

**BUKTI KORESPONDENSI ARTIKEL PADA JURNAL  
INTERNASIONAL BEREPUTASI**

**PENGUSUL: Dr. dr. Mahalul Azam, M.Kes**

**JUDUL ARTIKEL:**

**Predictors of smear non-conversion among new-treatment pulmonary tuberculosis: a single center case-control study in Indonesia**

**Publikasi**

Judul : Predictors of smear non-conversion among new-treatment pulmonary tuberculosis: a single center case-control study in Indonesia

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Penulis : Arulita Ika Fibriana, Muhamad Zakki Saefurrohimi, Akhriyah Atsna Setiana, Mahalul Azam, Avissena Dutha Pratama

Kepada Yth.  
Tim Penilai Usulan PAK

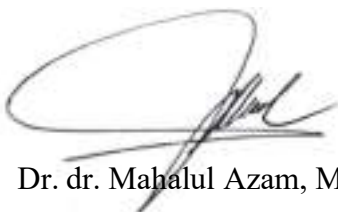
Bersama ini kami sertakan bukti korespondensi dan proses review artikel kami berjudul “Predictors of smear non-conversion among new-treatment pulmonary tuberculosis: a single center case-control study in Indonesia” dipublikasikan di Medical Journal of Indonesia Vol 29 No 4 tahun 2020 tanggal 30 Desember 2020.

#### Resume Kronologi

No	Tanggal	Aktivitas
1	18 September 2019	Artikel Submit di jurnal
2	27 September 2019	Submission dikonfirmasi Editor jurnal dan initial check, serta permintaan revisi fase initial check.
3	05 Desember 2019	Permintaan revisi pertama (komentar dapat dilihat di lampiran)
4	30 Desember 2019	- Respon perbaikan atas review 1 - Respon selengkapnya terlampir dalam lampiran
5	07 Februari 2020	Review dan masukan untuk perbaikan kedua
6	29 Februari 2020	Respon dan submit ulang perbaikan tahap kedua
7	22 April 2020	Pertanyaan ke editor atas perbaikan dan hasil revisi.
8	27 April 2020	Permohonan dari jurnal untuk perbaikan selanjutnya (tahap 3)
9	02 Mei 2020	Submit ulang perbaikan
10	30 Juni 2020	Permohonan perbaikan lanjut
11	07 Juli 2020	Submit ulang atas perbaikan
12	03 September 2020	

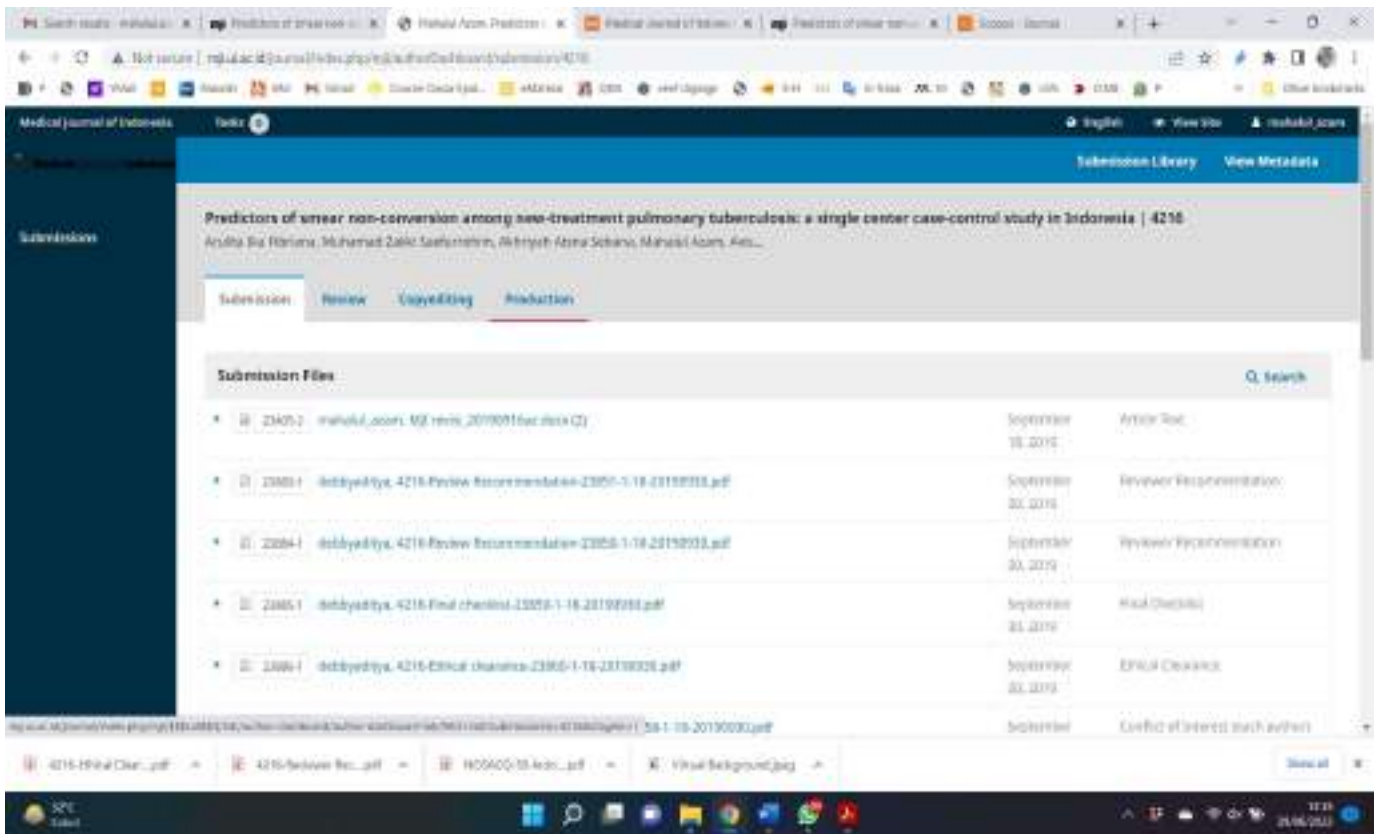
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Semarang, 28 Juni 2022



Dr. dr. Mahalul Azam, M.Kes

**Lampiran Rinci Kronologi dan Dokumen Email Korespondensi dengan Editor Jurnal terlampir sebagai berikut:**






## [MJI] Request for Completeness of Manuscript (ID:4216)

**Participants**

Debby Aditya (debbyaditya)

Mahalul Azam (mahalul\_azam)

**Messages**

Note	From
<p>Dear Mr. Mahalul Azam</p> <p>Thank you for sending us the interesting manuscript entitled "Smear grading predicts non-conversion pulmonary tuberculosis: study in Dr. Kariadi general hospital Semarang, Indonesia"</p> <p>We hereby inform you that before your manuscript can be processed further, please make sure to complete the following data on your manuscript, i.e.:</p> <ol style="list-style-type: none"><li>1. Fill in the enclosed reviewer recommendation form. The expert should be out of your affiliations and has no conflict of interest with one of the author.</li><li>2. The conflict of interest form enclosed, should be filled by all authors.</li><li>3. The enclosed final checklist form, should be assigned by all authors.</li><li>4. Ethical Clearance should be included</li></ol> <p>Please do complete and upload through the system within 2 weeks (Oct 11 , 2019), otherwise your manuscript will be automatically deleted from our system. Thank you for your collaboration.</p> <p>Best regards, Debby A Med J Indones</p> <p> <a href="#">debbyaditya, Conflict of Interest (each author).pdf</a></p> <p> <a href="#">debbyaditya, Final checklist.pdf</a></p> <p> <a href="#">debbyaditya, Review Recommendation.pdf</a></p>	<p>debbyaditya 2019-09-27 12:21 PM</p>

▶ Dear Debby A

mahalul azam

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<p>▶ Dear Dr. Felix F. Widjaya</p> <p>Managing Editor of Medical Journal of Indonesia,</p> <p>Thank you for the process and review of our manuscript, we have responded and made an appropriate revision to meet the reviewer's inputs. Enclosed the revision version of our paper, we tried to refine our manuscript's quality, and we hope the Editor consider to process and publish our work in The Medical Journal of Indonesia.</p> <p>Thank you very much for everything.</p>	<p>mahalul_azam 2019-12-30 01:07 PM</p>

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Regards,

Felix F. W

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- ▶ Thank you very much for the continuing review to improve our manuscript.

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2020-07-07

08:12 AM

We have revised our manuscript according to the review and enclosed is the revised version of the manuscript.

We are looking forward to furthering information from you regarding our manuscript.

Thank you very much for all the services given to us.

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## [MJI] Permohonan Perbaikan Naskah (ID: 4216)

**Participants**

Novi Arie Anggraeni (noviarie)

Mahalul Azam (mahalul\_azam)

**Messages**

Note	From
<p>Yth. dr. Mahalul Azam,</p> <p>Selamat siang, Dok. Proses review naskah sudah selesai dan naskah ini akan kami lanjutkan untuk proses produksi. Namun sebelum proses produksi kami ingin mengonfirmasi beberapa hal dan memohon sedikit perbaikan dari Dokter. Mohon dapat diperbaiki dalam waktu 4 hari (deadline 6 Sept 2020). Terima kasih atas perhatian Dokter.</p> <p>Salam, Novi AA</p> <p> <a href="#">noviarie, 16-4216-FFW.docx</a></p>	<p>noviarie 2020-09-02 11:20 AM</p>
<p>▶ Yth. Sdri Novi A. Anggraini</p> <p>Terima kasih atas informasi dan reviewnya. Berikut ini kami kirimkan file perbaikan dan konfirmasi manuskrip atas review tersebut. Kami menunggu untuk informasi selanjutnya. Sekali lagi terima kasih banyak atas pelayanan yang diberikan.</p> <p>Salam, Azam</p> <p> <a href="#">mahalul_azam, 4216-Article Text-33001-1-18-20200902_az.docx</a></p>	<p>mahalul_azam 2020-09-02 08:38 PM</p>

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2020-09-02  
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Novi AA [noviarie, 16-4216-FFW.docx](#)

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2020-09-02  
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Salam,  
Azam [mahalul\\_azam, 4216-Article Text-33001-1-18-20200902\\_az.docx](#)**Add Message**

