

ORIGINAL ARTICLE

Omega-6 and Omega-3 Intake Ratio in Pulmonary Tuberculosis Patients and Its Correlation with Depression Score

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ABSTRACT

Introduction: Depression affects 45.19% of pulmonary tuberculosis (TB) patients' adherence to treatment, resulting in increased morbidity and death, medication resistance, and continued disease transmission. This study aimed to examine the relationship between omega-6/omega-3 (ω -6/ ω -3) polyunsaturated fatty acids (PUFA) intake ratio and depression score in patients with pulmonary TB at Persahabatan National Respiratory Referral Hospital, Jakarta.

Methods: This was a cross-sectional study of 99 subjects with pulmonary TB. Data were collected using the Semi-Quantitative Food Frequency Questionnaire (SQ-FFQ), anthropometric measurements, and the Beck Depression Inventory-II (BDI-II).

Results: Correlation analysis used the Spearman test and revealed the ratio of ω -6/ ω -3 PUFAs intake of 7.78 ± 1.13 , the median value of depression score was 9 (10-36). There was no correlation between ω -6/ ω -3 PUFA intake and depression score ($r = 0.063$; $p = 0.534$).

Conclusion: There was no correlation between ω -6/ ω -3 PUFAs intake ratio and depression scores in pulmonary TB patients. This is the first study to examine the correlation between ω -6/ ω -3 PUFA intake ratio and depression score in pulmonary TB patients.

INTRODUCTION

Tuberculosis (TB) is an infectious disease that is a major source of health problems and one of the leading causes of death worldwide.¹ TB is transmitted through the bacterium *Mycobacterium tuberculosis* (MTB), which is spread through droplets in the air. TB is still a major public health issue in Indonesia.² According to data from the Indonesian Ministry of Health, there were 406,936 pulmonary TB patients in Indonesia in 2021, with an 86% treatment success rate. In 2021, the majority of global TB cases, comprising over two-thirds,

were reported in eight nations, India (28%), Indonesia (9.2%), China (7.4%), the Philippines (7.0%), Pakistan (5.8%), Nigeria (4.4%), Bangladesh (3.6%), and the Democratic Republic of the Congo (2.9%).^{2,3}

Depression is a common mental health problem among people with TB. Psychiatric illnesses, especially depression, are common among TB patients. Depression was found in 45.19% of TB patients in community-based investigations and increased to 54% in hospitalized patients. According to a 2020 systematic review and meta-analysis, people with TB are at high risk of developing depression, which negatively

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impacts patients' adherence to TB treatment, increasing morbidity and mortality, drug resistance, and ongoing disease transmission.⁴

Psychosocial, behavioral, and biological variables influence depression in TB patients. Concurrently, MTB infection causes persistent inflammation by inducing cytokines. Systemic inflammation affects the immune system's central response in the central nervous system, activating the hypothalamic-pituitary-adrenal (HPA) axis and sympathetic nerves, contributing to mental health problems.⁵ Age, gender, education, income, nutritional condition, phase of therapy, comorbidities, and human immunodeficiency virus (HIV) status also can affect depression in TB patients.⁶⁻⁹

The composition of fatty acids against inflammation impacts cell function, with arachidonic acid (AA), eicosapentaenoic acid (EPA), and docosahexaenoic acid (DHA) playing essential roles. The presence of high EPA and DHA and low AA in the cell membrane will alter the pattern of inflammation-related eicosanoids, resolvin, and protectin synthesis.¹⁰ Omega-6 (ω -6) and omega-3 (ω -3) fatty acids compete with each other using the same desaturase and elongase enzymes for bioconversion into their derivatives. Therefore, the ratio of ω -6 to ω -3 fatty acid intake is important to consider because it affects the bioconversion of alpha-linolenic acid (ALA) and linolenic acid (LA) into their derivatives in the human body. A low ω -6 diet in relation to ω -3 will result in higher levels of EPA and DHA in cell membranes and lower levels of AA.^{10,11} In addition, the presence of ω -3 polyunsaturated fatty acids (PUFAs) increases cell membrane fluidity compared to ω -6 PUFAs. This membrane fluidity affects the occurrence of depression. The ratio of ω -6 and ω -3 PUFAs impacts the monoaminergic system. Given the role of the monoaminergic system in the pathophysiology of depression, an increased ratio of ω -6 and ω -3 PUFAs appears to be an underlying factor in depression.¹¹ According to a meta-analysis, a positive association exists between a high ω -6/ ω -3 PUFA ratio and the incidence of depression.¹² In a study by Jayaatmaja, *et al.* (2020) regarding the ω -6/ ω -3 fatty acid intake ratio in TB patients, the result obtained was 10:1.¹³ This figure indicates a high ratio compared to the recommended ω -6 to ω -3 ratio of 1-4:1.¹³

