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The Analysis of The Effectiveness of Pulmonary Tuberculosis and HIV-Co-TB Treatment Therapies at Sulianti Saroso Infectious Diseases Hospital

(Analisis Keberhasilan Pengobatan Pasien TB Paru dan TB HIV di Rumah Sakit Penyakit Infeksi Sulianti Saroso)

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Abstract: *Mycobacterium tuberculosis* causes Tuberculosis (TB), an infectious disease. The study aims to evaluate DOTS therapy's impact on pulmonary TB and TB-HIV patients. This research used a descriptive qualitative study design with a retrospective descriptive research approach using secondary data for the period June 2017 to July 2020. The analysis uses the Miles and Huberman model. A study of 305 people found that 83% of pulmonary TB cases completed treatment within the initial phase, 64% completed the continuation phase. TB-HIV cases 93% completed treatment within the initial phase, 71% the continuation phase. The combination of OAT and ARV doses was successful in reducing initial smear conversion in pulmonary TB cases. The treatment was evaluated as cure in pulmonary TB cases, complete in pulmonary TB-HIV cases, and had no treatment failure status in both groups. Treatment success in pulmonary TB patients was not significantly related (p-value≥5%) with the type of OAT, type of PMO, gender, and age. Whereas in HIV co-infected pulmonary TB patients, treatment success was significantly related (p-value <5%) with the type of PMO, and not related (p-value≥5%) with the type of OAT, gender, and age.

Keywords: DOTS, HIV tuberculosis, pulmonary tuberculosis, tuberculosis (TB).

Abstrak : *Mycobacterium tuberculosis* menyebabkan Tuberkuloisis (TB), suatu penyakit menular yang paling sering menyerang paru. Penelitian bertujuan menganalisa keberhasilan terapi DOTS dilihat dari paramater pasien TB Paru dan TB Paru-HIV. Penelitian menggunakan desain studi kualitatif deskriptif dengan pendekatan penelitian deskriptif retrospektif menggunakan data sekunder periode Juni 2017 – Juli 2020. Analisis menggunakan model *Miles and Huberman*. Total sampel 305 orang, ditemukan sebanyak 83% kasus TBC paru menyelesaikan pengobatan pada fase awal dan 64% menyelesaikan fase lanjutan. Pada kasus TBC-paru HIV 93% menyelesaikan fase awal, dan 71% menyelesaikan fase lanjutan. Kombinasi dosis OAT dan ARV berhasil menurunkan konversi BTA awal pada kasus TB paru. Pengobatan dinilai sembuh pada kasus TB paru, tuntas pada kasus TB-HIV paru, dan tidak ada status kegagalan pengobatan pada kedua kelompok. Keberhasilan pengobatan pada pasien TB paru tidak berhubungan bermakna (p-value≥5%) dengan jenis OAT, jenis PMO, jenis kelamin, dan usia. Sedangkan pada pasien TB-HIV paru, keberhasilan pengobatan berhubungan bermakna (p-value <5%) dengan jenis PMO, dan tidak berhubungan (p-value≥5%) dengan jenis OAT, jenis kelamin, dan usia. Kombinasi OAT tablet FDC dan tablet lepasan yang diberikan pada kedua kasus sudah tepat dosis disertai pemberian ARV pada TB-HIV sudah tepat dosis dengan hasil evaluasi berupa sembuh.

Kata kunci: DOTS, tuberculosis (TB), TB paru-HIV.

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INTRODUCTION

TUBERCULOSIS (TB) is an infectious disease that is the main cause of poor health and one of the main causes of death worldwide after HIV (human immunodeficiency virus)/AIDS (acquired immuno-deficiency syndrome). TB disease is caused by the bacterium *Mycobacterium tuberculosis* (MTb) which usually attacks the lungs and spreads when a TB patient expels the bacteria into the air (for example, by coughing)[1,2]. Currently, almost a quarter of the world's population is infected with TB which 89% of TB sufferers are adults and 11% are children. Indonesia accounts for the third-highest TB sufferers in the world after India and China[3]. The risk of death in TB patients will be greater if a patient is also infected with HIV.