Yth. Dr. Mahalul Azam,

Penelitian Penulis dan tim yang berjudul "Smear grading predicts non-conversion pulmonary tuberculosis: study in Dr. Kariadi general hospital Semarang, Indonesia" sebenarnya sangat menarik, namun pembahasan dalam naskah ini masih belum mendalam dan komprehensif. Berikut poin-poin yang perlu Penulis perbaiki:

1. Metode penelitian juga tidak jelas menggambarkan bahwa ini adalah studi kasus kontrol. Kriteria inklusi dan eksklusi juga tidak jelas dan bagaimana sampling method perlu dijelaskan baik pada kasus maupun kontrol.
2. Waktu pengambilan sputum masih belum dijelaskan.
3. Tuliskan juga dengan rumus apa Penulis menentukan sample size.
4. Mengapa hanya satu perbandingan case dan control 1:1 melihat banyaknya subjek pada kontrol yang mungkin juga eligible? Disarankan untuk menambahkan pada kontrol menjadi 1:2 atau 1:3 supaya lebih sah dalam mengambil simpulan.
5. Secara logika tentu saja semakin tinggi smear grading semakin banyak kuman maka semakin sulit pula konversi. Tetapi bagaimana menjelaskan hal ini perlu didiskusikan lebih lanjut.
6. Dalam naskah ini masih terlalu banyak faktor yang dibahas tetapi jumlah subjek sedikit sehingga menyebabkan power menjadi sangat rendah.
7. Fokus banyak pada menjelaskan RS Kariadi dan bukan fokus bahwa prediktor ini berguna untuk apa.
8. Apa yang menarik dari penelitian ini dan bagaimana hasilnya dibandingkan dengan penelitian lain juga belum banyak dibahas terutama dalam kaitannya sebagai prediktor.
9. Penelitian lain bagaimana apakah ada prediktor lain yang lebih baik. Limitasi dari penelitian ini apa? Sebagai contoh DM saja mungkin tidak dapat menjadi prediktor, mungkin uncontrolled DM yang bisa menjadi prediktor. Itu juga tidak ada dalam diskusi. Perdalam diskusi agar lebih menarik.

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Terimakasih banyak atas kerjasamanya Penulis.

Editor,

dr. Felix F. Widjaja, Sp.PD



**Predictors of smear non-conversion among new-treatment pulmonary tuberculosis: a single center case-control study in Indonesia**

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Mahalul Azam,<sup>1</sup> Avissena Dutha Pratama<sup>2</sup>

<sup>1</sup>Public Health Department, Faculty of Sports Science, Universitas Negeri Semarang, Semarang, Indonesia

<sup>2</sup>Department of Pulmonology Medicine, Dr. Kariadi General Hospital, Semarang, Indonesia

**Disclaimer (if any)** : -

**Conflict of interest** : None

**Running title** : Predictors of non-conversion pulmonary TB

**Corresponding author**

**Name** : Mahalul Azam

**Full address** : FIK UNNES Gd. F1 Lt.2 Sekaran, Gunungpati, Semarang

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+628122853982 (Cell-phone)

**E-mail address** : [mahalul.azam@mail.unnes.ac.id](mailto:mahalul.azam@mail.unnes.ac.id)

Field Code Changed

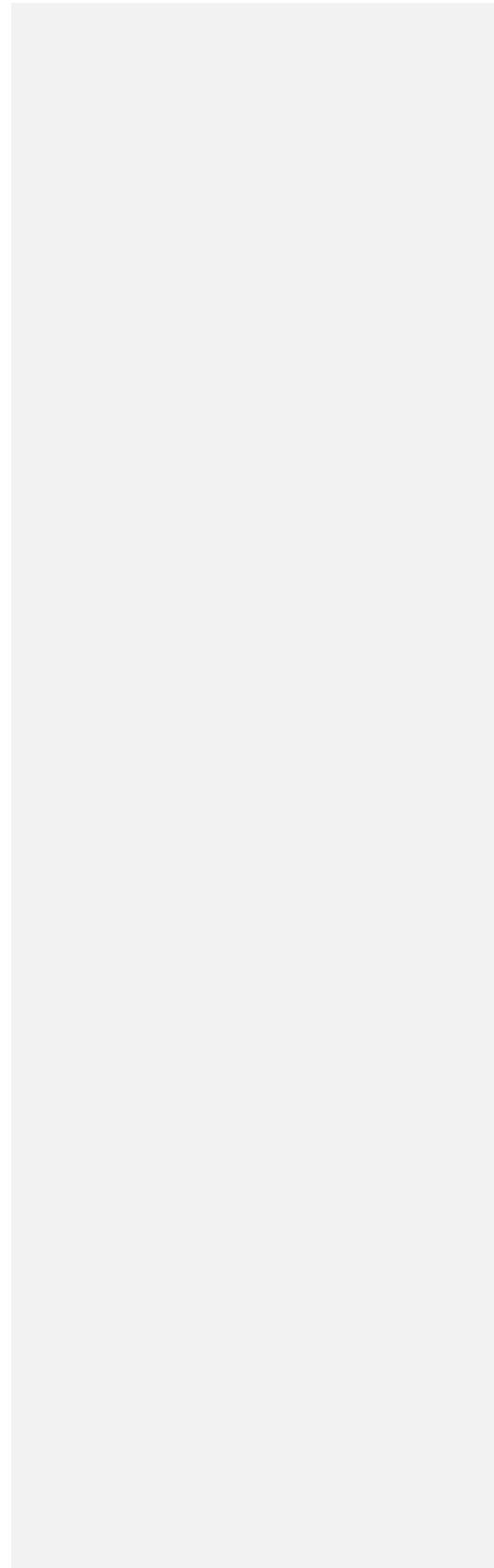
**Source(s) of support** :

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Universitas Negeri Semarang
2. Dr. Kariadi General Hospital, Semarang

**Word counts** : 2492

**Number of figures** : 2

**Number of tables** : 2



## ABSTRACT

**BACKGROUND** Previous studies concluded predictors of smear non-conversion pulmonary tuberculosis (TB) globally as well as in Indonesia. However, little has been exposed in Indonesian hospital setting. **This current** study aimed to explore predictors of smear non-conversion in Dr. Kariadi General Hospital, Semarang, Indonesia

**METHODS** A case-control study was conducted to explore the predictors of smear non-conversion among new-treatment pulmonary TB from 2017 to 2019. Number of subjects have been determined consecutively. Data were collected from secondary data accessed in medical records as well as from subjects directly. Non-conversion status in the case group was defined as persistent sputum smear-positive after two months of intensive phase of treatment. The study observed the subject's characteristics i.e. age, sex, BMI, level of education, occupational status, and the predictors of smear non-conversion, i.e. patient's compliance, smoking status, alcohol consumption, the presence of drugs side effects, health care access, acid-fast bacilli (AFB) smear grading, diabetes mellitus (DM), housing condition, housing density, and household income. Chi-square test and Binary logistic regression were used.

**RESULTS** Of 35 subjects determined in the case group while 76 subjects as the control group and involved in the final analysis. Age, sex, AFB smear grading, smoking status, housing condition, housing density, and DM were involved in the model of logistic regression. DM (OR = 3.4; 95%CI: 1.19–10.00) and AFB smear grading (OR = 11.2; 95%CI: 3.86–33.00) were concluded as the predictors of smear non-conversion.

**CONCLUSION** DM and AFB smear grading were the predictors of smear non-conversion among new-treatment pulmonary TB subjects.

**KEYWORDS:** pulmonary tuberculosis, mycobacterium, microbiological techniques

Commented [N1]: Maksudnya? Conclusionnya apa?

Commented [A2R1]: Supaya menghindari pengulangan dan pertimbangan jumlah kata, rincian prediktor diuraikan di metode

Commented [MJoI3]: Aim of study?

Commented [A4R3]: Sudah ditambahkan

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Commented [N6]: Yang penting dalam abstrak adalah apa saja yang dinilai jangan hanya menulis subject's characteristics and predictor. Bagaimana menilai smear non conversion dan kapan dinilainya penting dituliskan. Justru kalimat ini tidak perlu.

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Tuberculosis (TB) remains a serious public health problem, which includes in the top 10 causes of death in the world.<sup>1</sup> An estimated 10 million people got pulmonary TB, and 1.2 million of them died in 2018.<sup>1</sup> Geographically, most of the TB cases occur in Asia (44%). Indonesia ranks third (8%) after India (27%), and China (9%) contributes the most TB cases in the world.<sup>1</sup> Surprisingly, TB cases in Indonesia increased by 70%, from 331,703 in 2015 to 563,879 in 2018.<sup>1</sup> The failure in the management of pulmonary TB were highly caused by limited resources, low quality of health system, and high HIV infection rate.<sup>1,2</sup>

The critical parameters in evaluating pulmonary TB management are cure rate and smear conversion rate.<sup>3</sup> In 2018, TB cure rate in Indonesia was 71.08% which is lower than 85%, the rate determined by WHO.<sup>1</sup> Smear conversion rate was also decreased remarkably from 80.6% in 2013 to 50.5% in 2014.<sup>1</sup>

The decrease of smear conversion rate adjusts with the increase of smear non-conversion rate. Smear non-conversion will make the treatment longer and increase the risk of drug resistance, relapse, and mortality, as well as the TB transmission to others.<sup>4</sup> It has been proven that some factors, i.e., patient's compliance,<sup>3,5,6</sup> smoking status,<sup>3,7</sup> diabetes mellitus (DM),<sup>8</sup> HIV co-infection,<sup>9</sup> and smear acid-fast bacilli (AFB) grading<sup>9</sup> are associated with smear non-conversion pulmonary TB. AFB smear grading was identified as a significant predictor of smear conversion status.<sup>9</sup> Studies also showed that the conversion rate in Persahabatan General Hospital, Jakarta was 90.8% in 2014,<sup>10</sup> and Sri Venkateswara Ramnarain Ruia General Hospital, Tirupati, India was 90.4%,<sup>11</sup> however, the studies did not analyze the risk factors. Additionally, studies reported that drug side effects,<sup>12</sup> alcohol

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Reviewer

R1: Novelty for same title in Indonesia not available  
 Introduksi belum menggambar the known, the unknown and the gap of the study. Belum jelas definisi non-conversion pulmonary TB. Belum jelas mengapa tiba2 penulis mau menilai predictor smear non-conversion. Faktor-faktor ini seharusnya di RS manapun mempunyai faktor yang sama. Apakah kuman MTB di Semarang virulensi lebih tinggi? Mengapa banyak sekali menceritakan RS Kariadi. Bila dirasa ingin menjelaskan ini untuk mewakili populasi tulis satu kalimat di method.