No research has been conducted on the effect of the ω -6/ ω -3 PUFA intake ratio on depression scores in pulmonary TB patients. This study aimed to examine the relationship between ω -6/ ω -3 PUFA intake ratio and depression score in patients with pulmonary TB at Persahabatan National Respiratory Referral Hospital, Jakarta.

METHODS

Study Participants

From January 2023 to February 2023, a cross-sectional study with a consecutive sampling strategy was conducted at Persahabatan National Respiratory Referral Hospital, Jakarta. Inclusion criteria were TB patients currently undergoing treatment, both male and female, aged 18-60 years old. Exclusion criteria were patients with drug-resistant TB, those with psychiatric disorders or those taking psychiatric medications before being diagnosed with pulmonary TB, body mass index (BMI) <16 kg/m² (severely underweight), pregnant and breastfeeding women, unable to speak Indonesian, and illiterate. Before fulfilling the requirement, the participants signed a written consent form. Subjects completed a socio-demographic questionnaire. The Ethics Committee of Health Research Persahabatan National Respiratory Referral Hospital, Jakarta, approved the study procedure (No. 01/KEPK-RSUPP/01/2023).

Dietary Intake

A Semi-Quantitative Food Frequency Questionnaire (SQ-FFQ) was used in this study to collect dietary consumption of ω -6 and ω -3 PUFAs throughout the previous month. Food composition data from Asian and local countries were used to compute dietary intake.¹⁴

Anthropometric Measurement

A height measurement board (ShorrBoard, Olney, USA) was used to determine the height. SECA 876 was used to measure weight to determine body weight. The measurements were repeated twice, with the average value calculated.

Depression Score

The Beck Depression Inventory-II (BDI-II) questionnaire collected depression score data. It consisted of 21 questions about mood, pessimism, feelings of failure, lack of satisfaction, guilt, feelings of being punished, self-loathing, self-blame, self-punishment, crying episodes, irritability, social withdrawal, inability to make decisions, body image, a distraction from work, sleep disturbance, fatigue, loss of appetite, weight loss, somatic preoccupation, and loss of sexual desire.¹⁵

Data Analysis

The Statistical Package for the Social Sciences (SPSS) version 20 (SPSS Inc., Chicago, IL, USA) was used to analyze the data. Dietary intake was assessed using the NutriSurvey 2007 (Germany). The

Kolmogorov-Smirnov test was performed to determine the normality of data from subjects' demographics, nutritional consumption, anthropometric measurements, and depression scores. The Spearman correlation test was utilized to determine the correlation between the ω -6/ ω -3 PUFA ratio and the depression score. The correlation was deemed significant if $p < 0.05$.

RESULTS

Participant Characteristics

The total number of respondents was 104. After data cleaning, 99 respondents were included in the final data analysis. Five respondents could not be included as they did not complete the BDI-II questionnaire and did not proceed with the SQ-FFQ interview. Among the study population, 61.6% were males with a median age of 46 years old. Study participants were also predominantly of higher education level (68.7%) but low income (54.5%). According to the BMI classification, 42.4% of the study population were underweight. Most of the participants were in the continuation treatment phase (71.7%), did not have chronic disease comorbidities (57.6%), and did not have co-infection with HIV (89.9%) (Table 1).

Characteristics of Participants Based on Dietary Intake and Depression Score

Table 2 shows the distribution of dietary intake and depression scores. Most participants had a low intake of ω -6 PUFAs (55.6%) but an adequate intake of ω -3 PUFAs (55.6%). The median intake of ω -6 PUFAs was 11.9 (2.2-51.8) g/day and ω -3 PUFAs was 1.6 (0.3-7.3) g/day. According to this study, the mean of ω -6/ ω -3 PUFAs intake ratio was 7.78 ± 1.13 . The median depression score was 9 (0-36), with a predominantly normal score (79.8%).

