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LAMPIRAN



KEMENTERIAN PENDIDIKAN, KEBUDAYAAN, RISET DAN TEKNOLOGI
 UNIVERSITAS HASANUDDIN FAKULTAS KEDOKTERAN
 KOMITE ETIK PENELITIAN UNIVERSITAS HASANUDDIN
 RSPTN UNIVERSITAS HASANUDDIN
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REKOMENDASI PERSETUJUAN ETIK

Nomor : 327/UN4.6.4.5.31/ PP36/ 2022

Tanggal: 30 Juni 2022

Dengan ini Menyatakan bahwa Protokol dan Dokumen yang Berhubungan Dengan Protokol berikut ini telah mendapatkan Persetujuan Etik :

No Protokol	UH22050206	No Sponsor Protokol	
Peneliti Utama	dr. Andi Ita Maghfirah	Sponsor	
Judul Peneliti	KADAR FERITIN DAN ATAU INTERLEUKIN-1BETA (IL-1BETA) SERUM TERHADAP DERAJAT KEPARAHAN CORONAVIRUS DISEASE 2019 (COVID-19); SUATU META-ANALISIS		
No Versi Protokol	2	Tanggal Versi	20 Juni 2022
No Versi PSP	2	Tanggal Versi	20 Juni 2022
Tempat Penelitian	RS Universitas Hasanuddin, FKUH dan RS dr. Wahidin Sudirohusodo Makassar		
Jenis Review	<input type="checkbox"/> Exempted <input checked="" type="checkbox"/> Expedited <input type="checkbox"/> Fullboard Tanggal	Masa Berlaku 30 Juni 2022 sampai 30 Juni 2023	Frekuensi review lanjutan
Ketua KEP Universitas Hasanuddin	Nama Prof.Dr.dr. Suryani As'ad, M.Sc.,Sp.GK (K)	Tanda tangan 	
Sekretaris KEP Universitas Hasanuddin	Nama dr. Agussalim Bukhari, M.Med.,Ph.D.,Sp.GK (K)	Tanda tangan 	

Kewajiban Peneliti Utama:

- Menyerahkan Amandemen Protokol untuk persetujuan sebelum di implementasikan
- Menyerahkan Laporan SAE ke Komisi Etik dalam 24 Jam dan dilengkapi dalam 7 hari dan Laporan SUSAR dalam 72 Jam setelah Peneliti Utama menerima laporan
- Menyerahkan Laporan Kemajuan (progress report) setiap 6 bulan untuk penelitian resiko tinggi dan setiap setahun untuk penelitian resiko rendah
- Menyerahkan laporan akhir setelah Penelitian berakhir
- Melaporkan penyimpangan dari prokol yang disetujui (protocol deviation / violation)
- Mematuhi semua peraturan yang ditentukan

Meta-Analysis Feritin dan Severe COVID-19

Random-Effects Model (k = 9)

	Estimate	se	Z	p	CI Lower Bound	CI Upper Bound
Intercept	4.99	1.19	4.18	< .001	2.652	7.334

Note. Tau² Estimator: Restricted Maximum-Likelihood

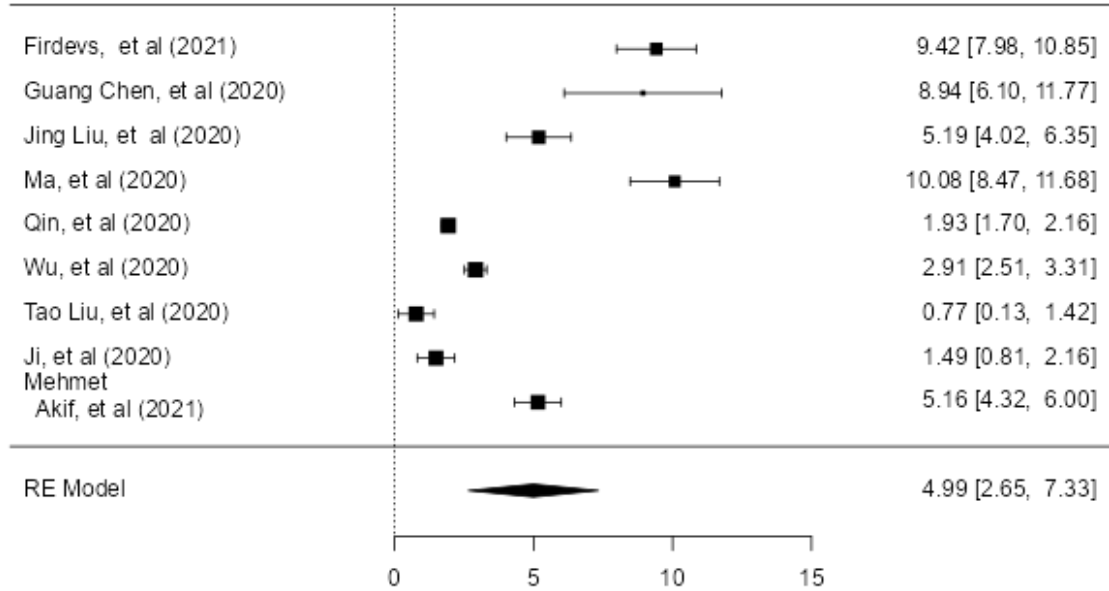
Heterogeneity Statistics

Tau	Tau ²	I ²	H ²	R ²	df	Q	p
3.523	12.4099 (SE= 6.4163)	99.19%	123.034	.	8.000	317.361	< .001

The analysis was carried out using the standardized mean difference as the outcome measure. A random-effects model was fitted to the data. The amount of heterogeneity (i.e., tau²), was estimated using the restricted maximum-likelihood estimator (Viechtbauer 2005). In addition to the estimate of tau², the Q-test for heterogeneity (Cochran 1954) and the I² statistic are reported. In case any amount of heterogeneity is detected (i.e., tau² > 0, regardless of the results of the Q-test), a prediction interval for the true outcomes is also provided. Studentized residuals and Cook's distances are used to examine whether studies may be outliers and/or influential in the context of the model. Studies with a studentized residual larger than the 100 x (1 - 0.05/(2 X k))th percentile of a standard normal distribution are considered potential outliers (i.e., using a Bonferroni correction with two-sided alpha = 0.05 for k studies included in the meta-analysis). Studies with a Cook's distance larger than the median plus six times the interquartile range of the Cook's distances are considered to be influential. The rank correlation test and the regression test, using the standard error of the observed outcomes as predictor, are used to check for funnel plot asymmetry.