Based on the 2021 health profile (B) data, HIV patients in 2021 are likely to increase over the last 10 years, although they tend to decrease compared to 2016[4]. Patients who are co-infected with TB and HIV have the potential to accelerate the decline in immune function so that the patient's condition will worsen. According to Getahun H et al. in Yong-Jia Ji et al[5]. The HIV population has a 20 times higher risk of latent TB activation than non-HIV infected patients. In Indonesia, TB control is important and targets a reduction in the incidence of TB to close to 65 cases per 10,000 population by 2030.

One of the efforts to control TB disease is through medication. The success of treating TB patients is expressed in the patient's recovery rate and treatment rate[4]. In 2021, the national TB treatment success rate is 86%, which shows that the success of TB treatment has been achieved according to the Ministry of Health's target of 85%. However, the provinces of DKI Jakarta (79.3%) and West Java (82.4%) are still below the Ministry of Health's treatment success target in 2021. DKI Jakarta Province ranks 4th (fourth) lowest in terms of TB treatment success for all provinces in Indonesia[3].

Several factors influence the successful treatment of TB patients, including socio-economic status, knowledge, stress levels, and ease of access to health services[6,7]. The successful treatment of TB patients is beneficial in suppressing the spread of TB disease both in Indonesia and around the world. As a form of tackling the spread of TB and increasing the success of TB treatment. In 1993, the WHO (World Health Organisation) declared TB as a global emergency, implementing a short-term strategy of direct observation therapy known as DOTS (directly observed therapy short course) therapy. DOTS is an action that combines practice in the diagnosis and treatment of TB patients. The term "DOTS" is defined as direct supervision of swallowing short-term drugs every day by the medication supervisor (PMO) for TB patients. A PMO is someone who supervises TB patients in swallowing and/or consuming good drugs, which aims to reduce the number of sufferers who do not take their antibiotic drugs properly. PMO itself is the third point in the DOTS strategy of the five WHO components[8,9]. Based on research conducted by Dailami et al. showed that PMO was not significantly related to the success of treatment for TB patients[7]. The quality of PMO in supervising TB patients taking medication will also tend to affect the success of treatment. PMO which can affect adherence to taking TB patients' medication will affect the success of TB treatment. The research showed that adherence to taking medication for TB patients affects the success of treatment for TB patients[10,11].

RSPI Prof. Dr. Sulianti Saroso is a facility that supports integrated TB DOTS services and integrated HIV polyclinic services that treat TB patients and HIV patients. The hospital is also the National Centre for Study and Referral for Infectious Diseases in Indonesia, which always strives to provide the best service supported by excellent services that support these quality facilities[12]. Based on these conditions, researchers wanted to analyse the success of DOTS therapy in patients with pulmonary TB and HIV co-infected TB based on the length of treatment, the number of combinations of drugs given, and the success of treatment based on clinical achievements.

MATERIAL AND METHODS

MATERIAL. The study was conducted in patients with pulmonary TB and HIV co-infected TB at RSPI Prof. Dr. Sulianti Saroso for the period July 2017–June 2020. Data was collected retrospectively using medical records of patients with pulmonary TB and TB HIV coinfection at RSPI Prof. Dr. Sullianti Saroso.

Equipments. The data was analyzed using statistical computing platform R Commander version 4.1.2.

METHODS. Study Design. The study was conducted in a qualitative descriptive manner in patients with pulmonary TB and HIV co-infected TB at RSPI Prof. Dr. Sulianti Saroso. The sampling technique in this study used Total Sampling where the entire population that met the inclusion and exclusion criteria was used as a sample.

Inclusion and Exclusion Criteria. The inclusion criteria in this study were adult patients 19–59 years old, patients with pulmonary TB and new cases of pulmonary TB coinfected with HIV, patients who

routinely carry out controls (at least once a month) for 6 months of treatment, and length of patient treatment. The exclusion criteria of this study were relapsed patients, patients treated after failure, patients treated after discontinuation of treatment, pregnant and lactating women, patients aged 0–18 years, and extrapulmonary TB patients. Samples that met the inclusion criteria were 305 people, of which 103 were HIV co-infected pulmonary TB patients and 202 were pulmonary TB patients.