Correlation of ω -6/ ω -3 PUFAs Intake and Depression Score in TB Patients

In the scatter plot results, the data points appear to be randomly scattered and do not form a clear line or

curve. This indicates no strong linear relationship between the two variables, as shown in Figure 1.

Table 1. Sociodemographic characteristics of the study population

Parameter	Frequency (n = 99)
Gender	
Male	61 (61.6)
Female	38 (38.4)
Age (years old)	46 (18-60)
Education level	
Elementary/no education	13 (13.1)
Middle school	18 (18.2)
High school/university	68 (68.7)
Income level	
Low	54 (54.5)
Enough	45 (45.5)
Body mass index	
Underweight	42 (42.4)
Normal	39 (39.4)
Overweight	8 (8.1)
Obese type I	8 (8.1)
Obese type II	2 (2)
Therapy phase	
Intensive phase	28 (28.3)
Continuation phase	71 (71.7)
Comorbidities	
Yes	42 (42.4)
No	57 (57.6)
HIV status	
Yes	5 (5.1)
No	89 (89.9)
Unknown	5 (5.1)

Table 2. Distribution of dietary intake and depression score

Parameter	Results (n = 99)
Level of ω -6	11.9 (2.2 – 51.8)
Low	55 (55.6)
High	44 (44.4)
Level of ω -3	1.6 (0.3 – 7.3)
Low	44 (44.4)
High	55 (55.6)
ω -6/ ω -3 ratio	7.78 ± 1.13
Depression score	9 (0-36)
Normal	79 (79.8)
Mild depression	10 (10.1)
Moderate depression	9 (9.1)
Severe depression	1 (1)

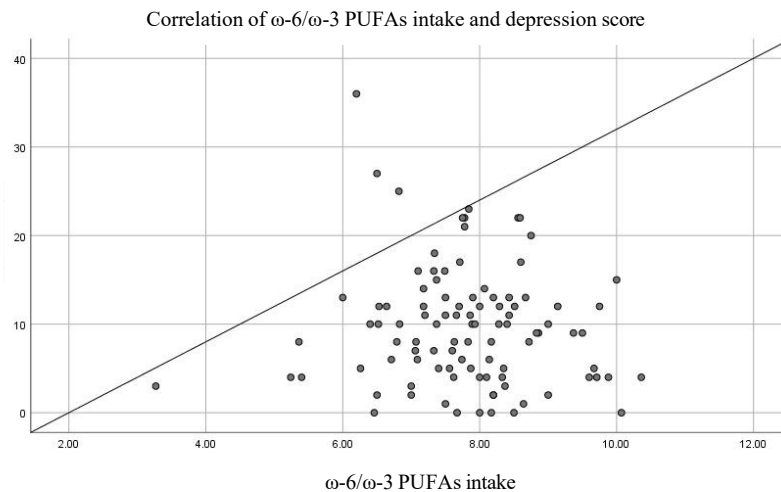


Figure 1. Scatter plot for ω -6/ ω -3 PUFAs intake and depression score correlation

The correlation of ω -6/ ω -3 PUFAs intake and depression score in TB patients was tested using the Spearman rank test because the data did not meet the normality assumption, as shown in Table 3. The correlation between ω -6/ ω -3 PUFA intake and depression score in TB patients had an r -value of -0.063. The p -value was 0.534 ($p > 0.05$), indicating that the correlation between ω -6/ ω -3 PUFA intake and depression score in TB patients in this study was not statistically significant.