A total of k=9 studies were included in the analysis. The observed standardized mean differences ranged from 0.7744 to 10.0785, with the majority of estimates being positive (100%). The estimated average standardized mean difference based on the random-effects model was $\hat{\mu} = 4.9931$ (95% CI: 2.6520 to 7.3342). Therefore, the average outcome differed significantly from zero (z = 4.1802, p < 0.0001). According to the Q-test, the true outcomes appear to be heterogeneous (Q(8) = 317.3612, p < 0.0001, tau² = 12.4099, I² = 99.1872%). A 95% prediction interval for the true outcomes is given by -2.2975 to 12.2837. Hence, although the average outcome is estimated to be positive, in some studies the true outcome may in fact be negative. An examination of the studentized residuals revealed that none of the studies had a value larger than ± 2.7729 and hence there was no indication of outliers in the context of this model. According to the Cook's distances, none of the studies could be considered to be overly influential. Both the rank correlation and the regression test indicated potential funnel plot asymmetry (p = 0.0446 and p = 0.0003, respectively).

Forest Plot

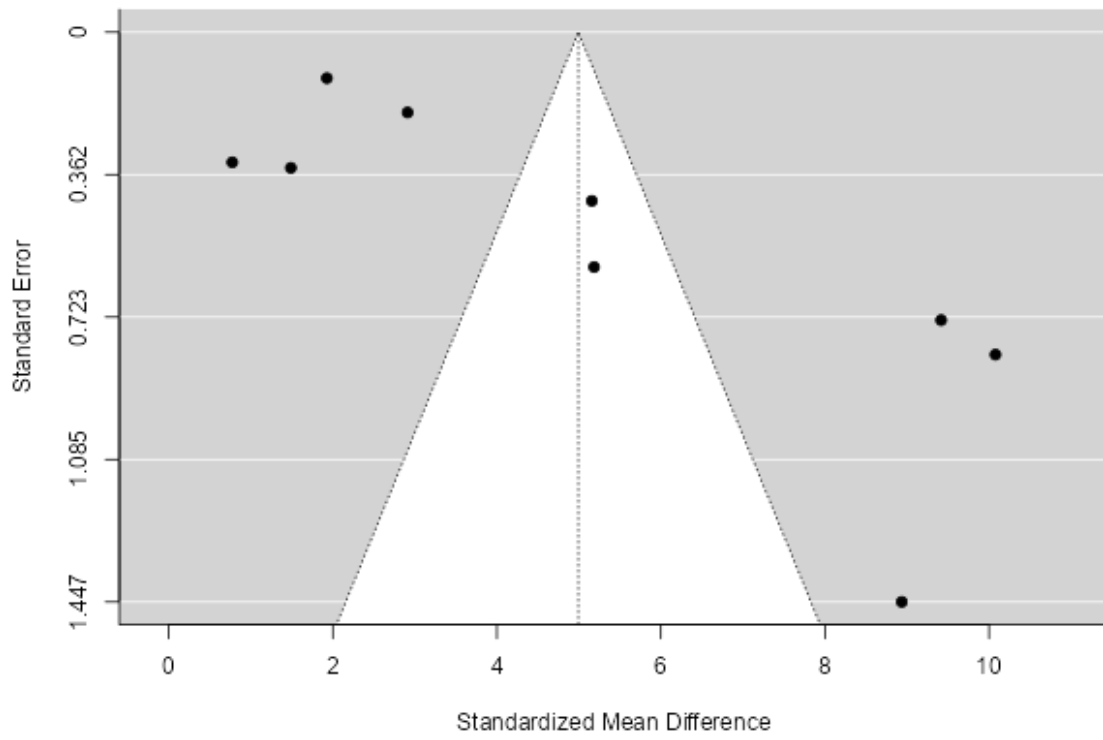


Publication Bias Assessment

Test Name	value	p
Fail-Safe N	2957.000	< .001
Begg and Mazumdar Rank Correlation	0.556	0.045
Egger's Regression	3.651	< .001
Trim and Fill Number of Studies	1.000	.

Note. Fail-safe N Calculation Using the Rosenthal Approach

Funnel Plot



Meta-Analysis feritin dan mortalitas COVID-19

Random-Effects Model (k = 4)

	Estimate	se	Z	p	CI Lower Bound	CI Upper Bound
Intercept	1.52	0.330	4.61	< .001	0.874	2.169

