Dr. dr. Afif Nurul Hidayati, SpKK-K <afif_nurulhidayati@fk.unair.ac.id>

Article submission received

2 pesan

editorial@f1000research.com <editorial@f1000research.com> 20 Desember 2021 13.28
Kepada: afif_nurulhidayati@fk.unair.ac.id

Dear Afif Nurul

Thank you for submitting your manuscript:

Efficacy of Vitamin D Supplementation on the Severity of Atopic Dermatitis in Children: Systematic Review and Meta-Analysis
Hidayati AN *et al.*

Funders: no grant funding was stated during submission.

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Please quote the article number 106957 in any correspondence.

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Kepada: desiana_ws@yahoo.co.id

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Begin forwarded message:

From: editorial@f1000research.com
Date: 20 December 2021 13.28.27 GMT+7
To: afif_nurulhidayati@fk.unair.ac.id
Subject: Article submission received

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Dr. dr. Afif Nurul Hidayati, SpKK-K <afif_nurulhidayati@fk.unair.ac.id>

Your article submission 106957

2 pesan

F1000.Research <research@f1000.com> 14 Januari 2022 23.59
Kepada: "afif_nurulhidayati@fk.unair.ac.id" <afif_nurulhidayati@fk.unair.ac.id>

Dear Afif Nurul Hidayati,

Hoping you are well. I am writing to provide you with an update on your submission to F1000Research.

I'm afraid that we're currently experiencing some delays in our editorial process due to a high volume of submissions over the Christmas period. I'm very sorry for the inconvenience caused. I can confirm that your article has passed initial checks and is waiting to undergo further checks. I will be in touch again next week as soon as the checks have been finalised.

In the meantime, if you have any questions, please do get in touch.

Thanks and best wishes,

Kitty Nolan (she/her)

Senior Assistant Editor

F1000

240 Blackfriars Rd
London SE1 8BF

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Dr. Afif Nurul Hidayati, dr., SpKK., FINSDV <afif_nurulhidayati@fk.unair.ac.id> 15 Januari 2022 07.54

Kepada: "F1000.Research" <research@f1000.com>

Dear Mrs. Kitty Nolan,

Thank you very much for your information about our manuscript and we are looking forward to see next confirmation about our manuscript.

Sincerely,
Afif Nurul Hidayati

Dermatologist, MD
Department of Dermatology and Venereology, Faculty of Medicines, Universitas Airlangga
Dr Soetomo Academic General Hospital
Universitas Airlangga Teaching Hospital
Surabaya, Indonesia

On 14 Jan 2022, at 23.59, F1000.Research <research@f1000.com> wrote:

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Payment for article APC in F1000Research (Article ID: 106957)

2 pesan

info@f1000.com <info@f1000.com> 21 Januari 2022 08.11
Kepada: afif_nurulhidayati@fk.unair.ac.id

Dear Dr. Afif Nurul Hidayati, dr., Sp.KK(K), FINSDV, FAADV

Efficacy of Vitamin D Supplementation on the Severity of Atopic Dermatitis in Children: Systematic Review and Meta-Analysis
Hidayati AN, Sawitri S, Sari DW, Prakoeswa CRS, Indramaya DM, Damayanti D, Zulkarnain I, Citrashanty I *et al.*

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Jl. Mayjen Prof. Dr. Moestopo No.6-8, Airlangga, Kec. Gubeng, Surabaya, East Java, Indonesia 60286
Jl. Dharmahusada Permai, Mulyorejo, Kec. Mulyorejo, Surabaya, East Java, Indonesia 60115
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Indonesia

The APC for this article, once any discounts have been taken into account, is $1350.00

If you have any questions, please contact us as soon as possible.

