Generic ceftriaxone n=43 (%)** | **Patient ceftriaxone n=20 (%)** |
| Age                              |                     |                                 |
| Toddlers (0–5 years)             | 35 (55.55)          | 22 (51.16)                      | 13 (65)                          |
| Children (>5–11 years)           | 25 (39.69)          | 18 (41.87)                      | 7 (35)                           |
| Adolescents (>11–19 years)       | 3 (4.76)            | 3 (6.97)                        | 0 (0)                            |
| Total                            | 63 (100)            | 43 (100)                        | 20 (100)                         |
| Sex                              |                     |                                 |
| Male                             | 28 (44.45)          | 18 (41.86)                      | 10 (50)                          |
| Female                           | 35 (55.55)          | 25 (58.14)                      | 10 (50)                          |
| Total                            | 63 (100)            | 43 (100)                        | 20 (100)                         |
| Payment source                   |                     |                                 |
| Self-found                       | 24 (38.1)           | 13 (30.23)                      | 11 (55)                          |
| BPJS (National Health Insurance) | 24 (38.1)           | 22 (51.16)                      | 2 (10)                           |
| Private Health Insurance         | 15 (23.8)           | 8 (18.61)                       | 7 (35)                           |
| Total                            | 63 (100)            | 43 (100)                        | 20 (100)                         |
| Treatment class                  |                     |                                 |
| Class I                          | 13 (20.63)          | 11 (25.58)                      | 2 (10)                           |
| Class II                         | 12 (19.04)          | 10 (23.25)                      | 2 (10)                           |
| Class III                        | 23 (36.50)          | 15 (34.88)                      | 8 (40)                           |
| First Class                      | 3 (4.76)            | 1 (2.32)                        | 2 (10)                           |
| VIP Class                        | 11 (17.49)          | 5 (11.65)                       | 6 (30)                           |
| VVIP Class                       | 1 (1.58)            | 1 (2.32)                        | 0 (0)                            |
| Total                            | 63 (100)            | 43 (100)                        | 20 (100)                         |
| Length of hospital stay          |                     |                                 |
| Median (days)                    | 4                   | 4                                | 4                                |
| Range                            | 3–7                 | 3–7                              | 3–7                              |

| Table 2: Comparison of medical cost between generic and patent ceftriaxone groups |
|----------------------------------|
| **Cost Type**                   | **Generic ceftriaxone (Rp)** | **Patent ceftriaxone (Rp)** | **p-value** |
| Median drug cost                | 97,000                      | 1,070,880                      | 0.000*      |
| Median laboratory cost          | 308,000                     | 365,000                        | 0.953       |
| Median medical device use cost  | 87,351                      | 133,529                        | 0.040*      |
| Median service cost             | 130,000                     | 260,000                        | 0.153       |
| Median hospitalization cost     | 1,555,000                   | 1,695,000                      | 0.170       |
| Median total medication cost    | 2,303,749                   | 3,554,407                      | 0.000*      |

*significant difference
Mann-Whitney U-test, the p-value obtained was 0.153 (p>0.05), indicating that service cost was not significantly different between the two groups.

Median hospitalization cost in the generic and patent ceftriaxone groups was Rp 1,555,000 and Rp 1,695,000, respectively. Based on non-parametric Mann-Whitney U-test, the p-value obtained was 0.000 (p<0.05), indicating that hospitalization was not significantly different between the two groups.

Median total medication cost for patent ceftriaxone (Rp 3,554,407) was higher than that for generic ceftriaxone (Rp 2,303,749). Based on non-parametric Mann-Whitney U-test, the p-value obtained was 0.000 (p<0.05), indicating that total medication cost was significantly different between the two groups. Median total medication cost for each medication was used further in CEA, which consisted of CER, CEIR, and sensitivity analysis.

CER

Mean CER was calculated by comparing median total medication cost with medication effectiveness in generic and patent ceftriaxone groups. Based on normality test, total cost data distribution was not normal; hence, median total medication cost used in the calculation was considered total medication cost. Medication effectiveness was defined as median length of hospital stay. The CER of each medication group is shown in Table 3.