Note. Tau² Estimator: Restricted Maximum-Likelihood

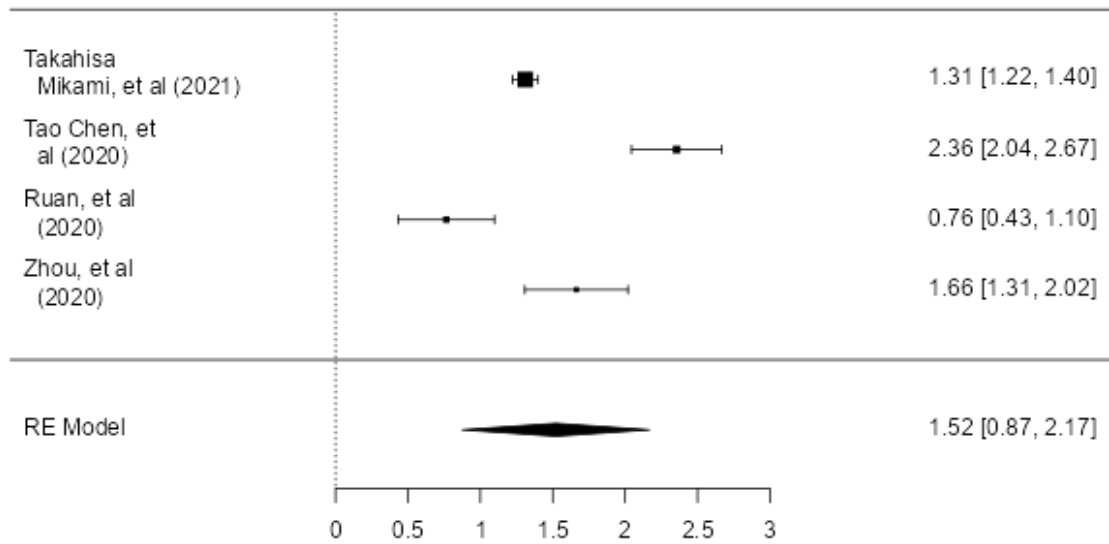
Heterogeneity Statistics

Tau	Tau ²	I ²	H ²	R ²	df	Q	p
0.644	0.4142 (SE= 0.3561)	96.22%	26.487	.	3.000	55.587	< .001

The analysis was carried out using the standardized mean difference as the outcome measure. A random-effects model was fitted to the data. The amount of heterogeneity (i.e., tau²), was estimated using the restricted maximum-likelihood estimator (Viechtbauer 2005). In addition to the estimate of tau², the Q-test for heterogeneity (Cochran 1954) and the I² statistic are reported. In case any amount of heterogeneity is detected (i.e., tau² > 0, regardless of the results of the Q-test), a prediction interval for the true outcomes is also provided. Studentized residuals and Cook's distances are used to examine whether studies may be outliers and/or influential in the context of the model. Studies with a studentized residual larger than the 100 x (1 - 0.05/(2 X k))th percentile of a standard normal distribution are considered potential outliers (i.e., using a Bonferroni correction with two-sided alpha = 0.05 for k studies included in the meta-analysis). Studies with a Cook's distance larger than the median plus six times the interquartile range of the Cook's distances are considered to be influential. The rank correlation test and the regression test, using the standard error of the observed outcomes as predictor, are used to check for funnel plot asymmetry.

A total of k=4 studies were included in the analysis. The observed standardized mean differences ranged from 0.7648 to 2.3553, with the majority of estimates being positive (100%). The estimated average standardized mean difference based on the random-effects model was $\hat{\mu} = 1.5215$ (95% CI: 0.8743 to 2.1686). Therefore, the average outcome differed significantly from zero (z = 4.6077, p < 0.0001). According to the Q-test, the true outcomes appear to be heterogeneous (Q(3) = 55.5866, p < 0.0001, tau² = 0.4142, I² = 96.2245%). A 95% prediction interval for the true outcomes is given by 0.1038 to 2.9392. Hence, even though there may be some heterogeneity, the true outcomes of the studies are generally in the same direction as the estimated average outcome. An examination of the studentized residuals revealed that none of the studies had a value larger than ± 2.4977 and hence there was no indication of outliers in the context of this model. According to the Cook's distances, none of the studies could be considered to be overly influential. Neither the rank correlation nor the regression test indicated any funnel plot asymmetry (p = 1.0000 and p = 0.8250, respectively).

Forest Plot

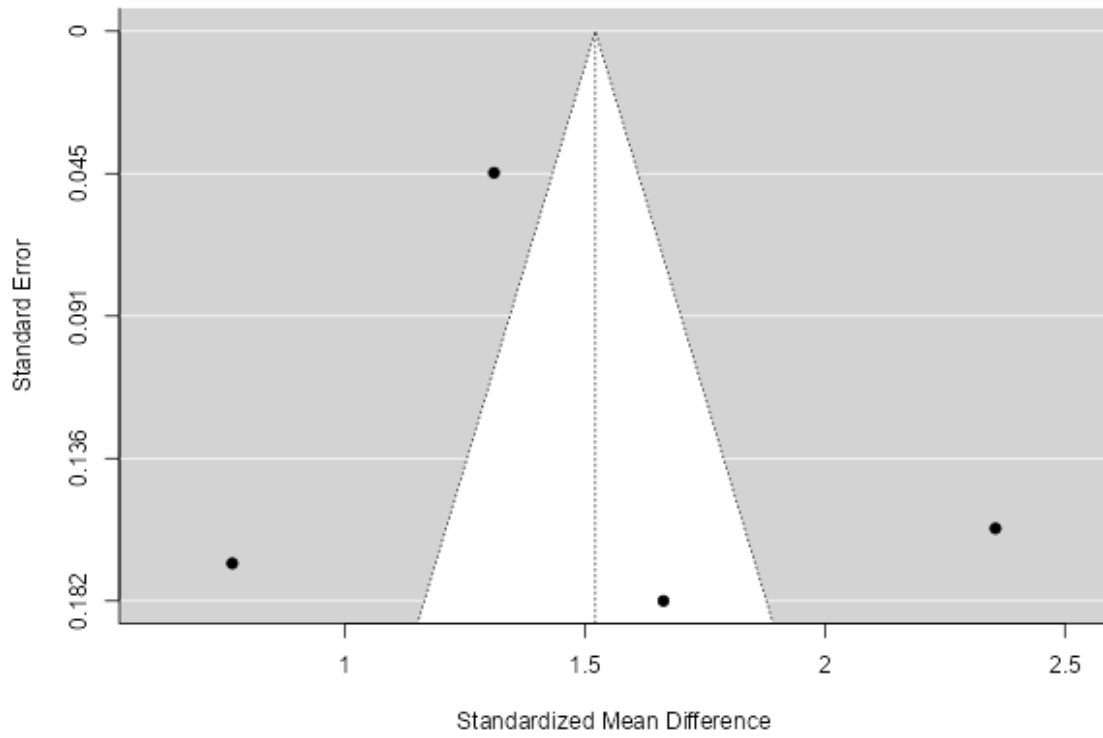


Publication Bias Assessment

Test Name	value	p
Fail-Safe N	1218.000	< .001
Begg and Mazumdar Rank Correlation	0.000	1.000
Egger's Regression	0.221	0.825
Trim and Fill Number of Studies	0.000	.