Data Analysis. Data analysis techniques in this study used two approaches: descriptive analysis using descriptive statistical approaches and inferential analysis. Descriptive analysis was carried out on patient characteristics data, OAT combinations, and treatment outcomes of patients with pulmonary TB and HIV co-infected pulmonary TB. Inferential analysis was carried out to see the relationship between the combination of antituberculosis drugs as part of treatment and treatment success. In this study, the success of treatment was divided into successful and unsuccessful outcomes. Success is achieved if the results of the treatment are complete and cured, whereas it is not successful if the results of the treatment move to the health facility, die, default, or drop out of treatment and are not evaluated.

Relationship analysis in this study used two tests, namely the chi-square test on the contingency table and the Spearman correlation test. The Chi-Square test on the contingency table was used to see the relationship between treatment success and the type of antituberculosis drug, Medication Supervisor (PMO) type, and gender, while the Spearman Correlation Test was used to see the relationship between treatment success and age.

RESULT AND DISCUSSION

Patient Characteristic. This study used data on pulmonary TB and HIV co-infected pulmonary TB at RSPI Prof. Dr. Sulianti Saroso for the period July 2017–June 2020 which met the inclusion and exclusion criteria of 305 patients. The characteristics of the patients in this study are presented in Table 1 including age, gender, residence status of medication supervisor (PMO), type of diagnosis, HIV status, and acid fast bacilli (AFB) conversion.

According to age, the proportion of patients with pulmonary TB tended to be evenly distributed across the age range of 19 to 58 years, with the greatest percentages of 25% in the age ranges of 29 to 38 and 49 to 58 years. The ages of HIV co-infected pulmonary TB patients tended to be uneven, with the highest percentage in the age group 29–38 years of 40%. This situation was consistent with the research findings of Sikumbang RH et al., which found that productive age had a higher vulnerability to pulmonary TB than unproductive age[13]. The distribution of productive age had the highest percentage of getting pulmonary TB, which was also in accordance with the Indonesian Health Profile data released by the Ministry of Health of the Republic of Indonesia in 2021, where the age with the highest percentage was 45–54 years old at 17.5%, followed by 25–34 years old at 17.1%. The productive age group, which included those between the ages of 29 and 38, tended to be highly mobile and socially active, to be tired, and to lead unhealthy lifestyles that increase the rate of transmission, especially when combined with lowered immunity.

The male sex group's tendency for pulmonary TB and pulmonary TB to be HIV-infected were greater than the female sex group, where the male sex was pulmonary TB by 57% and pulmonary TB HIV coinfection was 77%. This condition could be caused by men tending to have a higher level of mobility than women. In addition, larger men had unhealthy lifestyles such as smoking and drinking alcohol (and having sex with many partners)[14]. Male sex in HIV-pulmonary TB could also be caused by a lifestyle that had multiple partners, so that patients exposed to the HIV virus which causes decreased immunity.

Patients with TB at RSPI Prof. Dr. Sulianti Saroso were given complete access to a Medication Supervisor (PMO), which was divided into two groups: those who lived in one house and those who did not. According to Table 1's data, 98% of PMOs live in one home, whereas 98% of PMOs do not. This means that the proportion of PMOs who live in one home was higher than the percentage of PMOs who do not. PMOs who share a home tended to make it simpler for TB patients to follow instructions and take the prescribed TB treatment. The type of diagnosis in patients with pulmonary TB was a greater percentage through bacteriological diagnosis with sputum and positive HIV-positive acid fast bacteria (BTA) test results of 67% compared to clinical diagnosis through Thorax photos with negative smears. The results of examinations using sputum or smear tests have supported the diagnosis of pulmonary tuberculosis in patients. However, this was different from HIV co-infected pulmonary TB patients who have a clinical diagnosis percentage that is 62% higher than a bacteriological diagnosis (positive AFB). HIV co-infected pulmonary TB patients were HIV patients who were exposed to TB bacteria more easily because the symptoms appeared and were supported by chest photos, so the clinical diagnosis was more percentage based on bacteriology.

Table 1. Characteristics of outpatient pulmonary TB and TB HIV coinfection at RSPI Prof. Dr. Sulianti Saroso year 2017-2020.