MA

Penjelasan the known: penelitian sebelumnya telah menyimpulkan predictor non-conversion pulmonary TB  
 The unknown: meskipun dalam setting RS juga sudah diteliti di bbrp negara, namun predictor non-conversion dengan setting RS di Indonesia masih terbatas; bisa diduga bahwa predictor tersebut adalah sama/serupa, namun penelitian ini akan membuktikannya dan memberikan pembahasan terkait dengan hasilnya  
 Relevant study di Indonesia ditambahkan 2 referensi no: 12 dan 17  
 Ulasan tentang RS Kariadi dipindahkan di metode  
 Definisi non-conversion pulmonary TB dijelaskan di metode

Reviewer round 2

Penulis perlu lebih menjelaskan novelty dari penelitian ini selain data di Indonesia masih sedikit. Penjelasan ini belum menggambarkan.  
 Mengapa menurut Penulis hasilnya diduga akan berbeda? Karena bila tujuan hanya untuk menilai predictor di RS Kariadi saja amat bersifat lokal dan tentu tidak cocok untuk diterbitkan di MJJ. Belum ada penjelasan apa yang kira2 membuat perbedaan hasil di RS Kariadi dengan rumah sakit lain atau bahkan negara lain?

MA respon round 2

Konsumsi lakohol, ESO, health care access, income, housing characteristics terbukti berhubungan dengan treatment outcome pada peneltian sebelumnya, namun sangat sedikit diketahui hubungannya dengan status non-konversi, karenanya penelitian ini mencoba mengungkap apakah predictor treatment outcome ... [1]

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consumption,<sup>13</sup> health care access,<sup>14</sup> household income,<sup>13</sup> and housing characteristics<sup>15,16</sup> i.e., housing condition, and housing density were associated with TB treatment outcome.

Previous studies<sup>3,7,9,17</sup> ~~were conducted and~~ concluded the risk factors of smear non-conversion in TB. However, to the best of our knowledge, little is known regarding the relationship between drug side effects, alcohol consumption, household income, health care access, housing characteristics, and smear non-conversion; moreover, a few data are known in the Indonesian hospital setting. ~~This~~ ~~current~~ study aimed to explore predictors of smear non-conversion pulmonary TB in Dr. Kariadi General Hospital. It hypothesized that AFB smear grading, patient's compliance, drug side effects, alcohol consumption, smoking, DM, household income, housing condition, and housing density were the predictors of smear non-conversion among new-treatment pulmonary TB.

## METHODS

This case-control study was conducted from 2017 to 2019. The secondary data were ~~taken~~ ~~captured~~ from medical records and TB patients' monitoring sheets, whereas the primary data were collected from an interview and observation of the subjects recorded in the pulmonary TB registry in Dr. Kariadi General Hospital. All procedures performed in this study were approved by the Institutional Review Board Committee, Public Health Department, Universitas Negeri Semarang (No.052/KEPK/EC/2019). The sample size was determined to meet the minimum sample according to the formula for a case-control study published previously.<sup>18</sup> Thirty subjects with smear non-conversion of new-treatment pulmonary TB were assigned as a case group, meanwhile twice were assigned in the

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Reviewer 1  
Tidak jelas bagaimana memilih kasus dan memilih kontrol dan apa kriteria inklusi dan eksklusi dari masing2 kelompok.

MA  
Ada di penjelasan di paragraf 2 bagian ini dan ditambahkan juga exclude HIV/AIDS

Reviewer 2  
Belum adekuat kriteria kasus dan kontrol. Seharusnya cara rekrutmen kasus dan kontrol menyambung paragraph yang dipindahkan. Tidak perlu menulis terlalu detail dengan angka tidak apa2 karena sudah ada dalam figure

MA  
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Reviewer  
New treatment pulmonary TB? Atau smear non-conversion?  
MA  
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control group. Both of the groups were added a minimum of 10 % for the anticipation of incompleteness, rejection, and another thing.

Non-conversion status was defined as persistent sputum smear-positive after two months of the intensive phase of treatment. It was categorized as the case group. Smear examinations were conducted for three sputum smear specimens, i.e., first spot, second spot, and morning sample sputum. Results determined as positive if at least one of the specimens is positive, while negative if all of them are negative. Subjects with negative results then categorized as the control group.

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A number of 674 subjects with TB directly observed treatment short-course, which recorded in the Dr. Kariadi General Hospital TB registry from 2017 to 2019. Meanwhile, four hundred and twenty of them were excluded because of negative AFB or TB with HIV/AIDS or extrapulmonary TB or re-treatment cases, 254 subjects diagnosed pulmonary TB with positive AFB. Of them, and 209 subjects diagnosed with conversion status. The rest 45 subjects diagnosed with smear non-conversion. Subjects in the control group were obtained sequentially from the last visit to the hospital until the number was obtained as determined. The detailed study subjects recruitment illustrated in Figure 1.

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Secondary data were collected to determine smear non-conversion status. The subjects' characteristics include age, sex, body mass index (BMI), level of education, and occupational status. Level of education categorized as high and low. High-level education is for a subject who passed high school or above. The study also observed determinants of non-conversion pulmonary TB, i.e., patient's compliance, smoking status, alcohol

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consumption, the presence of drugs side effects, health care access, AFB smear grading, DM, housing condition, housing density, and household income.

Patients who paused the treatment for one or more weeks consecutively or total interruption of 12 days in non-consecutive days considered as non-compliant. Current or former alcohol routine usage in any dosage and frequency categorized as alcohol user as well as a current and former smoker. The presence of drug side effects involved the presence of the subject's complaint after medication, i.e., nausea, itching, arthralgia, hearing disorder, anorexia, and abnormal urine color. The limitation of the health service access determined by cost and distance.

AFB examination was conducted by the clinical microbiologist in the Clinical Microbiology Laboratory, Central Laboratory Unit, Dr. Kariadi General Hospital. The data obtained from medical records. The AFB were stratified into: 0: nil, 1+:  $\leq 1$  AFB, 2+:  $>1$  but  $<10$  AFB, 3+:  $\geq 10$  AFB per 10 fields of view, respectively. AFB smear ratings were categorized as high if the results were either 3+ or 2+ and low if the results were either 1+ or scanty. The housing condition consists of wall conditions, floor conditions, and lighting. The housing density determined as a number of the building area divided by a number of family members living in the same house. The condition that met the criterion as published elsewhere<sup>15</sup> used to determine the status. Household income considered fair when it met the regional minimum salary determined by the local Government government.

Data were presented in frequency and percentage based on the case and the control group. Chi-square test was performed to analyze the association of predictors and the

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smear non-conversion pulmonary TB status. P-value <0.05 was considered as statistically significant. The predictors with the P-value lower than 0.25 involved in the logistic regression analysis. All statistical analysis was performed using SPSS 16.0 (IBM Corporation, NY, USA).

(Figure 1)

## RESULTS

Of the 45 non-conversion subjects were in the case group (~~non-conversion rate=17.7%~~); however, only 35 subjects completed primary and secondary data. Five subjects refused to be interviewed, two subjects died, and three subjects were lost to follow-up. A number of 76 subjects with smear conversion was determined as a control group. The subject's characteristics, i.e., age, sex, level of education, and occupational status based on case and control group, were presented in Table 1. The frequency of subjects' age was significantly different between the groups ( $p=0.013$ ). For the non-conversion group, subject with age  $\geq 55$  years old (57.1%) is higher than subject with age 15–54 years old (42.9%). In contrast, for the conversion group, the proportion of subjects aged  $\geq 55$  years old is lower than 15–54 years old; 30.3% and 69.7% respectively. The frequency of sex was not comparable between groups. It did not meet the significant difference ( $p=0.080$ ). Regarding the gender, males (68.6%) were higher than females (31.4%) for the non-conversion group. In contrast, for the conversion group, males (48.7%) were lower than females (51.3%). The two other characteristics, namely level of education and occupational status, were comparable between the groups (P-value >0.05).

(Table 1)

**Commented [N39]:** directly mention, which group higher? Case or control?

**Commented [N40]:** Rephrase. Intinya yang lebih tua lebih banyak yg tidak konversi? Detilnya lihat tabel

**Commented [N41]:** Rephrase. Langsung intinya saja. Detilnya lihat di tabel

**Commented [N42]:** Rephrase.



Table 2 showed the association between predictors and smear non-conversion status among new-treatment pulmonary TB, i.e., AFB smear grading, BMI, drug side effects, smoking status, alcohol consumption, DM, patient's compliance, access to health service, housing condition, housing density, and household income. The Chi-square test results showed that AFB smear grading, smoking status, and DM were ~~the predictors associated with~~of smear non-conversion pulmonary TB status. Proportion of non-conversion group was higher in AFB smear  $\geq 2+$  (82.9%) than in AFB smear  $< 2+$  (17.1%). In contrast the proportion of conversion group was lower in AFB smear  $\geq 2+$  (26.3%) than AFB smear  $< 2+$  (73.7%) with significance level  $p=0.0001$ .

The proportion of non-conversion subjects in the smoking group was higher than the non-smoking group, 60%, and 40%, respectively. In line, the proportion of conversion subjects was lower in the smoking group than the non-smoking group, 30.3%, and 69.7%, respectively. Surprisingly, the proportion of the non-conversion group was lower in the DM group (48.6%) compare to in non-DM group (51.4%), whereas the proportion of conversion group was also lower (14.5%) than in non-DM group (85.5%), with p-value was 0.0001.

There was no significant difference in BMI between groups ( $p>0.05$ ). The proportion of drug side effects were also comparable between groups ( $p=0.10$ ). Alcohol consumption proportion in a non-conversion group was higher (11.4 %) than in the conversion group (4.9 %), but the difference was not significant ( $p=0.28$ ). Access to the health services between groups was also comparable ( $p=0.61$ ). Housing conditions, housing density, and household income were also comparable between groups.