Note. Fail-safe N Calculation Using the Rosenthal Approach

Funnel Plot



Meta-Analysis IL-1 β and Severe COVID-19

Random-Effects Model (k = 4)

	Estimate	se	Z	p	CI Lower Bound	CI Upper Bound
Intercept	0.579	0.426	1.36	0.174	-0.256	1.413

Note. Tau² Estimator: Restricted Maximum-Likelihood

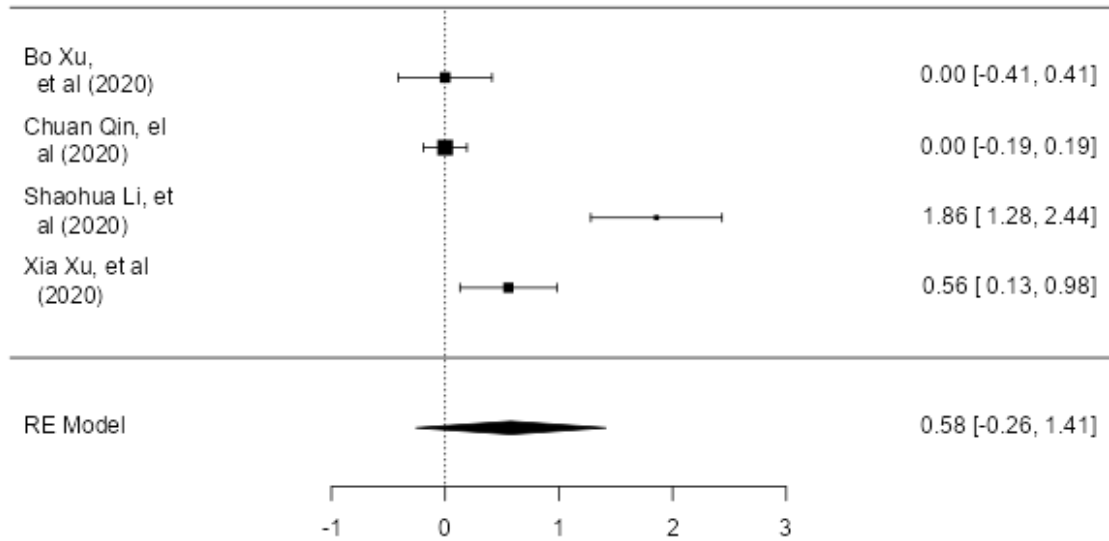
Heterogeneity Statistics

Tau	Tau ²	I ²	H ²	R ²	df	Q	p
0.824	0.6797 (SE= 0.5925)	95.04%	20.169	.	3.000	39.479	< .001

The analysis was carried out using the standardized mean difference as the outcome measure. A random-effects model was fitted to the data. The amount of heterogeneity (i.e., tau²), was estimated using the restricted maximum-likelihood estimator (Viechtbauer 2005). In addition to the estimate of tau², the Q-test for heterogeneity (Cochran 1954) and the I² statistic are reported. In case any amount of heterogeneity is detected (i.e., tau² > 0, regardless of the results of the Q-test), a prediction interval for the true outcomes is also provided. Studentized residuals and Cook's distances are used to examine whether studies may be outliers and/or influential in the context of the model. Studies with a studentized residual larger than the 100 x (1 - 0.05/(2 X k))th percentile of a standard normal distribution are considered potential outliers (i.e., using a Bonferroni correction with two-sided alpha = 0.05 for k studies included in the meta-analysis). Studies with a Cook's distance larger than the median plus six times the interquartile range of the Cook's distances are considered to be influential. The rank correlation test and the regression test, using the standard error of the observed outcomes as predictor, are used to check for funnel plot asymmetry.

A total of k=4 studies were included in the analysis. The observed standardized mean differences ranged from 0.0000 to 1.8583, with the majority of estimates being negative (0%). The estimated average standardized mean difference based on the random-effects model was $\hat{\mu} = 0.5787$ (95% CI: -0.2561 to 1.4135). Therefore, the average outcome did not differ significantly from zero (z = 1.3586, p = 0.1743). According to the Q-test, the true outcomes appear to be heterogeneous (Q(3) = 39.4795, p < 0.0001, tau² = 0.6797, I² = 95.0418%). A 95% prediction interval for the true outcomes is given by -1.2401 to 2.3975. Hence, although the average outcome is estimated to be positive, in some studies the true outcome may in fact be negative. An examination of the studentized residuals revealed that one study (Shaohua Li, et al (2020)) had a value larger than ± 2.4977 and may be a potential outlier in the context of this model. According to the Cook's distances, none of the studies could be considered to be overly influential. Neither the rank correlation nor the regression test indicated any funnel plot asymmetry (p = 0.0833 and p = 0.0557, respectively).