CER of the generic ceftriaxone group was lower (Rp 575,937.25/day) than that of the patent ceftriaxone group (Rp 888,601.75/day). Moreover, CER was calculated according to the treatment class of patients. CER of each medication group based on their treatment class is shown in Table 4.

The length of hospital stay in the generic and patent ceftriaxone groups was similar, showing effectiveness equality between the two medication groups. However, total medication cost in the generic ceftriaxone group was lower than that in the patent group; hence, generic ceftriaxone was in a dominant position in the effectiveness and cost table (Table 5). Meanwhile, the patent ceftriaxone group was in the dominant position. A clear position between the medication groups showed that generic ceftriaxone was more cost-effective than patent ceftriaxone; hence, calculation of the CER was not necessary. Subsequently, a sensitivity analysis was performed to measure uncertainty from various data used as well as resulting from the pharmacoeconomic analysis.

Sensitivity Analysis

Sensitivity analysis was performed by simulating 25% or 50% increase and decrease in median total medication cost. The results of the sensitivity analysis are shown in Table 6.

The results of the sensitivity analysis showed that even though median total medication cost from generic ceftriaxone was decreased by 25% and 50% or increasing by 25% and 50%, CER of the generic ceftriaxone group remained lower than that of the baseline CER of the patent ceftriaxone group (Rp 888,601.8). Meanwhile, a significant difference in the CER of the patent ceftriaxone was observed only at 50% decrease median total medication cost, at which point the CER of the patent ceftriaxone group (Rp 444,300.88) became lower than the baseline CER of the generic ceftriaxone group (Rp 575,937.3).

DISCUSSION

Of the 63 patients in this study, 43 and 20 patients were administered generic or patent ceftriaxone of a brand, respectively. The analysis was performed by comparing total medicinal cost and treatment effectiveness of the generic and patent ceftriaxone groups.

Among the patients who met the inclusion criteria, the number of patients using generic ceftriaxone (71.67%) was more than that of patients using patent ceftriaxone (28.33%). This might be explained by the fact that a majority of patients were covered under BPJS health insurance (National Health Insurance), and the use of generic ceftriaxone was recommended according to BPJS terms and conditions in 2014 stated in National Formularies based on Keputusan Menkes RI No.328/Menkes/SK/2013 [5].

Based on the payment source type, 24 patients paid total medication cost independently (38.09%); 24 patients paid total medication cost independently.
Pharmacoeconomic analysis was performed to account for uncertainty more cost-effective group [7-10]. Medication alternative position in on treatment class showed that CER of the generic ceftriaxone group was lower than that of the patent ceftriaxone group, except when median total medicinal cost of patent ceftriaxone was decreased by 50%. This study is suggested to be taken as evaluation consideration for the regulator so that generic ceftriaxone can be taken as it is more cost-effective than branded ceftriaxone. However, further study is needed and if it possible, to consider other effectiveness parameters such as number of anti-salmonella immunoglobulin M counted, number of decreased fever temperature, and the count of leukocytes. It is also suggested to consider including indirect cost and intangible cost in further study.

### CONCLUSION

The medication effectiveness of generic ceftriaxone was equal to that of patent ceftriaxone, as evident by the equal median length of hospital stay (4 days) for both drug types. Statistically, there was no significant difference in medication effectiveness between generic and patent ceftriaxone in terms of median total medication cost (p=0.548). Median total medication cost of patent ceftriaxone was higher (Rp 3,554,407) than that of generic ceftriaxone (Rp 2,303,749), and there was a statistically significant difference in medication effectiveness between generic and patent ceftriaxone in terms of median total medication cost (p<0.001). Based on CEA, generic ceftriaxone (CER: Rp 575,937.25/day) was more cost-effective than patent ceftriaxone (CER: Rp 888,601.75/day).

### CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest.

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