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(Table 2)

Table 2 and Figure 2 showed the results of Binary logistic regression. The final model concluded that DM and high smear grading were significantly predicting smear non-conversion status among new-treatment pulmonary TB with a contribution of 68.19% and the rest 31.81% influenced by other predictors ( $R^2$ : 0.465; Nagelkerke). DM predicts non-conversion with an adjusted odds ratio (OR) was 3.44, and 95% confident interval (CI) was 1.186–10.003 ( $p=0.023$ ) while high smear grading predicts non-conversion with an adjusted odds ratio (OR) was 11.22 and 95% CI was 3.861–33.007 ( $p=0.0001$ ).

(Figure 2)

## DISCUSSION

The present study found that DM and high AFB smear grading were the predictors of smear non-conversion status among new-treatment pulmonary TB in Dr. Kariadi General Hospital with the contribution of 68.19% (OR=3.44; 95% CI=1.186–10.003 and OR=11.22; 95% CI=3.861–33.007, respectively). Present This study also analyzed the association of drug side effects, alcohol consumption, household income, and housing characteristics with smear non-conversion; however, these novel predictors did not reach the statistical significance. These findings contribute to add knowledge on some predictors of non-conversion status among new-treatment pulmonary TB in Indonesia, which previously there had been limited in the hospital setting.

Current study adds the evidence and strengthening previous studies that concluded DM and AFB smear grading as major predictors of smear non-conversion among new-

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**Commented [MJoI46]:** Diskusi tidak tajam, tidak mendiskusikan tentang mengapa hanya satu faktor yang dapat menjadi predictor atau ada confounding lain yang dapat menyebabkan perbedaan ini. Kondisi komorbid pasti berhubungan seperti HIV pasti berhubungan dengan hal ini tetapi tidak ada dalam data sehingga perlu dicantumkan sbg limitasi

**Commented [A47R46]:** Dengan menambah jumlah responden pada kontrol akhirnya kami menyimpulkan DM dan AFB grading sebagai predictor non-conversion Kami juga menambahkan pembahasan dan keterbatasan karena penelitian mengeksklude HIV/AIDS dan re-treatment status, dimana mempunyai kontribusi besar terhadap status non-konversi

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**Commented [N52]:** Ini bersifat sangat lokal

**Commented [A53R52]:** Meskipun hipotesis tidak terbukti, namun laporan ini memberikan pengetahuan baru scr global bahwa prediktor baru yang diteliti yang sebelumnya terbukti berpengaruh pada treatment outcome yaitu variabel drug side effects, alcohol consumption, household income, and housing characteristics tidak terbukti berhubungan dengan smear non-conversion

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treatment pulmonary TB. A study in Egypt concluded that delay in sputum culture conversion, moderate and extensive lung lesions, and DM were the predictors for the unsuccessful treatment of multidrug-resistant TB cases.<sup>19</sup>

High AFB smear grading was found playing a vital role in predicting non-conversion status with adjusted OR of 11.22, which means subjects with high smear grading have the risk of non-conversion 11.22 times higher than subjects with low smear grading. It has been reported that AFB smear 3+ has a higher risk of getting non-conversion after the intensive phase of treatment<sup>20</sup> and pulmonary TB subjects with AFB 2+ and 3+ only 34% with smear conversion after two months intensive phase of treatment.<sup>20</sup> AFB grading plays an important role in the management of pulmonary TB, which is describing pulmonary TB severity and transmission ability<sup>21</sup> as well as indicating the late drug resolution that related to the existence of lung cavity and the density of the mycobacterium.

DM proved as a predictor for non-conversion among new-treatment pulmonary TB with the OR=3.44; 95% CI=1.186–10.003. It means that new-treatment pulmonary TB with DM has the risk of non-conversion 3.44 higher than non-DM. Unfortunately, the present study did not report the status of controlled or un-controlled DM that had a meaningful impact. Study reported that DM was associated with failure to sputum smear convert at two months and treatment failure.<sup>8</sup> Another study also reported that pulmonary TB cases with DM were common to be delayed sputum conversion and failure.<sup>22</sup> On the contrary, a study reported that DM influenced the clinical presentation and response to the treatment, but there was no difference in the drug resistance and relapse rates.<sup>22</sup>

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Current study also found that the conversion rate of new-treatment pulmonary TB subjects in Dr. Kariadi General Hospital was 82.3%. This finding was in accordance with previous studies globally and Indonesia as well, which ranged from 74.7 to 90.8.<sup>3,9,10,23</sup> However, some crucial predictors, i.e., HIV/AIDS and re-treatment status that obviously will implicate to the conversion rate<sup>9</sup> were excluded from this study.

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Present study also showed that the presence of drug side effects has a higher proportion to the smear non-conversion and almost reaches the significance level ( $p=0.05$ ). However, this condition did not match the condition of the non-compliant patient, which has a very minimum number, i.e., 5.7% for non-conversion status. Indeed, previous study concluded the presence of side effects implicate in treatment outcome,<sup>12</sup> but in the previous study, the observed population was the multi-drugs resistance TB, which most of them took a long period of a treatment since they were re-treatment cases. No statistical significance in the present study also showed in alcohol consumption status, while in the previous study concluded alcohol consumption was related to the treatment outcome particularly in the multi-drugs resistance TB.<sup>13</sup> Similarly, health care access, household income, and housing characteristics were well established as predictors of TB treatment outcome.<sup>13-16</sup> However, present study concluded that all these predictors were not related to the smear non-conversion status. These current findings add the evidence that predictors of TB treatment outcome did not exactly the same as predictors of smear non-conversion status in the intensive phase of treatment.

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Smoking status was not involved in the final model of Binary logistic regression; however, smoking status was significantly related to the smear non-conversion among new-

treatment pulmonary TB based on the Chi-square test. Previous study reported that smoking is related to adherence to anti-tuberculosis treatment.<sup>24</sup> Previous study also concluded that cigarette smoking in active pulmonary TB is related to delayed culture conversion. The frequency of delayed culture conversion after two months of treatment increasingly in sequentially in a group of never smokers, ex-smokers, current non-smokers, and current smokers.<sup>25</sup>

The current study was conducted based on hospital data as achieving the primary goal of the study. Indeed, this study did not represent the general population condition; moreover, the status of the hospital is national referral implies the pulmonary TB cases tend to be more complicated. ~~The current study was also using primary data; however, prior secondary data were used in medical records.~~ The use of culture to diagnose and its conversion after two months of treatment was not observed in the present study. The most vital confounding variables, i.e., HIV/AIDS and re-treatment status, were excluded from the study implies not a comprehensive understanding of the predictors. Based on several limitations of the current study described above, further research is needed to understand the related predictors thoroughly for smear non-conversion among new-treatment pulmonary TB.

#### **CONFLICTS OF INTEREST**

The authors affirm no conflict of interest in this study.

#### **FUNDING SOURCES**

This study was supported by a grant of DIPA PNBPN UNNES 2019 No. 1603/UN37.3.1/TU/2019.

## **ACKNOWLEDGMENT**

We acknowledge the Lembaga Penelitian dan Pengabdian Masyarakat (LPPM) Universitas Negeri Semarang for financial support, Dr. Kariadi General Hospital, Semarang, Indonesia for providing data, and all subjects of the study.

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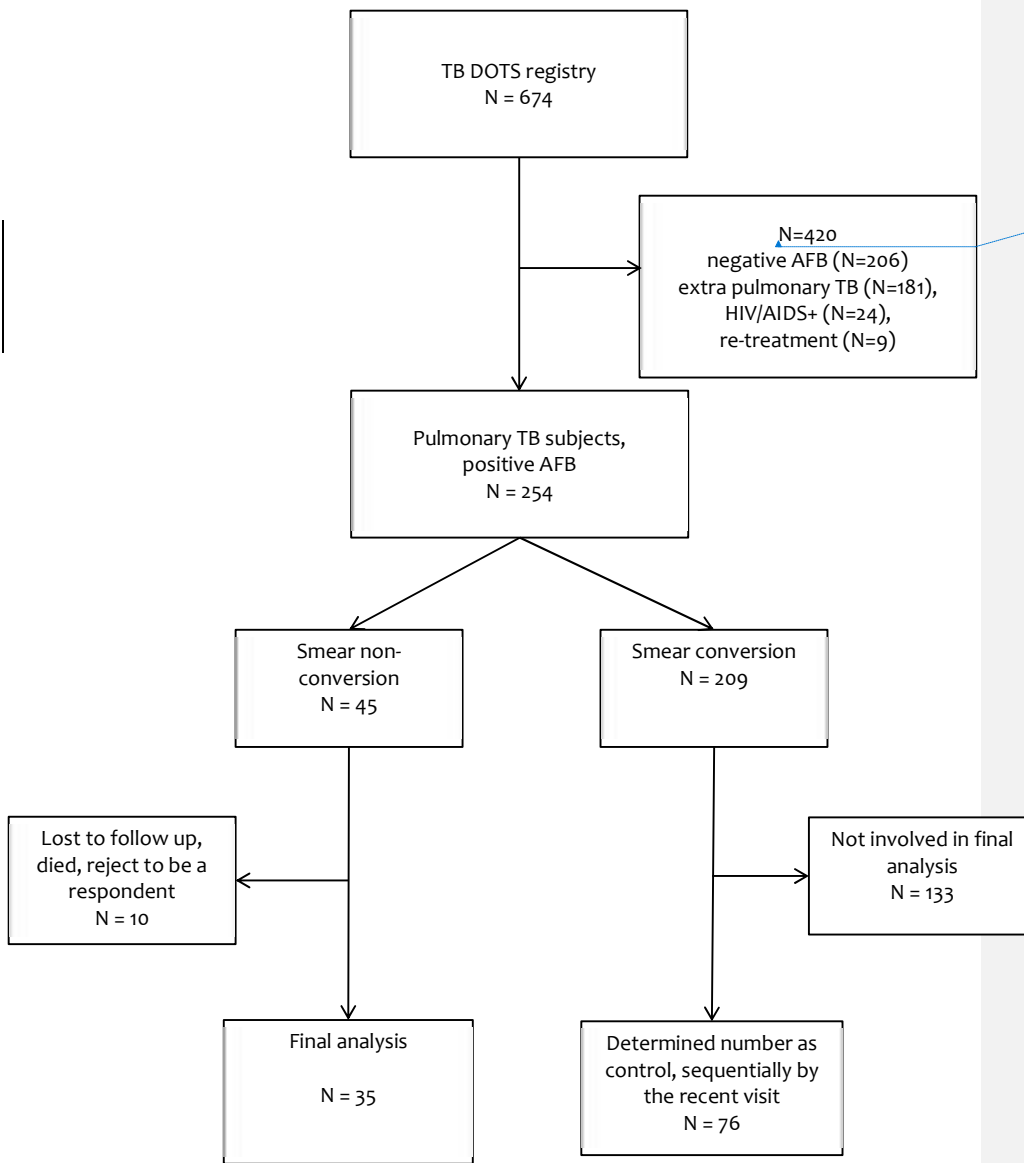
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Figure 1. Subject recruitment