Forest Plot

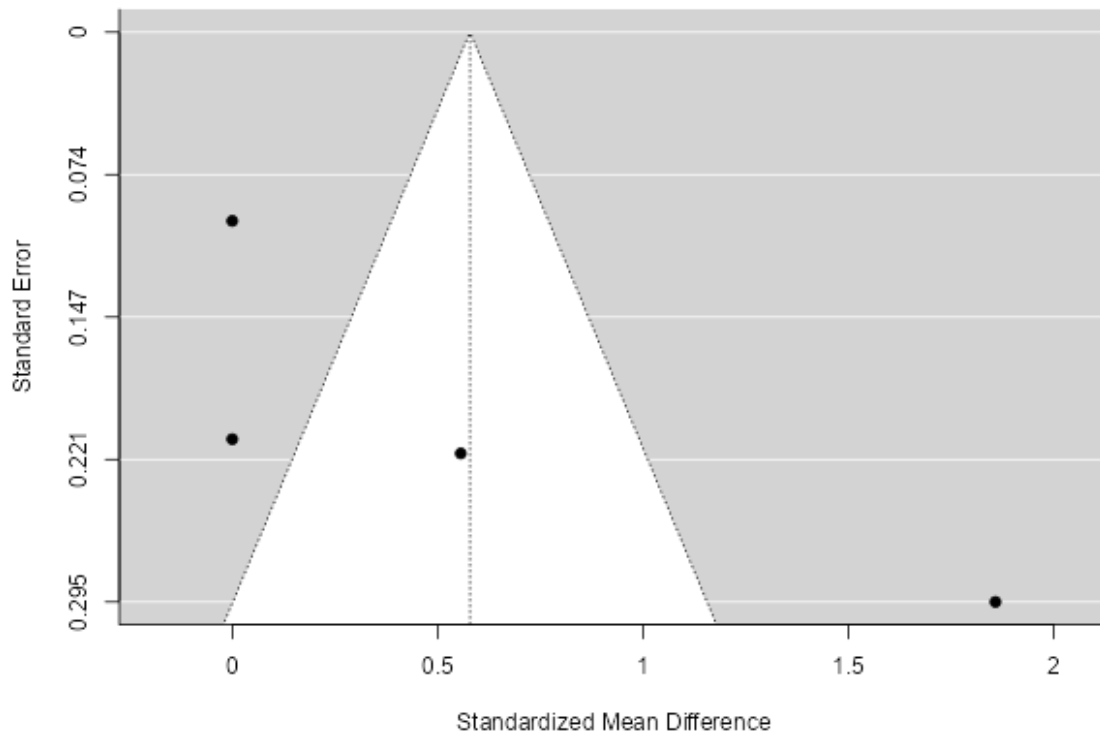


Publication Bias Assessment

Test Name	value	p
Fail-Safe N	26.000	< .001
Begg and Mazumdar Rank Correlation	1.000	0.083
Egger's Regression	1.914	0.056
Trim and Fill Number of Studies	0.000	.

Note. Fail-safe N Calculation Using the Rosenthal Approach

Funnel Plot



Meta-Analysis IL-1 β dan mortalitas COVID-19

Random-Effects Model (k = 4)

	Estimate	se	Z	p	CI Lower Bound	CI Upper Bound
Intercept	0.270	0.297	0.909	0.363	-0.313	0.853

Note. Tau² Estimator: Restricted Maximum-Likelihood

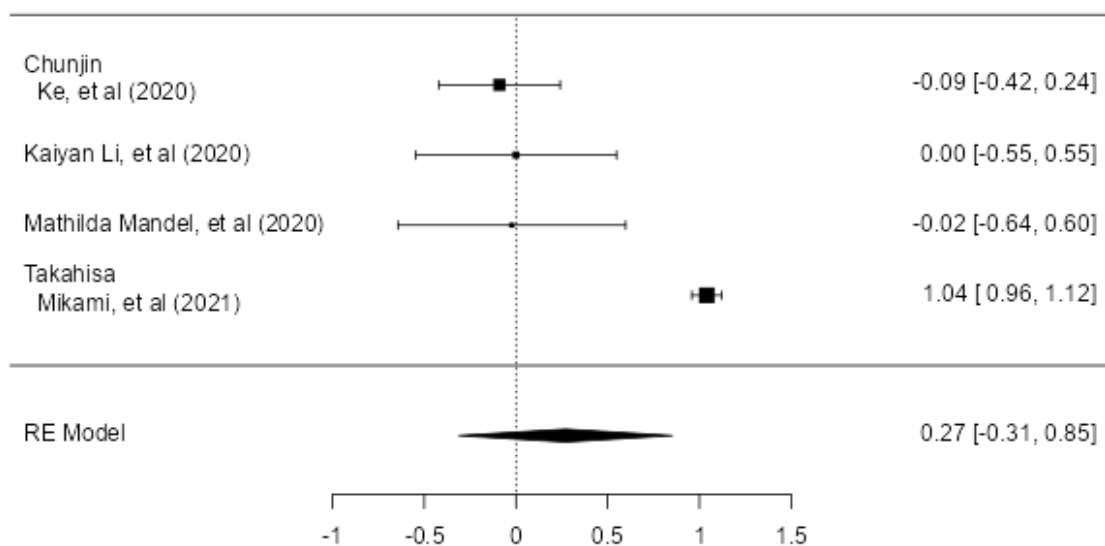
Heterogeneity Statistics

Tau	Tau ²	I ²	H ²	R ²	df	Q	p
0.553	0.3059 (SE= 0.2888)	91.68%	12.016	.	3.000	63.582	< .001

The analysis was carried out using the standardized mean difference as the outcome measure. A random-effects model was fitted to the data. The amount of heterogeneity (i.e., tau²), was estimated using the restricted maximum-likelihood estimator (Viechtbauer 2005). In addition to the estimate of tau², the Q-test for heterogeneity (Cochran 1954) and the I² statistic are reported. In case any amount of heterogeneity is detected (i.e., tau² > 0, regardless of the results of the Q-test), a prediction interval for the true outcomes is also provided. Studentized residuals and Cook's distances are used to examine whether studies may be outliers and/or influential in the context of the model. Studies with a studentized residual larger than the 100 x (1 - 0.05/(2 X k))th percentile of a standard normal distribution are considered potential outliers (i.e., using a Bonferroni correction with two-sided alpha = 0.05 for k studies included in the meta-analysis). Studies with a Cook's distance larger than the median plus six times the interquartile range of the Cook's distances are considered to be influential. The rank correlation test and the regression test, using the standard error of the observed outcomes as predictor, are used to check for funnel plot asymmetry.