Table 3. Correlation between variables

Variables	R coefficient*	P-value**
ω -6/ ω -3 PUFAs intake and depression score	11.9 (2.2 – 51.8)	0.534

*R 0.01-0.19 = negligible relationship

**Statistically significant ($p < 0.05$)

DISCUSSION

Based on this study, there was no correlation between the ratio of ω -6/ ω -3 fatty acid intake and depression scores in pulmonary TB patients at Persahabatan National Respiratory Referral Hospital, Jakarta, although most subjects met their daily ω -3 requirements. However, the ω -6/ ω -3 ratio remained high. In this study, the most common food presentation was fried. The cooking method can affect the retention of fatty acids in fish as a food source of ω -3. After experimenting with various cooking methods in terms of cooking time and temperature, lipid content decreased dramatically. When cooking time and temperature are increased, lipid oxidation increases. Fatty acids, especially ω -6 and ω -3, are easily oxidized. High temperatures and cooking duration accelerate this reaction. Therefore, the cooking process can change the contents.¹⁶

Although the ω -3 fatty acids content in most of the subjects met the recommended dietary allowance (RDA) value, it should be noted that ω -6 and ω -3 fatty acids compete with each other to undergo bioconversion into their derivatives using the same desaturase and elongase enzymes. The ratio of ω -6 to ω -3 intake is important to note as this affects the bioconversion of ALA and LA to their derivatives in the human body. A low ω -6 to ω -3 ratio diet results in lower levels of EPA and DHA in cell membranes and lower levels of AA.^{10,11}

From structured interviews of pulmonary TB patients with depression and filling out the BDI-II questionnaire, a median value of 9 (normal) was obtained. As many as 20% of subjects experienced depression. Compared to people without TB, adults with TB had 1.98, 1.75, and 3.68 times the incidence of subsyndromal depression and brief depressive episodes, respectively, according to a meta-analysis of data from low- and middle-income nations.¹⁷

The effects of treatment on TB patients should also be taken into consideration. According to Doherty, *et al.* (2013), isoniazid (INH) has mood-enhancing effects because it acts as a monoamine oxidase inhibitor (MAOI), which can increase the availability of serotonin, a neurotransmitter known for its antidepressant properties.¹⁸ As a result, some TB patients may exhibit normal mood or mild depressive symptoms. It is important to note that all subjects included in this study were taking INH, which can be a reason for the absence of a relationship between the two variables.¹⁸

This study found that the median ratio of ω -6/ ω -3 fatty acid intake was 7.78 ± 1.13 . The ideal ratio of ω -6/ ω -3 fatty acids for health and for preventing non-communicable diseases is 1:1 to 4:1. In this study, the most common food preparation method was frying using

coconut oil, which has a high ω -6 content, leading to an increase in the ω -6/ ω -3 ratio. In a study conducted by Jayaatmaja, *et al.* (2020) regarding the ratio of ω -3/ ω -6 fatty acid intake in multidrug-resistant (MDR) TB patients, the results obtained were 0.11 or the equivalent of 1:9.¹³ In the study conducted by Fabiani, *et al.* (2021), the maximum ratio of ω -6/ ω -3 fatty acids in adults in Jakarta was 18:1.¹⁴

A previous study suggested that a high ω -6 to ω -3 PUFA ratio could increase the risk of depression.¹⁹ Increased ω -6/ ω -3 was associated with significant depression and increased production of pro-inflammatory cytokines in students, according to a randomized controlled experiment. This study discovered that lowering the ω -6/ ω -3 ratio decreased anxiety and encouraged decreases in IL-6 and TNF- α production, as well as minor variations in serum TNF- α .¹⁹ A study conducted by Thesing, *et al.* (2020) found no protective benefit for major depression disorder (MDD) recurrence from high levels of ω -3 PUFA, DHA, EPA, low ω -6 PUFA levels, or a high ω -3/ ω -6 PUFA ratio in MDD patients who recovered for a maximum of eight years of follow-up.²⁰ A study by Matsuoka, *et al.* (2017) on fish diet, consumption of ω -3 PUFAs, and risk of depression in Japan discovered no statistically significant correlation between the ratio of ω -6 and ω -3 and depression risk.²¹

The chronic nature of TB infection with symptoms of decreased appetite leading to weight loss, combined with socioeconomic factors, becomes a risk factor for depression in TB patients.²² In the study by Ambaw, *et al.* (2017), it was stated that TB patients with malnutrition, specifically being underweight, are at risk of developing depression.⁷ However, after conducting additional analysis in this study regarding the correlation between nutritional status and depression, no significant results were found. This may be attributed to the fact that the subjects participating in this study had a BMI >16, and the majority were in the advanced treatment phase, which resulted in improved dietary patterns. In a study by Rouf *et al.* (2021), a significant association was found between depression and TB treatment outcomes.²³ Initially, the prevalence of depression among TB patients was notably high at 50.5%. However, after 2 months of treatment, this prevalence dropped to 9.4%, and by the end of the treatment period, it further decreased to 2.5%.²³