DOTS: Directly observed treatment short-course

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Negative AFB (n=...)  
Extrapulmonal TB (n=...)  
And so on

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**Table 1.** Subject's characteristics

Characteristics	Non-conversion status		p*
	Yes, n (%)	No, n (%)	
Age (yo)			
≥ 55	20 (57.1)	23 (30.3)	0.013
15–54	15 (42.9)	53 (69.7)	
Sex			
Male	24 (68.6)	37 (48.7)	0.080
Female	11 (31.4)	39 (51.3)	
Level of education			
Low	6 (17.1)	19 (25.0)	0.499
High	29 (82.9)	57 (75.0)	
Occupational status			
Un-employee	12 (34.3)	32 (42.1)	0.566
Employee	23 (65.7)	44 (57.9)	

\*Chi-square test  
yo: years old

**Table 2.** Predictors of smear non-conversion status Pulmonary TB

Predictors	Non-conversion status		p value*	OR (95% CI)	p value**	adjusted OR (95% CI)
	Yes	No				
AFB smear grading						
≥2+	29 (82.9)	20 (26.3)	0.000	13.533 (4.897–37.401)	0.000	11.223 (3.861–33.007)
<2+	6 (17.1)	56 (73.7)				
BMI						
Under (<18.5)	14 (40.0)	27 (35.5)	0.616	1.383 (0.575–3.323)	-	-
Overweight (>23)	6 (17.1)	9 (11.8)	0.525	0.562 (0.171–1.851)	-	-
Normal (18.5–23)	15 (42.9)	42 (52.6)	Ref	Ref	-	-
Drugs side effects						
Yes	11 (31.4)	38 (50.0)	0.104	0.458 (0.197–1.065)	0.050	0.346 (0.119–1.000)
No	24 (68.6)	38 (50.0)				
Smoking status						
Yes	21 (60.0)	23 (30.3)	0.006	3.457 (1.500–7.965)	0.139	2.136 (0.781–5.842)
No	14 (40.0)	53 (69.7)				
Alcohol consumption						
Yes	4 (11.4)	3 (4.9)	0.277	3.140 (0.663–14.864)	-	-
No	31 (88.6)	69 (96.1)				
DM						
Yes	17 (48.6)	11 (14.5)	0.000	5.581 (2.222–14.014)	0.023	3.444 (1.186–10.003)
No	18 (51.4)	65 (85.5)				
Compliance						
No	2 (5.7)	6 (7.9)	0.986	0.707 (0.135–3.693)	-	-
Yes	33 (94.3)	70 (92.1)				
Access to health services						
Limited access	10 (28.6)	27 (35.5)	0.613	0.726 (0.304–1.734)	-	-
Fair	25 (71.4)	49 (64.5)				
Housing condition						
Bad	8 (22.9)	8 (10.5)	0.153	2.519 (0.858–7.391)	0.307	1.992 (0.530–7.484)
Fair	27 (77.1)	68 (89.5)				
Housing density						
Very density	10 (28.6)	12 (15.8)	0.189	2.133 (0.818 – 5.561)	0.779	0.832 (0.230–3.011)
Fair	25 (71.4)	64 (84.2)				
Household income						
Low	26 (74.3)	52 (68.4)	0.686	1.333 (0.543–3.277)	-	-
Fair	9 (25.7)	24 (31.6)				

\* Chi-square test

\*\* Binary logistic regression test R<sup>2</sup>=0.465 (Nagelkerke)

CI: confidence interval

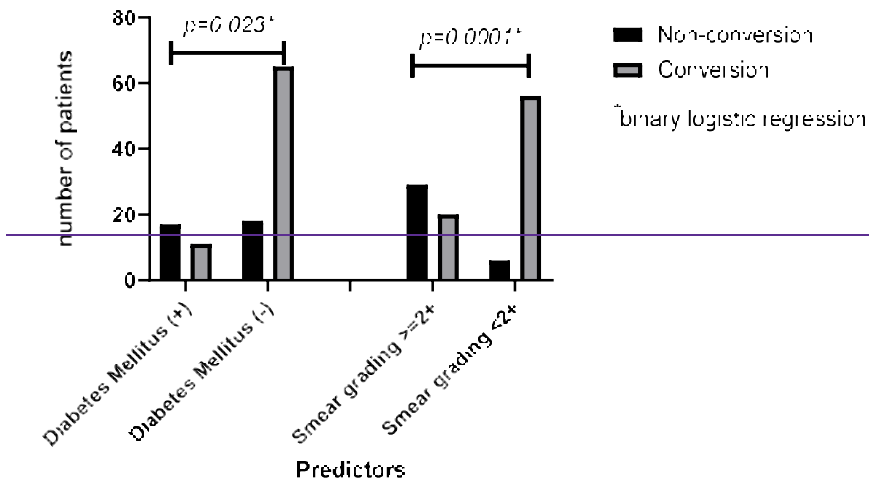


Figure 2. Predictors of smear non-conversion pulmonary TB.

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## Reviewer

R1: Novelty for same title in Indonesia not available

Introduksi belum menggambar the known, the unknown and the gap of the study. Belum jelas definisi non-conversion pulmonary TB. Belum jelas mengapa tiba2 penulis mau menilai predictor smear non-conversion. Faktor-faktor ini seharusnya di RS manapun mempunyai faktor yang sama. Apakah kuman MTB di Semarang virulensi lebih tinggi? Mengapa banyak sekali menceritakan RS Kariadi. Bila dirasa ingin menjelaskan ini untuk mewakili populasi tulis satu kalimat di method.

## MA

Penjelasan the known: penelitian sebelumnya telah menyimpulkan prediktor non-conversion pulmonary TB

The unknown: meskipun dalam setting RS juga sudah diteliti di bbrp negara, namun prediktor non-conversion dengan setting RS di Indonesia masih terbatas; bisa diduga bahwa prediktor tersebut adalah sama/serupa, namun penelitian ini akan membuktikannya dan memberikan pembahasan terkait dengan hasilnya

Relevant study di Indonesia ditambahkan 2 referensi no: 12 dan 17

Ulasan tentang RS Kariadi dipindahkan di metode

Definisi non-conversion pulmonary TB dijelaskan di metode

## Reviewer round 2

Penulis perlu lebih menjelaskan novelty dari penelitian ini selain data di Indonesia masih sedikit. Penjelasan ini belum menggambarkan.

Mengapa menurut Penulis hasilnya diduga akan berbeda? Karena bila tujuan hanya untuk menilai predictor di RS Kariadi saja amat bersifat lokal dan tentu tidak cocok untuk diterbitkan di MJJ. Belum ada penjelasan apa yang kira2 membuat perbedaan hasil di RS Kariadi dengan rumah sakit lain atau bahkan negara lain?

## MA respon round 2

Konsumsi lakohol, ESO, health care access, income, housing characteristics terbukti berhubungan dengan **treatment outcome** pada penelitian sebelumnya, namun **sangat sedikit** diketahui hubungannya dengan status **non-konversi**, karenanya penelitian ini mencoba mengungkap apakah prediktor treatment outcome sejalan/sama dengan prediktor non-conversion; meskipun pada akhirnya hasil tidak terbukti

**Smear grading predicts non-conversion pulmonary tuberculosis: a case control study in Indonesia**

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**Disclaimer (if any)** : -

**Conflict of interest** : None

**Running title** : Smear grading predicts non-conversion TB

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**Number of tables** : 3

## ABSTRACT

**BACKGROUND** Non-conversion is the most important indicator of pulmonary tuberculosis (TB) management. Non-conversion after 2 months of treatment of the intensive phase tends to be a failure after completing treatment. The previous study concluded predictors for smear non-conversion globally as well as in Indonesia. However, little is known in the population setting of the hospital in Indonesia. The current study explored the predictors for smear non-conversion PTB in Dr. Kariadi General Hospital.

**METHODS** A case-control study was conducted. Data were collected both either secondary and primarily accessed in medical records and subjects directly. Study observed the subject's characteristics as well as the predictors for smear non-conversion. Chi-square test and Binary logistic regression were conducted to conclude the association of predictors and the smear non-conversion.

**RESULTS** A number of 254 subjects were diagnosed as PTB with positive acid-fast bacilli (AFB), consisting of 209 subjects with conversion status after 2 months of intensive treatment (82.3%), while 45 subjects with non-conversion (17.7%). A number of 35 subjects determined both in the case and control status and involved in the final analysis. Chi-square test concludes that age, sex, AFB smear grading, smoking status, and diabetes mellitus (DB) were the predictors for smear non-conversion PTB status. Household income and AFB smear grading finally involved in the model of binary logistic regression and conclude that only AFB smear grading was the predictor for smear non-conversion.