A total of k=4 studies were included in the analysis. The observed standardized mean differences ranged from -0.0901 to 1.0404, with the majority of estimates being negative (50%). The estimated average standardized mean difference based on the random-effects model was $\hat{\mu} = 0.2703$ (95% CI: -0.3125 to 0.8532). Therefore, the average outcome did not differ significantly from zero (z = 0.9090, p = 0.3634). According to the Q-test, the true outcomes appear to be heterogeneous (Q(3) = 63.5824, p < 0.0001, tau² = 0.3059, I² = 91.6778%). A 95% prediction interval for the true outcomes is given by -0.9604 to 1.5010. Hence, although the average outcome is estimated to be positive, in some studies the true outcome may in fact be negative. An examination of the studentized residuals revealed that one study (Takahisa Mikami, et al (2021)) had a value larger than ± 2.4977 and may be a potential outlier in the context of this model. According to the Cook's distances, none of the studies could be considered to be overly influential. The regression test indicated funnel plot asymmetry (p = 0.0372) but not the rank correlation test (p = 1.0000).

Forest Plot

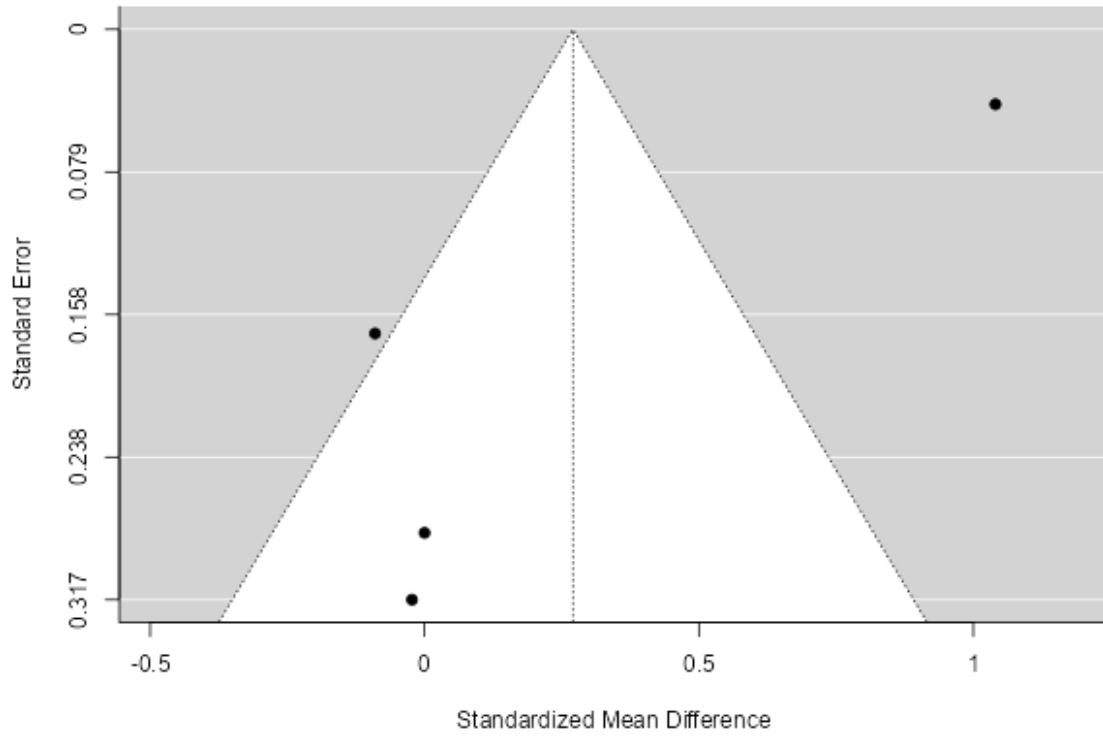


Publication Bias Assessment

Test Name	value	p
Fail-Safe N	217.000	< .001
Begg and Mazumdar Rank Correlation	0.000	1.000
Egger's Regression	-2.084	0.037
Trim and Fill Number of Studies	1.000	.

Note. Fail-safe N Calculation Using the Rosenthal Approach

Funnel Plot



PubMed Search History Feritin pada COVID-2

Search number	Query	Sort By	Filters	Search Details	Results	Time
5	(ferritin) AND (Severe COVID- 19)		Abstract, Free full text, Full text, Associated data, Comparative Study, Observational Study, Humans, English, Adult: 19+ years, from 2019 – 2022	((("ferritin s"[All Fields] OR "ferritine"[All Fields] OR "ferritins"[MeSH Terms] OR "ferritins"[All Fields] OR "ferritin"[All Fields]) AND (("sever"[All Fields] OR "severe"[All Fields] OR "severed"[All Fields] OR "severely"[All Fields] OR "severer"[All Fields] OR "severes"[All Fields] OR "severing"[All Fields] OR "severities"[All Fields] OR "severity"[All Fields] OR "severs"[All Fields]) AND ("covid 19"[All Fields] OR "covid 19"[MeSH Terms] OR "covid 19 vaccines"[All Fields] OR "covid 19 vaccines"[MeSH Terms] OR "covid 19 serotherapy"[All Fields] OR "covid 19 serotherapy"[Supplementary Concept] OR "covid 19 nucleic acid testing"[All Fields] OR "covid 19 nucleic acid testing"[MeSH Terms] OR "covid 19 serological testing"[All Fields] OR "covid 19 serological testing"[MeSH Terms] OR "covid 19 testing"[All Fields] OR "covid 19 testing"[MeSH Terms] OR "sars cov 2"[All Fields] OR "sars cov 2"[MeSH Terms] OR "severe acute respiratory syndrome coronavirus 2"[All Fields] OR "ncov"[All Fields] OR "2019 ncov"[All Fields] OR ("coronavirus"[MeSH Terms] OR "coronavirus"[All Fields] OR "cov"[All Fields]) AND 2019/11/01:3000/12/31[Date - Publication]))) AND ((ffrft[Filter] AND fha[Filter] AND (comparativestudy[Filter] OR observationalstudy[Filter]) AND fft[Filter]) AND (humans[Filter] AND (2019:2022[pdat]) AND (data[Filter]) AND (english[Filter] AND (alladult[Filter]))	27	20:21:09