Although no significant association was found between the ω -6 and ω -3 PUFAs intake ratio and depression scores in pulmonary TB patients in this study, this ratio should be considered because Nienaber, *et al.* (2021) found that a balanced ratio of ω -6 and ω -3 with high EPA and DHA, can reduce bacterial load and inflammation in the lungs and improve body

weight.²⁴ Therefore, although there was no observed correlation between the ω -6 to ω -3 intake ratio and depression scores among TB patients, reducing this ratio to 1-4:1 remains essential to support TB treatment.

The limitations of this study encompass several aspects. Firstly, the assessment of dietary intake in this study utilized a semi-quantitative FFQ aided by enumerators. During the data collection process, the potential for interviewer and recall bias exists, although efforts were made to minimize these biases through training, ensuring consistency in perception between the researchers and enumerators, and employing a food photo book in conducting the SQ-FFQ. Furthermore, limitations associated with the SQ-FFQ include the difficulty in accurately recalling the quantity or portion sizes of food consumed over the past month, which could introduce bias into the SQ-FFQ results reported by the subjects. Additionally, structured interviews regarding prior treatment history were not conducted in this study, and more suitable instruments were not used to distinguish between depressive symptoms caused by depression and those arising from other factors, such as depressive mood disorders or adjustment disorders. Another limitation of this study is the absence of research on other variables that might contribute to depression in pulmonary TB patients, such as the consumption of anti-inflammatory drugs.

CONCLUSION

There was no correlation between ω -6/ ω -3 PUFA intake ratio and depression score in pulmonary TB patients. Further research can be conducted on more homogeneous populations. In addition, future studies can use measurements through erythrocytes to see a more objective ratio of ω -6/ ω -3. It is suggested to research the intake of other nutrients that might affect depression scores in pulmonary TB patients.

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Conflict of Interest

The authors declared there is no conflict of interest.

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Authors' Contributions

Conceiving the study, designing the experiment, gathering, analyzing, and interpreting the data, making

tables and figures, and writing the manuscript: NF. Providing guidance, contributing significant intellectual content during drafting, and revising the manuscript: FN, WL, HA, and AAH. All authors contributed and approved the final version of the manuscript.