**CONCLUSION** AFB smear grading was the predictor for smear non-conversion PTB subjects.

**KEYWORDS:** pulmonary tuberculosis, mycobacterium, microbiological techniques

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**Commented [MJoI2]:** R2: Please add time and place of study in abstract (method)

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Pulmonary tuberculosis (TB) is the most burden of morbidity and mortality, especially in developing countries.<sup>1,2,3</sup> The failure in management of PTB in developing countries related to the limited resources, low quality of health system, and the high of HIV infection rate. In 2016, 10.4 million new PTB cases over the world, which is 6.2 million cases occur in men, 3.2 million in women, and 1 million cases in children.<sup>4</sup> Indonesia ranks second place of the highest number of tuberculosis (TB) cases after India.<sup>4,5</sup>

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The important parameter for evaluating PTB management is cure rate and smear conversion rate.<sup>6,7,8</sup> TB cure rate in Indonesia on 2018 was 71.08% which is still low compare to the rate determined by WHO i.e. 85%.<sup>4,5</sup> Smear conversion rate was also decreased extremely from 80.6% in 2013 to 50.5% in 2014.<sup>4</sup> Smear non-conversion will make the treatment longer and increase the risk of drug resistance, relapse, and mortality as well as the TB transmission to others.<sup>1,9,10</sup> Previous study concluded that smear non-conversion PTB was associated with some factors i.e. patient's compliance,<sup>11,6</sup> smoking status,<sup>6,7,8,12</sup> diabetes mellitus (DM),<sup>13,14</sup> drugs side effects,<sup>15</sup> and smear acid-fast bacilli (AFB) grading.<sup>7,11</sup> AFB smear grading identified as important predictor of smear conversion status.<sup>7,11</sup>

Conversion rate in Dr. Kariadi General Hospital in 2017 was 77 % and increasing to be 88% in 2018, a high number although still below 90%.<sup>16</sup> Conversion rate in Persahabatan General Hospital, Jakarta was 90.8% in 2014,<sup>16</sup> and Sri Venkateswara Ramnarain Ruia General Hospital, Tirupati, India was 90,4%.<sup>17</sup> Previous studies were conducted and concluded the risk factors of smear non-conversion TB, however to the best of our knowledge little is known in the setting population of the hospital in Indonesia. Current study aimed to explore predictors for smear non-conversion PTB in Dr. Kariadi General Hospital. The

present study hypothesized that AFB smear grading, body mass index (BMI), drugs side effect, smoking, and household income were the predictors for smear non-conversion PTB.

## METHODS

Present study conducted a case-control study, by secondary data usage captured from medical records as well as primary data collected from an interview and observation directly in subjects recorded in the PTB registry in Dr. Kariadi General Hospital during 2017–2019. The study protocol was approved by the Institutional Review Board Committee, Public Health Department, Universitas Negeri Semarang (No.052/KEPK/EC/2019).

Secondary data were collected to determine smear non-conversion status in the intensive phase of treatment, subjects' characteristics i.e. age, sex, BMI, level of education, and occupational status. Level of education categorized as high for subject who passed the high school and undergraduate degree. This study also observed determinant of non-conversion PTB i.e. patient's compliance, smoking status, alcohol consumption, the presence of drugs side effects, health care access, AFB smear grading, DM, the housing condition, house density, and household income. Access to the health services limited for subjects who limited in the distance and finance matter. AFB smear ratings were determined as high if the results were either 3+ or 2+ while low if they were either 1+ or scanty. Housing condition consists of wall condition, floor condition, and the lighting. Housing density determined as a calculation result of the building area divided by the number of family members living in the same house. A condition which met the criterion

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Introduksi belum menggambarkan the known, the unknown and the gap of the study. Belum jelas definisi non-conversion pulmonary TB. Belum jelas mengapa tiba2 penulis mau menilai predictor smear non-conversion. Faktor-faktor ini seharusnya di RS manapun mempunyai faktor yang sama. Apakah kuman MTB di Semarang virulensi lebih tinggi? Mengapa banyak sekali menceritakan RS Kariadi. Bila dirasa ingin menjelaskan ini untuk mewakili populasi tulis satu kalimat di method.

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Tuliskan juga dengan rumus apa Anda menentukan sample size.

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of housing condition and house density as published elsewhere used to determine the status.<sup>18</sup>

Data were presented in frequency and the percentage based on case and control group. Chi-square analysis was performed to conclude the association of predictors and the smear non-conversion PTB status. P value <0.05 was considered as statistically significant. The predictors with the p value lower than 0.25 involved in the Binary logistic regression analysis. All statistical analysis was performed using SPSS 16.0 (IBM Corporation, NY, USA). (Figure 1)

## RESULTS

Of 674 subjects which recorded in the Dr. Kariadi General Hospital TB registry during 2017–2019, 254 subjects diagnosed PTB with positive AFB and 209 subjects with conversion status (conversion rate=82.3%). The rest 45 subjects with non-conversion (non-conversion rate=17.7%). Of the 45 non-conversion subjects only 35 subjects completed primary and secondary data, 5 subjects rejected to be interviewed, 2 subjects died, and 3 subjects were lost to follow up. The same number of 35 subjects with conversion status were determined as control group and obtained sequentially from the last visit to the hospital until the number was obtained as determined. The detailed study subjects recruitment illustrated in Figure 1.

Subject's characteristics i.e. age, sex, level of education, and occupational status based on case and control group presented in Table 1. The frequency of subjects' age was significantly different between the group ( $p=0.03$ ). Proportion of subject in the non-

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conversion group was higher in subject with age  $\geq$  55 years old (57.1%) than subject with 15–54 years old (42.9%) and contrary the proportion of subject in the conversion group was lower in subject with age  $\geq$ 55 years old than 15–54 years old; 28.6% and 71.4% respectively. The frequency of sex was also significantly different between the group ( $p=0.031$ ). Proportion of subjects in the non-conversion group was higher for male than female, 68.6% and 31.4%, respectively. In contrary, proportion of subjects in conversion group was lower in male (40%) compare to female (60%). The other characteristics i.e. level of education and occupational status were comparable between the group ( $p$  value  $>0.05$ ).

(Table 1)

Table 2 showed the association between predictors and smear non-conversion status i.e. AFB smear grading, BMI, drugs side effects, smoking status, alcohol consumption, DM, patient's compliance, access to the health services, housing condition, housing density, and household income. Chi square test results showed that AFB smear grading, smoking status, and DM were the predictors for smear non-conversion PTB status. Proportion of non-conversion group was higher in AFB smear  $\geq 2+$  (82.9%) than in AFB smear  $<2+$  (17.1%), contrary proportion of conversion group was lower in AFB smear  $\geq 2+$  (25.7%) than AFB smear  $<2+$  (74.3%) with significance level  $p=0.0001$ .

Proportion of non-conversion group in the smoking group was higher than non-smoking group, 60% and 40%, respectively and as well as the proportion of conversion group was lower in the smoking group than non-smoking group, 31.4%, and 68.6%, respectively. Surprisingly, proportion of non-conversion group was lower in the DM group (48.6%)

compare to in non-DM group (51.4%), although the proportion of conversion group was also lower (8.6%) than in non-DM group (91.4%), with p value was 0.001.

There was no significant difference in BMI between groups (p value=0.805). The proportion of drug side effects was also comparable between groups (p value=0.801). Alcohol consumption proportion in non-conversion group higher (11.4 %) than in conversion group (5.7 %) but was also not different significantly (p value=0.669). Access to the health services between groups was also comparable (p value=0.784). Housing conditions, housing density, and household income were also comparable between groups, however, housing conditions and household income tend to have different proportions. The proportion of bad housing conditions higher in the non-conversion group (22.9 %) than the conversion group (5.7 %), although the statistical significance still not different (p value=0.088). Similarly, the low household income proportion in the non-conversion group was higher (74.3 %) than in the conversion group (51.4 %) but was also not statistically different (p value=0.083).

(Table 2)

Table 3 and Figure 2 showed the results of binary logistic regression. The final model involved predictor household income and smear grading. The analysis concluded that only smear grading that significantly predicts smear non-conversion PTB status with adjusted odds ratio (OR) was 14.18 and 95% confident interval (CI) was 4.279–47.006 (p=0.0001).

(Table 3)

(Figure 2)

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## DISCUSSION

Present study found that the conversion rate of PTB subjects in Dr. Kariadi General Hospital were 82.3%. This finding was in accordance with previous study globally or in Indonesia which ranged 74.7 to 90.8.<sup>3,6,11,16</sup> The current study also found that AFB smear grading was the single predictor for smear non-conversion PTB status in Dr. Kariadi General Hospital (OR=14.18; 95% CI=4.279–47.006). This finding contributed to add knowledge of predictor for non-conversion PTB status in Indonesia, which had a limited related study especially in the hospital setting, notably in Dr. Kariadi General Hospital. This finding strengthening previous study that concluded AFB smear grading as a predictor for smear non-conversion PTB status, however to the best of our knowledge, this finding was the first finding that conclude single major predictor i.e. AFB smear grading. Previous study also concluded AFB smear grading together with other factors are the risk factors for smear non-conversion PTB status. Study concluded AFB smear 3+ have a higher risk to get non-conversion after intensive phase of treatment.<sup>10</sup> Another study concluded PTB subjects with AFB 2+ and 3+ only 34 % with smear conversion after 2 months intensive phase of treatment.<sup>19</sup> AFB grading plays an important role in the management of PTB which is describing PTB severity and transmission ability<sup>20</sup> as well as indicating the late drugs resolution that related to the existence of lung cavity and the density of the mycobacterium.

The binary logistic regression analysis involved household income in the final model, although did not meet the significance level ( $p=0.096$ ). The previous study in Ethiopia concluded that the lower-income have a risk of 2.83 times to be non-conversion compared to the higher income.<sup>21</sup> Another study reported that lower income is related to the poor treatment outcome.<sup>22</sup> Indeed, the level of income plays a pivotal role in the prevention and

**Commented [MJo18]:** Diskusi tidak tajam, tidak mendiskusikan tentang mengapa hanya satu faktor yang dapat menjadi predictor atau ada confounding lain yang dapat menyebabkan perbedaan ini. Kondisi komorbid pasti berhubungan seperti HIV pasti berhubungan dengan hal ini tetapi tidak ada dalam data sehingga perlu dicantumkan sbg limitasi

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treatment of diseases moreover the disease with long-time treatment include PTB. A systematic review reported financial burden for TB patients that consist of direct medical cost, direct non-medical cost, and indirect cost. The mean total costs ranged from USD 55 to USD 8198, with an average of USD 847.<sup>21</sup>

Smoking status and DM was not involved in the final model of binary logistic regression, however, smoking status and DM were significantly related to the smear non-conversion PTB based on the Chi-square test. Previous study reported that smoking is related to the adherence to the anti-tuberculosis treatment.<sup>23</sup> Previous study also concluded that cigarette smoking in active PTB is related to delayed culture conversion. The frequency of delayed culture conversion after 2 months of treatment increasingly in sequentially in a group of ex-smokers, current non-smokers, never smokers, ever smokers, and current smokers.<sup>24</sup> Regarding DM status, previous study reported that DM was associated with failure to sputum smear convert at 2 months and failure.<sup>13</sup> Other study also reported that PTB cases with DM were common to be delayed sputum conversion and failure.<sup>25</sup> On the contrary, a study reported DM influenced the clinical presentation and response to the treatment, but there was no difference in the drug resistance and relapse rates.<sup>25</sup>

The current study conducted in the setting of hospital-based data in Dr. Kariadi General Hospital which is not represented the general population condition, moreover the status of the hospital is national referral imply the PTB cases tend to be complex referral cases. The current study was also using primary data, however, prior secondary data were used in medical records. The use of culture to diagnose and its conversion after 2 months of

treatment was not conducted in the present study. Further research is needed to understand well the related predictors for smear non-conversion PTB.