4	(ferritin) AND (Severe COVID- 19)	Abstract, Free full text, Full text, Associated data, Comparative Study, Multicenter Study, Observational Study, Humans, English, Adult: 19+ years, from 2019 – 2022	(("ferritin s"[All Fields] OR "ferritine"[All Fields] OR "ferritins"[MeSH Terms] OR "ferritins"[All Fields] OR "ferritin"[All Fields]) AND (("sever"[All Fields] OR "severe"[All Fields] OR "severed"[All Fields] OR "severely"[All Fields] OR "severer"[All Fields] OR "severes"[All Fields] OR "severing"[All Fields] OR "severities"[All Fields] OR "severity"[All Fields] OR "severs"[All Fields]) AND ("covid 19"[All Fields] OR "covid 19"[MeSH Terms] OR "covid 19 vaccines"[All Fields] OR "covid 19 vaccines"[MeSH Terms] OR "covid 19 serotherapy"[All Fields] OR "covid 19 serotherapy"[Supplementary Concept] OR "covid 19 nucleic acid testing"[All Fields] OR "covid 19 nucleic acid testing"[MeSH Terms] OR "covid 19 serological testing"[All Fields] OR "covid 19 serological testing"[MeSH Terms] OR "covid 19 testing"[All Fields] OR "covid 19 testing"[MeSH Terms] OR "sars cov 2"[All Fields] OR "sars cov 2"[MeSH Terms] OR "severe acute respiratory syndrome coronavirus 2"[All Fields] OR "ncov"[All Fields] OR "2019 ncov"[All Fields] OR ("coronavirus"[MeSH Terms] OR "coronavirus"[All Fields] OR "cov"[All Fields]) AND 2019/11/01:3000/12/31[Date - Publication]))) AND ((ffrft[Filter] AND (fha[Filter] AND (comparativestudy[Filter] OR multicenterstudy[Filter] OR observationalstudy[Filter]) AND (fft[Filter] AND (humans[Filter] AND (2019:2022[pdat] AND (data[Filter] AND (english[Filter] AND (alladult[Filter]))	33	20:20:52
3	(ferritin) AND (Severe COVID- 19)	Abstract, Free full text, Full text, Associated data, Multicenter Study, Observational Study, Humans, English, Adult: 19+ years, from 2019 - 2022	(("ferritin s"[All Fields] OR "ferritine"[All Fields] OR "ferritins"[MeSH Terms] OR "ferritins"[All Fields] OR "ferritin"[All Fields]) AND (("sever"[All Fields] OR "severe"[All Fields] OR "severed"[All Fields] OR "severely"[All Fields] OR "severer"[All Fields] OR "severes"[All Fields] OR "severing"[All Fields] OR "severities"[All Fields] OR "severity"[All Fields] OR "severs"[All Fields]) AND ("covid 19"[All Fields] OR "covid 19"[MeSH Terms] OR "covid 19	25	20:20:43

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2	(ferritin) AND (Severe COVID-19)	Abstract, Free full text, Full text, Associated data, Multicenter Study, Humans, English, Adult: 19+ years, from 2019 - 2022	<p>((("ferritin s"[All Fields] OR "ferritine"[All Fields] OR "ferritins"[MeSH Terms] OR "ferritins"[All Fields] OR "ferritin"[All Fields]) AND (("sever"[All Fields] OR "severe"[All Fields] OR "severed"[All Fields] OR "severely"[All Fields] OR "severer"[All Fields] OR "severes"[All Fields] OR "severing"[All Fields] OR "severities"[All Fields] OR "severity"[All Fields] OR "severs"[All Fields]) AND ("covid 19"[All Fields] OR "covid 19"[MeSH Terms] OR "covid 19 vaccines"[All Fields] OR "covid 19 vaccines"[MeSH Terms] OR "covid 19 serotherapy"[All Fields] OR "covid 19 serotherapy"[Supplementary Concept] OR "covid 19 nucleic acid testing"[All Fields] OR "covid 19 nucleic acid testing"[MeSH Terms] OR "covid 19 serological testing"[All Fields] OR "covid 19 serological testing"[MeSH Terms] OR "covid 19 testing"[All Fields] OR "covid 19 testing"[MeSH Terms] OR "sars cov 2"[All Fields] OR "sars cov 2"[MeSH</p>	13	20:20:35

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1	(ferritin) AND (Severe COVID-19)	Abstract, Free full text, Full text, Associated data, Humans, English, Adult: 19+ years, from 2019 - 2022	((("ferritin s"[All Fields] OR "ferritine"[All Fields] OR "ferritins"[MeSH Terms] OR "ferritins"[All Fields] OR "ferritin"[All Fields]) AND (("sever"[All Fields] OR "severe"[All Fields] OR "severed"[All Fields] OR "severely"[All Fields] OR "severer"[All Fields] OR "severes"[All Fields] OR "severing"[All Fields] OR "severities"[All Fields] OR "severity"[All Fields] OR "severs"[All Fields]) AND ("covid 19"[All Fields] OR "covid 19"[MeSH Terms] OR "covid 19 vaccines"[All Fields] OR "covid 19 vaccines"[MeSH Terms] OR "covid 19 serotherapy"[All Fields] OR "covid 19 serotherapy"[Supplementary Concept] OR "covid 19 nucleic acid testing"[All Fields] OR "covid 19 nucleic acid testing"[MeSH Terms] OR "covid 19 serological testing"[All Fields] OR "covid 19 serological testing"[MeSH Terms] OR "covid 19 testing"[All Fields] OR "covid 19 testing"[MeSH Terms] OR "sars cov 2"[All Fields] OR "sars cov 2"[MeSH Terms] OR "severe acute respiratory syndrome coronavirus 2"[All Fields] OR "ncov"[All Fields] OR "2019 ncov"[All Fields] OR (("coronavirus"[MeSH Terms] OR "coronavirus"[All Fields] OR "cov"[All Fields]) AND 2019/11/01:3000/12/31[Date - Publication]))) AND ((ffrft[Filter] AND (fha[Filter] AND (fft[Filter] AND (humans[Filter] AND (2019:2022[pdat] AND (data[Filter] AND (english[Filter] AND (alladult[Filter])))	110	20:20:02