Variable	Category	Pulmonary TB (N = 202)		Pulmonary TB HIV Coinfection (N = 103)	
		Number of Patient	Percentage (%)	Number of Patient	Percentage (%)
Age	19 – 28 years old	45	22	25	24
	29 – 38 years old	51	25	41	40
	39 – 48 years old	49	24	28	27
	49 – 58 years old	50	25	8	8
	59 years old	7	3	1	1
Sex	Female	86	43	24	23
	Male	116	57	79	77
Medication Supervisor (PMO)	Live in same house	198	98	101	98
	Don't Live in one house	4	2	2	2
Diagnostis	Bacteriology (AFB positive)	135	67	39	38
	Clinical (AFB Negative)	67	33	64	62
HIV Status	Positive	0	0	103	100
	Negative	151	75	0	0
	Unknown	51	25	0	0
Initial BTA Conversion	Negative	63	31	66	64
	1+	80	40	19	18
	2+	19	9	5	5
	3+	28	14	6	6
	Scanty	11	5	7	7
	Do not check sputum	1	0.09	0	0

Note: FDC=*Fixed Dose Combination*

The HIV status of pulmonary TB patients showed the highest percentage was negative, 75% were HIV co-infected pulmonary TB patients, and 100% tested positive for HIV. Initial AFB was the result of the AFB test in the initial treatment period. The majority of initial BTA conversion outcomes in patients with pulmonary TB were 1+ (40%), while the majority of results in patients with pulmonary TB and HIB were negative (64%). The initial conversion of AFB in pulmonary TB patients to the category of not examining sputum (0.09%) was caused because the patient could not excrete sputum, so he was not tested with smears.

Types of Anti-tuberculosis Drugs for Patients. The choice of the type of antituberculosis were given to a patient suspected of having TB was seen from the symptoms experienced by the patient as well as the results of the patient's sputum examination, which showed the level of AFB contained in one microscopic field of view. Types of antituberculosis drugs (OAT) for outpatient pulmonary TB and TB-HIV was presented in Table 2. The use of OAT in pulmonary TB cases resulted in 80 people (40%) using the release tablet, 105 people (54%) using the FDC tablet, and as many as 17 people (8%) using the FDC tablet in the initial phase, then replacing it with the release tablet in the continuation phase. In the case of pulmonary TB co-infected with HIV, the results obtained were that 67 people (65%) used the release tablet, 19 people (18%) used the FDC tablet, and as many as 17 people (17%) used the FDC tablet in the initial phase and then replaced the release tablet in the continuation phase.

The principle of using Antituberculosis Drug was expected to prevent TB resistance. Doses were given at the right dose and were given for a sufficient period of time according to the conditions could prevent recurrence. TB treatment included treatment at the initial and advanced stages by prioritising FDC tablets as the main choice and selecting release tablets. The use of one type of antituberculosis medication from the initial phase to the continuation phase was finished, but if the patient did not exhibit any clinical improvement during the continuation phase, the type of medication could be changed. For instance, switching from FDC tablets in the initial phase to a release tablet during the continuation phase. The principle of providing Antituberculosis Drug referred to the National Guidelines for Administrative Medical Services regulated by the Ministry of Health[15].

Treatment Result. Treatment outcomes were measured based on the type of Antituberculosis drug regimen used and based on the clinical condition of the patient during the treatment phase. The distribution

of treatment outcomes included recovery, complete treatment, dropout/default, failure, death, not being evaluated, and moving health facilities[14]. The treatment outcomes assessed in this study were only based on TB treatment therapy because treatment for people with HIV/AIDS (PLWHA) takes a lifetime, while TB treatment therapy could be monitored over a period of 6–9 months. Table 3 shows the patient's final results after passing treatment.

Based on the results of the Late AFB (Table 3), it showed that the negative category in pulmonary TB patients increased while HIV co-infected pulmonary TB patients decreased compared to the results of the initial AFB. The increase in the percentage of negative Late AFB and the decrease in the percentage in categories 1+, 2+, 3+, and scanty show the success of TB treatment. However, 54% of pulmonary TB patients and 78% of HIV co-infected pulmonary TB patients did not perform sputum examinations. The percentage of patients who were not examined for sputum in both pulmonary TB and HIV co-infected pulmonary TB was quite high because it was above 50%. Some of the reasons why sputum examinations were not carried out were because patients could not collect their sputum, died, moved to health facilities, dropped out of treatment, and could not be evaluated. Figure 1 shows a comparison of the initial and final AFB conditions in patients with pulmonary TB and pulmonary TB coinfected with HIV, where there was an increase in late smear negatives in pulmonary TB patients but a decrease. The decrease in negative Late AFB in HIV Coinfected Pulmonary TB patients was due to the condition of HIV patients tending to have low immunity, but when viewed from other categories, namely 1+, 2+, 3+, and scanty decreased.