#### **CONFLICTS OF INTEREST**

The authors affirm no conflict of interest in this study.

#### **FUNDING SOURCES**

This study was supported by grant of DIPA PNBPN UNNES 2019 No. 1603/UN37.3.1/TU/2019.

#### **ACKNOWLEDGMENT**

We acknowledge the Lembaga Penelitian dan Pengabdian Masyarakat (LPPM) Universitas Negeri Semarang for the financial support and Dr. Kariadi General Hospital, Semarang, Indonesia for providing data and permission to meet subjects.



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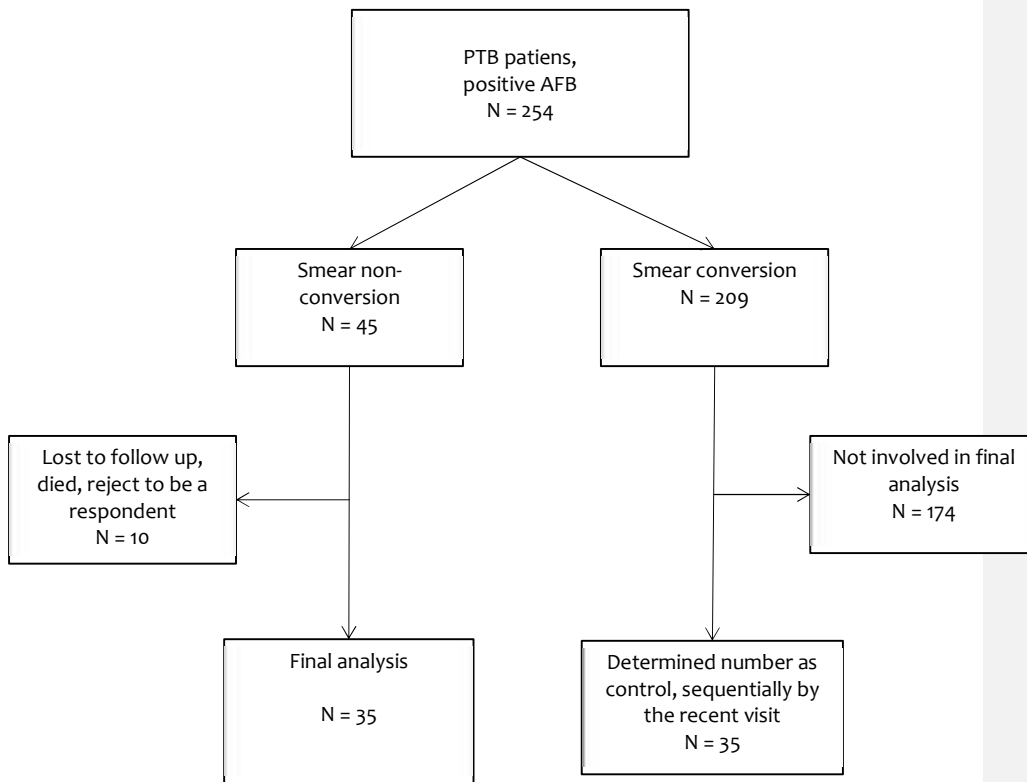
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**Figure 1.** Subject recruitment

**Table 1.** Subject's characteristics

Characteristics	Non-conversion status		p value*
	Yes, n (%)	No, n (%)	
Age (yo)			
≥ 55	20; 57.1	10; 28.6	0.030
15–54	15; 42.9	25; 71.4	
Sex			
Male	24; 68.6	14; 40.0	0.031
Female	11; 31.4	21; 60.0	
Level of education			
Low	6; 17.1	4; 11.4	0.733
High	29; 82.9	31; 88.6	
Occupational status			
Un-employee	12; 34.3	11; 31.4	1.000
Employee	23; 65.7	24; 68.6	

\*Chi-square test  
yo: years old

**Commented [MJo122]:** Mohon diubah dalam bentuk n (%)  
contoh  
20 (57.1)  
15 (42.9)  
dst

**Table 2.** Predictors for smear non-conversion status PTB

Predictors	Non-conversion status		p value*	OR (CI 95%)
	Yes	No		
AFB smear grading				
≥2+	29; 82.9	9; 25.7	0.000	13.963 (4.374–44.573)
<2+	6; 17.1	26; 74.3		
BMI				
Under (<18.5)	14; 40.0	12; 34.3	0.805	1.278 (0.483–3.377)
Normal (>18.5)	15; 42.9	18; 51.4		
Overweight (>23)	6; 17.1	5; 14.3		
Drugs side effects				
Yes	11; 31.4	13; 37.1	0.801	0.776 (0.288–2.087)
No	24; 66.6	22; 62.9		
Smoking status				
Yes	21; 60.0	11; 31.4	0.031	3.273 (1.224–8.748)
No	14; 40.0	24; 68.6		
Alcohol consumption				
Yes	4; 11.4	2; 5.7	0.669	2.129 (0.364–12.459)
No	31; 88.6	33; 94.3		
DM				
Yes	17; 48.6	3; 8.6	0.001	10.074 (2.595–39.111)
No	18; 51.4	32; 91.4		
Compliance				
No	2; 5.7	2; 5.7	1.000	1.000 (0.133–7.527)
Yes	33; 94.3	33; 94.3		
Access to the health services				
Limited access	10; 28.6	8; 22.9	0.784	1.350 (0.460–3.964)
Fair	25; 71.4	27; 77.1		
Housing condition				
Bad	8; 22.9	2; 5.7	0.088	4.889 (0.957–24.973)
Fair	27; 77.1	33; 94.3		
Housing density				
Very density	10; 28.6	5; 14.3	0.244	2.400 (0.725–7.949)
Fair	25; 71.4	30; 85.7		
Household income				
Low	28; 74.3	18; 51.4	0.083	2.728 (0.997–7.468)
Fair	9; 25.7	17; 48.6		

\* Chi-square test

BMI: body mass index

**Commented [N23]:** Gabungkan table 2 dan table 3. Tuliskan juga yang dimasukkan dalam analisis multivariate walupun hasil tidak bermakna.

**Commented [MJoI24]:** Mohon cara penulisan disamakan dengan komentar sebelumnya n (%)

**Table 3.** Binary logistic regression.

Predictors	$\beta$	Adjusted OR (95% CI)	p value*
Household income	1.041	2.83 (0.831–9.657)	0.096
AFB smear grading	2.652	14.18 (4.279–47.006)	0.000
Constant	-2.134	0.118	0.001

\*Binary logistic regression test

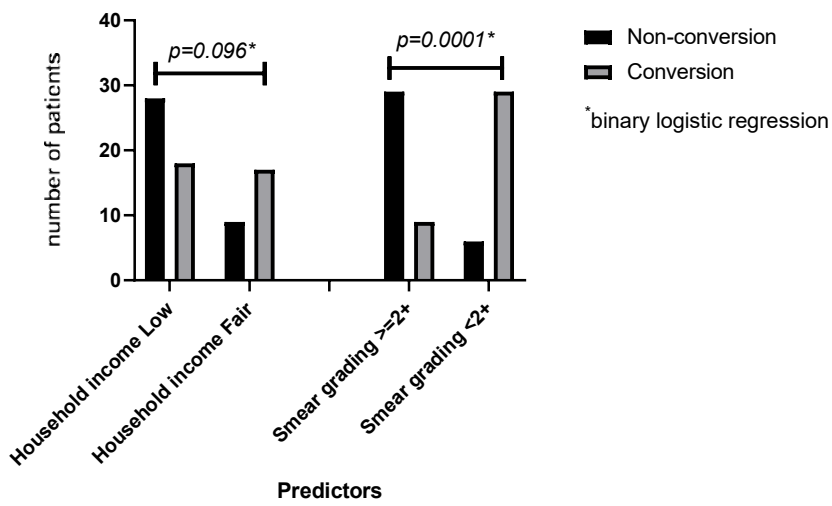


Figure 2. Predictors for smear non-conversion PTB.



Yth. Editor Medical Journal of Indonesia.

Bersama ini kami kirimkan kembali hasil revisi manuskrip kami dengan judul “ **Diabetes mellitus and smear grading predict non-conversion among new-treatment pulmonary tuberculosis: a case-control study in Indonesia**” setelah mendapatkan masukan dari Reviewer.

Berikut ini daftar masukan dari Reviewer dan perbaikan dari kami

Penelitian Penulis dan tim yang berjudul “Smear grading predicts non-conversion pulmonary tuberculosis: study in Dr. Kariadi general hospital Semarang, Indonesia” sebenarnya sangat menarik, namun pembahasan dalam naskah ini masih belum mendalam dan komprehensif. Berikut poin-poin yang perlu Penulis perbaiki:

1. Metode penelitian juga tidak jelas menggambarkan bahwa ini adalah studi kasus kontrol. Kriteria inklusi dan eksklusi juga tidak jelas dan bagaimana sampling method perlu dijelaskan baik pada kasus maupun kontrol.
  - Metode penelitian menggunakan desain case-control study, dengan menetapkan kelompok kasus dan kontrol sebagaimana dijelaskan di bagian metode.
  - Kriteria inklusi; adalah penderita pengobatan baru dengan BTA + dan mengeklusi: HIV/AIDS, TB ekstra paru, kasus kambuh (re-treatment)
  - Telah ditambahkan di metode
2. Waktu pengambilan sputum masih belum dijelaskan.
  - Sudah dijelaskan di metode juga
  - Smear examinations were done for three sputum smear specimens, i.e., first spot, morning, and second spot sputum. Results determined as positive if at least one of the specimens is positive, while negative if all of them are negative
3. Tuliskan juga dengan rumus apa Penulis menentukan sample size.
  - Formula sampling merujuk Rumus Lemeshow (Adequacy of Sample Size in Health Studies) untuk desain kasus kontrol

4. Mengapa hanya satu perbandingan case dan control 1:1 melihat banyaknya subjek pada kontrol yang mungkin juga eligible? Disarankan untuk menambahkan pada kontrol menjadi 1:2 atau 1:3 supaya lebih sah dalam mengambil simpulan.