REFERENCES

- (WHO) WHO. *Global Tuberculosis Report 2021*. Geneva, <https://www.who.int/publications-detail-redirect/9789240037021> (2021).
- Kementerian Kesehatan Republik Indonesia. *Pedoman Nasional Pelayanan Kedokteran Tata Laksana Tuberculosis*. Jakarta: Kementerian Kesehatan Republik Indonesia, 2020.
- Indonesia KKR. *Dashboard TB Indonesia*. Jakarta, <https://tbindonesia.or.id/dashboard-tb-indonesia/> (2021).
- Duko B, Bedaso A, Ayano G. The Prevalence of Depression among Patients with Tuberculosis: A Systematic Review and Meta-Analysis. *Ann Gen Psychiatry* 2020; 19: 30.
- D'Attilio L, Santucci N, Bongiovanni B, *et al*. Tuberculosis, the Disrupted Immune-Endocrine Response and the Potential Thymic Repercussion as a Contributing Factor to Disease Physiopathology. *Front Endocrinol (Lausanne)* 2018; 9: 214.
- Fekadu N, Shibeshi W, Engidawork E. Major Depressive Disorder: Pathophysiology and Clinical Management. *J Depress Anxiety*; 6. Epub ahead of print 6 September 2016.
- Ambaw F, Mayston R, Hanlon C, *et al*. Burden and Presentation of Depression among Newly Diagnosed Individuals with TB in Primary Care Settings in Ethiopia. *BMC Psychiatry* 2017; 17: 57.
- Nahda ND, Kholis FN, Wardani ND, *et al*. Faktor-Faktor yang Berpengaruh terhadap Kejadian Depresi pada Pasien Tuberculosis di RSUP Dr. Kariadi Semarang. *J Kedokt Diponegoro* 2017; 6: 1529–1542.
- Kehbila J, Ekabe CJ, Aminde LN, *et al*. Prevalence and Correlates of Depressive Symptoms in Adult Patients with Pulmonary Tuberculosis in the Southwest Region of Cameroon. *Infect Dis Poverty* 2016; 5: 51.
- Saini RK, Keum Y-S. Omega-3 and Omega-6 Polyunsaturated Fatty Acids: Dietary Sources, Metabolism, and Significance - A Review. *Life Sci* 2018; 203: 255–267.
- Husted KS, Bouzinova E V. The Importance of n-6/n-3 Fatty Acids Ratio in the Major Depressive Disorder. *Medicina (Kaunas)* 2016; 52: 139–147.
- Wang Y, Dong L, Pan D, *et al*. Effect of High Ratio of n-6/n-3 PUFAs on Depression: A Meta-Analysis of Prospective Studies. *Frontiers in Nutrition* 2022; 9: 889576.
- Jayaatmaja FH. *Hubungan Rasio Asupan Asam Lemak Omega-3/Omega-6 dengan Selera Makan yang Dimediasi oleh Tumor Necrosis Factor-Alpha pada Penyandang Multidrug Resistant Tuberculosis Paru*. Universitas Indonesia, <https://lib.ui.ac.id/detail?id=20513104&lokasi=loka1> (2020).
- Fabiani H, Mudjihartini N, Lestari W. Dietary Omega-6 to Omega-3 Fatty Acids Ratio is Correlated with High Molecular Weight Adiponectin Level in Indonesian Office Workers. *Int J Nutr Pharmacol Neurol Dis*; 11, https://journals.lww.com/ijnp/fulltext/2021/11010/dietary_omega_6_to_omega_3_fatty_acids_ratio_is.8.aspx (2021).
- Ginting H, Näring G, van der Veld WM, *et al*. Validating the Beck Depression Inventory-II in Indonesia's General Population and Coronary Heart Disease Patients. *Int J Clin Heal Psychol* 2013; 13: 235–242.
- Bastías JM, Balladares P, Acuña S, *et al*. Determining the Effect of Different Cooking Methods on the Nutritional Composition of Salmon (*Salmo salar*) and Chilean Jack Mackerel (*Trachurus murphyi*) Fillets. *PLoS One* 2017; 12: e0180993.
- Koyanagi A, Vancampfort D, Carvalho AF, *et al*. Depression Comorbid with Tuberculosis and Its Impact on Health Status: Cross-Sectional Analysis of Community-Based Data from 48 Low- and Middle-Income Countries. *BMC Med* 2017; 15: 209.
- Doherty AM, Kelly J, McDonald C, *et al*. A Review of the Interplay between Tuberculosis and Mental Health. *Gen Hosp Psychiatry* 2013; 35: 398–406.
- Kiecolt-Glaser JK, Belury MA, Andridge R, *et al*. Omega-3 Supplementation Lowers Inflammation and Anxiety in Medical Students: A Randomized Controlled Trial. *Brain Behav Immun* 2011; 25: 1725–1734.
- Thesing CS, Lok A, Milaneschi Y, *et al*. Fatty Acids and Recurrence of Major Depressive Disorder: Combined Analysis of Two Dutch Clinical Cohorts. *Acta Psychiatr Scand* 2020; 141: 362–373.
- Matsuoka YJ, Sawada N, Mimura M, *et al*. Dietary Fish, n-3 Polyunsaturated Fatty Acid Consumption, and Depression Risk in Japan: A Population-Based Prospective Cohort Study. *Transl Psychiatry* 2017; 7: e1242–e1242.
- Amin Z, Bahar A. Tuberculosis Paru. In: *Buku Ajar Ilmu Penyakit Dalam*. 2014, pp. 863–872.
- Rouf A, Masoodi MA, Dar MM, *et al*. Depression among Tuberculosis Patients and Its Association with Treatment Outcomes in District Srinagar. *J Clin Tuberc Other Mycobact Dis* 2021; 25: 100281.
- Nienaber A, Ozturk M, Dolman RC, *et al*. Beneficial Effect of Long-Chain n-3 Polyunsaturated Fatty Acid Supplementation on Tuberculosis in Mice. *Prostaglandins, Leukot Essent Fat Acids* 2021; 170: 102304.