PubMed Search History IL-1 β pada COVID-19

Search number	Query	Sort By	Filters	Search Details	Results	Time
5	(Interleukin-1beta) AND (Severity COVID-19)		Full text, Associated data, in the last 5 years, English, Adult: 19+ years	((("interleukin 1beta"[MeSH Terms] OR "interleukin 1beta"[All Fields] OR ("interleukin"[All Fields] AND "1beta"[All Fields]) OR "interleukin 1beta"[All Fields]) AND (("sever"[All Fields] OR "severe"[All Fields] OR "severed"[All Fields] OR "severely"[All Fields] OR "severer"[All Fields] OR "severes"[All Fields] OR "severing"[All Fields] OR "severities"[All Fields] OR "severity"[All Fields] OR "severs"[All Fields]) AND ("covid 19"[All Fields] OR "covid 19"[MeSH Terms] OR "covid 19 vaccines"[All Fields] OR "covid 19 vaccines"[MeSH Terms] OR "covid 19 serotherapy"[All Fields] OR "covid 19 serotherapy"[Supplementary Concept] OR "covid 19 nucleic acid testing"[All Fields] OR "covid 19 nucleic acid testing"[MeSH Terms] OR "covid 19 serological testing"[All Fields] OR "covid 19 serological testing"[MeSH Terms] OR "covid 19 testing"[All Fields] OR "covid 19 testing"[MeSH Terms] OR "sars cov 2"[All Fields] OR "sars cov 2"[MeSH Terms] OR "severe acute respiratory syndrome coronavirus 2"[All Fields] OR "ncov"[All Fields] OR "2019 ncov"[All Fields] OR ("coronavirus"[MeSH Terms] OR "coronavirus"[All Fields] OR "cov"[All Fields]) AND 2019/11/01:3000/12/31[Date - Publication]))) AND ((y_5[Filter]) AND (fft[Filter]) AND (data[Filter]) AND (english[Filter]) AND (alladult[Filter]))	8	20:56:19

7	(Interleukin-1beta) AND (Severity COVID-19)	Full text, Associated data, Observational Study, in the last 5 years, English, Adult: 19+ years		0	20:56:12
6	(Interleukin-1beta) AND (Severity COVID-19)	Full text, Associated data, Observational Study, in the last 5 years, English, Adult: 19+ years	(("interleukin 1beta"[MeSH Terms] OR "interleukin 1beta"[All Fields] OR ("interleukin"[All Fields] AND "1beta"[All Fields]) OR "interleukin 1beta"[All Fields]) AND (("sever"[All Fields] OR "severe"[All Fields] OR "severed"[All Fields] OR "severely"[All Fields] OR "severer"[All Fields] OR "severes"[All Fields] OR "severing"[All Fields] OR "severities"[All Fields] OR "severity"[All Fields] OR "severs"[All Fields]) AND ("covid 19"[All Fields] OR "covid 19"[MeSH Terms] OR "covid 19 vaccines"[All Fields] OR "covid 19 vaccines"[MeSH Terms] OR "covid 19 serotherapy"[All Fields] OR "covid 19 serotherapy"[Supplementary Concept] OR "covid 19 nucleic acid testing"[All Fields] OR "covid 19 nucleic acid testing"[MeSH Terms] OR "covid 19 serological testing"[All Fields] OR "covid 19 serological testing"[MeSH Terms] OR "covid 19 testing"[All Fields] OR "covid 19 testing"[MeSH Terms] OR "sars cov 2"[All Fields] OR "sars cov 2"[MeSH Terms] OR "severe acute respiratory syndrome coronavirus 2"[All Fields] OR "ncov"[All Fields] OR "2019 ncov"[All Fields] OR ("coronavirus"[MeSH Terms] OR "coronavirus"[All Fields] OR "cov"[All Fields]) AND 2019/11/01:3000/12/31[Date - Publication]))) AND ((y_5[Filter]) AND (observationalstudy[Filter]) AND (fft[Filter]) AND	1	20:56:03

			(data[Filter]) AND (english[Filter]) AND (alladult[Filter]))		
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2	(Interleukin-1beta) AND (Severe COVID-19)	in the last 5 years, English, Adult: 19+ years	((("interleukin 1beta"[MeSH Terms] OR "interleukin 1beta"[All Fields] OR ("interleukin"[All Fields] AND "1beta"[All Fields]) OR "interleukin 1beta"[All Fields]) AND ("sever"[All Fields] OR "severe"[All Fields] OR "severed"[All Fields] OR "severely"[All Fields] OR "severer"[All Fields] OR "severes"[All Fields] OR "severing"[All Fields] OR "severities"[All	47	20:55:08

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1	(Interleukin-1beta) AND (COVID-19)	in the last 5 years, English, Adult: 19+ years	((("interleukin 1beta"[MeSH Terms] OR "interleukin 1beta"[All Fields] OR ("interleukin"[All Fields] AND "1beta"[All Fields]) OR "interleukin 1beta"[All Fields]) AND ("covid 19"[All Fields] OR "covid 19"[MeSH Terms] OR "covid 19 vaccines"[All Fields] OR "covid 19 vaccines"[MeSH Terms] OR "covid 19 serotherapy"[All Fields] OR "covid 19 serotherapy"[Supplementary Concept] OR "covid 19 nucleic acid testing"[All Fields] OR "covid 19 nucleic acid testing"[MeSH Terms] OR "covid 19 serological testing"[All Fields] OR "covid 19 serological testing"[MeSH Terms] OR	104	20:54:29

			"covid 19 testing"[All Fields] OR "covid 19 testing"[MeSH Terms] OR "sars cov 2"[All Fields] OR "sars cov 2"[MeSH Terms] OR "severe acute respiratory syndrome coronavirus 2"[All Fields] OR "ncov"[All Fields] OR "2019 ncov"[All Fields] OR ("coronavirus"[MeSH Terms] OR "coronavirus"[All Fields] OR "cov"[All Fields]) AND 2019/11/01:3000/12/31[Date - Publication]])) AND ((y_5[Filter] AND (english[Filter] AND (alladult[Filter]))		
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