Table 2. Types of anti tuberculosis srugs (OAT) for outpatient pulmonary TB and TB HIV coinfection at RSPI Prof. Dr. Sulianti Saroso year 2017-2020.

Variable	Category	Pulmonary TB (N = 202)		Pulmonary TB HIV Coinfection (N = 103)	
		Number of patients	%	Number of patients	%
BTA after treatment (pre BTA)	Negative	88	44	22	21
	1+	0	0	0	0
	2+	0	0	0	0
	3+	2	1	0	0
	Scanty	3	1	1	1
	Do not check sputum	109	54	80	78

Note: FDC=*Fixed Dose Combination*

Table 3. BTA Outpatient Pulmonary TB and TB HIV Coinfection after treatment at RSPI Prof. Dr. Sulianti Saroso Year 2017-2020.

Type of Anti Tuberculosis Drug	Pulmonary TB		Pulmonary TB HIV Coinfection	
	Number of patients	%	Number of patients	%
Release Tablet	80	40	67	65
Tablet FDC*	105	52	19	18
Tablet FDC and release tablet	17	8	17	17

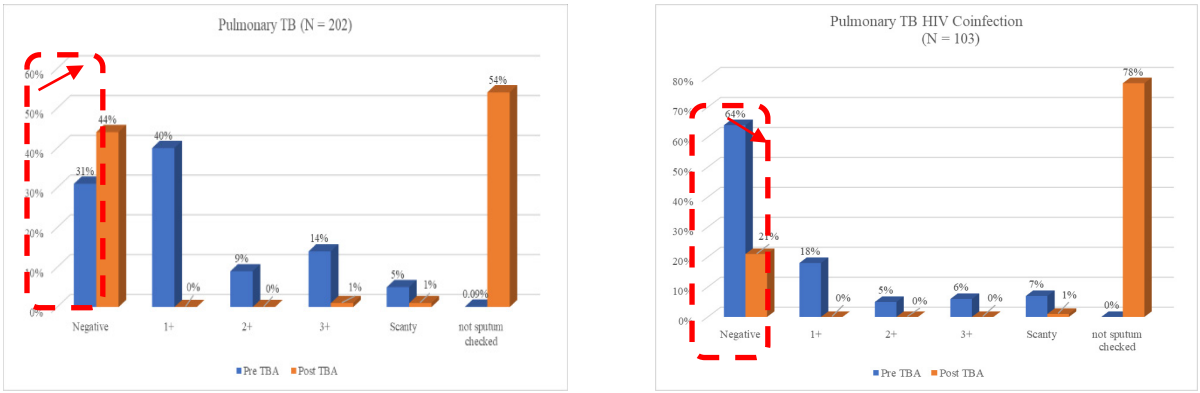

Figure 1. Comparison of initial and final BTA results at RSPI Prof. Dr. Sulianti Saroso year 2017-2020.

Table 4. shows the results of treatment for pulmonary TB patients with cured (45%) and complete (20%) treatment results. This showed that 65% of patients with pulmonary TB were successful. In HIV co-infected pulmonary TB patients, the treatment outcome was 22% cured and 47% complete, so the treatment was successful in HIV co-infected pulmonary TB patients by 69%. RSPI Prof. Dr. Sulianti Saroso has implemented the DOTS strategy in the treatment of TB patients, one of which is the existence of a Medication Supervisor (PMO). Based on the data, Table 1 showed TB patients in %. RSPI Prof. Dr. Sulianti Saroso had been 100% assisted by the PMO. The success of treating TB patients was influenced by the presence of a PMO accompanying TB patients[14,15]. The PMO was tasked with observing and supervising every drug intake so that the OAT swallowed by the patient was the right drug, the right dose, and the right interval, so that a PMO who doesn't monitor would cause the success rate of treatment to decrease.

Table 4. Treatment results for pulmonary TB and HIV coinfected pulmonary TB at RSPI Prof. Dr. Sulianti Saroso year 2017-2020.