→ Kami menetapkan perbandingan kasus:kontrol = 1:2 dengan kembali turun ke lapangan untuk mengambil/menambah data kontrol

5. Secara logika tentu saja semakin tinggi smear grading semakin banyak kuman maka semakin sulit pula konversi. Tetapi bagaimana menjelaskan hal ini perlu didiskusikan lebih lanjut.

→ Kami telah menambahkan penjelasan pada bagian pembahasan, dengan menambah rujukan dan menjelaskan kontribusi confounding utama yaitu HIV/AIDS dan status pengobatan baru (kasus baru) yang memang dalam penelitian kami, kami batasi

6. Dalam naskah ini masih terlalu banyak faktor yang dibahas tetapi jumlah subjek sedikit sehingga menyebabkan power menjadi sangat rendah.

→ Sesuai saran yang diberikan kami menambahkan jumlah responden kontrol sehingga didapatkan sejumlah total 76 kontrol.

7. Fokus banyak pada menjelaskan RS Kariadi dan bukan fokus bahwa prediktor ini berguna untuk apa.

→ Telah diperbaiki di pembahasan

8. Apa yang menarik dari penelitian ini dan bagaimana hasilnya dibandingkan dengan penelitian lain juga belum banyak dibahas terutama dalam kaitannya sebagai prediktor.

→ Kami tambahkan keterangan di pembahasan

9. Penelitian lain bagaimana apakah ada prediktor lain yang lebih baik. Limitasi dari penelitian ini apa? Sebagai contoh DM saja mungkin tidak dapat menjadi prediktor, mungkin uncontrolled DM yang bisa menjadi prediktor. Itu juga tidak ada dalam diskusi. Perdalam diskusi agar lebih menarik.

→ Kami tambahkan keterangan di pembahasan

Kami berharap Penulis bersedia memperbaiki artikel ini sesuai saran reviewer, agar menjadi layak muat di Med J Indones, dan diterima untuk publikasi.

Bersama ini saya kirimkan artikel yang sudah diberi comment untuk mempermudah perbaikan. Perbaikan harap dilakukan pada file ini dengan balon tidak dibuang serta diberikan highlight kuning pada bagian yang diubah.

Terimakasih banyak atas kerjasamanya Penulis.

Demikian, kiranya perbaikan ini dapat menjadikan pertimbangan Editor agar naskah kami dapat diterima di Medical Journal of Indonesia.

Atas masukan, review dan diprosesnya naskah kami, atas nama seluruh penulis kami mengucapkan terima kasih.

Salam,

Mahalul Azam

(Correspondent author)

## Notifications

**[MJI] Editor Decision (ID:4216)**

2020-09-03 11:17 AM

Dear Dr. Mahalul Azam, Dr. Arulita Ika Fibriana, Muhamad Zakki Saefurrohimi, Akhriyah Atsna Setiana, Avissena Dutha Pratama:

We have reached a decision regarding your submission to Medical Journal of Indonesia, "Smear grading predicts non-conversion pulmonary tuberculosis: study in Dr. Kariadi general hospital Semarang, Indonesia".

Our decision is to: accept your submission.

Agus Rizal Hamid  
Editor-in-chief Medical Journal of Indonesia  
rizalhamid.urology@gmail.com

## Notifications

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Our decision is to: accept your submission.

Agus Rizal Hamid  
Editor-in-chief Medical Journal of Indonesia  
rizalhamid.urology@gmail.com

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**article submission**

2 messages

**Mahalul Azam** <mahalul.azam@mail.unnes.ac.id>  
 To: mji@ui.ac.id

Sat, Sep 21, 2019 at 7:15 AM

Dear Editor of the Medical Journal of Indonesia

Firstly may I introduce myself, my name Mahalul Azam. We have submitted a manuscript to the Medical Journal of Indonesia (MJI) on September, 18th 2019, however, until now we have not received confirmation from the Journal's Editor.

Just want to make sure that everything runs well or perhaps are there any mistakes that we must revise the submission?

The title of the manuscript was **Smear grading predicts non-conversion pulmonary tuberculosis: study in Dr. Kariadi general hospital Semarang, Indonesia.** (Arulita Ika Fibriana et al)

Manuscript ID was: **4216**

We will be waiting for your confirmation and thank you very much for the response.

Best regards

Assoc. Prof. Mahalul Azam, MD, MPH, PhD  
*Vice Dean for Academic Affairs*

Public Health Department  
 Faculty of Sport Sciences  
 Universitas Negeri Semarang  
 Semarang, Indonesia  
 Phone: **+62-8122853982** (Whatsapp available)  
 Fax: +62-24-8505422  
 email: [mahalul.azam@mail.unnes.ac.id](mailto:mahalul.azam@mail.unnes.ac.id)








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**Medical Journal of Indonesia** <mji@ui.ac.id>  
 To: Mahalul Azam <mahalul.azam@mail.unnes.ac.id>

Thu, Sep 26, 2019 at 3:57 PM

Dear authors

Thank you for submitting your manuscript to MJI.  
 Your manuscript now is in submission stage, and our staff are currently checking the completeness of your manuscript.  
 We will notify you for further information.

Thank you

[Quoted text hidden]

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**[MJI] Copyediting Request (ID: 4216)**

4 messages

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**Medical Journal of Indonesia** < mji@ui.ac.id >  
To: Mahalul Azam < mahalul.azam@mail.unnes.ac.id >

Tue, Sep 15, 2020 at 10:53 AM

Dear Dr. Mahalul Azam,

We have now copyedited your submission "**Smear grading predicts non-conversion pulmonary tuberculosis: study at Dr. Kariadi General Hospital, Semarang, Indonesia**" for Medical Journal of Indonesia. To review the proposed changes and respond to Author Queries, please follow these steps:

1. Click on the Submission URL below.
2. Log into the journal and click on the File that appears in Step 1.
3. Consult Copyediting Instructions posted on the webpage.
4. Open the downloaded file and review the copyediting, making changes using Track Changes in Word, and answer queries while adding Author Queries as needed.
5. Save the copyedited file, and upload it to Step 1 of Copyediting.
6. Send the COMPLETE email to the editor.

This is the last opportunity that you have to make substantial changes. You will be asked at a later stage to proofread the galleys, but at that point, only minor typographical and layout errors can be corrected. Please do complete the copyedit in **one week (Due: September 22, 2020)**.

Medical Journal of Indonesia URL: <https://mji.ui.ac.id/journal/index.php/mji>  
Submission URL: <https://mji.ui.ac.id/journal/index.php/mji/workflow/access/4216>  
Username: mahalul\_azam

If you are unable to undertake this work at this time or have any questions, please contact me. Thank you for your contribution to this journal.

--  
Warm regards,  
Dania Clarisa (Editorial Assistant)  
Medical Journal of Indonesia  
[clarisadania@gmail.com](mailto:clarisadania@gmail.com)

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Education Tower 6th Floor, IMERI FKUI, [Salemba Raya Street No. 6, Kenari, Senen, Central Jakarta, 10430, Indonesia](#)  
Contact Number: +622129189160 ext. 201605; +62-811-1400-115

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**Mahalul Azam** < mahalul.azam@mail.unnes.ac.id >  
To: Medical Journal of Indonesia < mji@ui.ac.id >

Wed, Sep 16, 2020 at 11:56 PM

Dear Dania Clarisa,  
Thank you very much for the further processing of our manuscript.  
We have revised the copyediting as reviewed and enclosed is the copyedited version file.  
Hopefully, it can meet the journal standard and could be processed in the next step. However, if there are still any corrections, we will do the needful edit.

Thank you very much and we are looking forward to hearing from you

Best regards

Assoc. Prof. Mahalul Azam, MD, MPH, PhD  
Vice Dean for Academic Affairs

Public Health Department  
Faculty of Sport Sciences  
Universitas Negeri Semarang  
Semarang, Indonesia  
Phone: +62-8122853982 (Whatsapp available)  
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email: [mahalul.azam@mail.unnes.ac.id](mailto:mahalul.azam@mail.unnes.ac.id)



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**Medical Journal of Indonesia** <[mji@ui.ac.id](mailto:mji@ui.ac.id)>  
To: Mahalul Azam <[mahalul.azam@mail.unnes.ac.id](mailto:mahalul.azam@mail.unnes.ac.id)>

Tue, Dec 22, 2020 at 7:09 PM

Dear dr. Mahalul Azam,

Enclosed the final correction of the copyediting manuscript, there are some comments on the result section that need to be clarified by the authors. Please do the revision within a short time.

Thank you.

Regards,  
Dania Clarisa  
Editorial Assistant  
Med J Indones  
[Quoted text hidden]

--  
Warm regards,  
Med J Indones  
[Quoted text hidden]

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**Mahalul Azam** <[mahalul.azam@mail.unnes.ac.id](mailto:mahalul.azam@mail.unnes.ac.id)>  
To: Medical Journal of Indonesia <[mji@ui.ac.id](mailto:mji@ui.ac.id)>

Wed, Dec 23, 2020 at 6:06 AM

Dear Dania Clarisa

Thank you very much for sending us the final correction. Some clarifications are as follows

1. We corrected some typing errors as shown in Track and Changes
2. We omit Figure 2 as requested in the comment "Better to show the binary logistic regression on the Table, you can omit the figure 2 since it represents the same result"
3. We clarified that We considered variables with  $p < 0.25$  to be continued in Binary logistic regression as stated in the Methods section (page 5 2<sup>nd</sup> paragraph)

Reference:

Kleinbaum, D. G., Dietz, K., Gail, M., Klein, M., & Klein, M. (2002). Logistic regression. New York: Springer-Verlag.  
for the comment "This result in inconsistent with the result in Table 2. Only the significant ones that should be continued with the analysis. Please check again"

The final version of the manuscript is attached.

Thank you very much.  
Best regards



Assoc. Prof. Mahalul Azam, MD, MPH, PhD  
*Vice Dean for Academic Affairs*

Public Health Department  
Faculty of Sport Sciences  
Universitas Negeri Semarang  
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