Tretament Result	Pulmonary TB		Pulmonary TB HIV Coinfection	
	Number of patients	%	Number of patients	%
Moved to other facilities	29	14%	11	11%
Completed	41	20%	48	47%
Cured	90	45%	23	22%
Died	1	0.50%	3	3%
Dropped out of treatment	28	14%	13	13%
Not Evaluated	13	6%	5	5%
Total	202	100%	103	100%

Relationship Analysis of Treatment Success with Types of Antituberculosis Drug. Treatment of pulmonary TB and HIV co-infected pulmonary TB was expected to be successful in one phase of treatment. In this study, treatment success was divided into two parts of treatment outcomes which are described in Table 5. The definition of treatment outcome categories referred to the Ministry of Health's guidelines regarding National Guidelines For Tuberculosis Medical Services[14]. Treatment was said to be "Successful" if the results of the treatment are "Cured" and "Complete", while the treatment was said to be "Unsuccessful" if the results of the treatment were "Moved Health Facilities", "Discontinued Treatment", "Died", and "Not Evaluated". Analysis of the relationship between treatment success and type of OAT, type of PMO, gender, and age was described in Table 6.

Based on the results of the correlation test, it showed that treatment success had a relationship with the type of Antituberculosis drug given to pulmonary TB patients (P-value <5%), while success had no relationship with the type of PMO, gender, and age (P-value>5%). This was accordance to research at Rimba Jaya Health which showed the success of TB treatment didn't affect to age, gender, and type of PMO[16].

Based on the results of research conducted by Yusmaniar et.al, it was found that one of the factors that influences the success of therapy was medication adherence. This validates the results of our study that medication, age, gender and type of PMO are not related to the success of TB treatment, but influenced by the poor level of medication adherence[17].

Table 5. Analysis of the relationship between treatment outcomes and the type of OAT, type of PMO, gender, and age of pulmonary TB patients at RSPI Prof. Dr. Sulianti Saroso year 2017-2020.

Variable	Category	Treatment Result		Total	P-value	Conclusion
		Succeed	not succeed			
Type of OAT	FDC (Fixed Dose Combination)	74	31	105	0.18	No
	Kombipak	43	37	80		Relationship
	FDC (Fixed Dose Combination), Kombipak	14	3	17		
Type of PMO (drug supervisor)	Family members living together	129	69	198	0.53	No
	Neighbours / relatives are not in the same house	2	2	4		Relationship
Sex	Female	59	27	86	0.336	No
	Male	72	44	116		Relationship
	Age (19- 59 years)			202	0.696	No Relationship

Table 6. Analysis of the relationship between treatment outcomes and the type of OAT, type of PMO, gender, and age of pulmonary TB HIV coinfection patients at RSPI Prof. Dr. Sulianti Saroso year 2017-2020.

Variable	Category	Succeed	Not Succeed	Total	P-value	Conclusion
Type of OAT	FDC (Fixed Dose Combination)	12	7	19	0.166	No Relationship
	Release tablet	44	23	67		
	FDC (Fixed Dose Combination), Release Tablet	15	2	17		
Type of PMO (Medication Supervisor)	Family members living together	71	30	101	0.033	Relationship
	Neighbours / relatives are not in the same house	0	2	2		
Sex	Female	59	27	86	0.818	No Relationship
	Male	72	44	116		
	Age (19- 59 years)			103	0.091	No Relationship

CONCLUSION

Pulmonary TB patients in the study were mostly in the 29-38 year age category (51%), with male sex (57%), and the PMO type living in one house (98%), while the most HIV-coinfected pulmonary TB patients were in the age category 29-38 years (40%), with male sex (77%), and type of the PMO living in one house (98%). The type of antituberculosis drug used fixed dose combination (FDC) and release tablet. The success of treatment with complete and cured treatment status in pulmonary TB patients was 65% and in HIV pulmonary TB patients was 69%. Treatment success in pulmonary TB patients was not significantly related (p-value≥5%) with the type of OAT, type of PMO, gender, and age. Whereas in HIV co-infected pulmonary TB patients, treatment success was significantly related (p-value <5%) with the type of PMO, and not related (p-value ≥5%) with the type of OAT, gender, and age.

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