Best regards

The F1000Research team

Dr. Afif Nurul Hidayati, dr., SpKK., FINSDV <afif_nurulhidayati@fk.unair.ac.id> 21 Januari 2022 20.28
Kepada: desiana_ws@yahoo.co.id

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Date: 21 January 2022 08.11.13 GMT+7
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Dr. Afif Nurul Hidayati, dr., Sp.KK(K), FINSDV, FAADV
Department of Dermatology and Venereology, Faculty of Medicine, Universitas Airlangga/ Dr. Soetomo General Academic Hospital
Jl. Mayjen Prof. Dr. Moestopo No.6-8, Airlangga, Kec. Gubeng, Surabaya, East Java, Indonesia 60286
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Best regards

The F1000Research team

UNTUK INDONESIA ADIL & BERADAB

Dr. dr. Afif Nurul Hidayati, SpKK-K <afif_nurulhidayati@fk.unair.ac.id>

Manuscript 106957 conditionally accepted for publication

10 pesan

editorial@f1000research.com <editorial@f1000research.com> 19 Januari 2022 22.50
Kepada: afif_nurulhidayati@fk.unair.ac.id

Dear Afif Nurul,

Efficacy of Vitamin D Supplementation on the Severity of Atopic Dermatitis in Children: Systematic Review and Meta-Analysis
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Best wishes,

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The Editorial Team, F1000Research

Dr. Afif Nurul Hidayati, dr., SpKK., FINSDV <afif_nurulhidayati@fk.unair.ac.id> 20 Januari 2022 05.25
Kepada: desiana_ws@yahoo.co.id

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From: editorial@f1000research.com
Date: 19 January 2022 22.50.17 GMT+7
To: afif_nurulhidayati@fk.unair.ac.id
Subject: Manuscript 106957 conditionally accepted for publication

Dear Afif Nurul,

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Best wishes,

Kitty
The Editorial Team, F1000Research

Dr. Afif Nurul Hidayati, dr., SpKK., FINSDV <afif_nurulhidayati@fk.unair.ac.id> 20 Januari 2022 05.43
Kepada: editorial@f1000research.com

Dear Mrs.Kitty Nolan
F1000Research Senior Assistant Editor

Thank you very much for your information about our manuscript, 106957 entitled "Efficacy of Vitamin D Supplementation on the Severity of Atopic Dermatitis in Children: Systematic Review and Meta-Analysis". We will revise the manuscript as soon as possible as the advice.

Again, thank you for your consideration.

Sincerely,
Afif Nurul Hidayati,
Dermatologist, MD
Department of Dermatology and Venereology, Faculty of Medicines, Universitas Airlangga
Dr Soetomo Academic General Hospital
Universitas Airlangga Teaching Hospital
Surabaya, Indonesia

On 19 Jan 2022, at 22.50, editorial@f1000research.com wrote:

Dear Afif Nurul,

Efficacy of Vitamin D Supplementation on the Severity of Atopic Dermatitis in Children: Systematic Review and Meta-Analysis
Hidayati AN, Sawitri S, Sari DW, Prakoeswa CRS, Indramaya DM, Damayanti D, Zulkarnain I, Citrashanty I *et al.*

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Best wishes,

Kitty
The Editorial Team, F1000Research

F1000.Research <research@f1000.com> 20 Januari 2022 23.51
Kepada: "Dr. Afif Nurul Hidayati, dr., SpKK., FINSDV" <afif_nurulhidayati@fk.unair.ac.id>

Dear Dr. Afif Nurul Hidayati,

Many thanks for your email, we look forward to receiving your revisions. If you have any questions in the meantime, please don't hesitate to ask.

Thanks and best wishes,

Kitty Nolan (she/her)

Senior Assistant Editor

F1000

240 Blackfriars Rd
London SE1 8BF

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[Kutipan teks disembunyikan]

> [Kutipan teks disembunyikan]
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> Dear Afif Nurul,
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Kitty
The Editorial Team, F1000Research

Dr. dr. Afif Nurul Hidayati, SpKK-K <afif_nurulhidayati@fk.unair.ac.id> 31 Januari 2022 16.29
Kepada: editorial@f1000research.com

Dear Mrs. Kitty Nolan
F1000Research Senior Assistant Editor

We have received the amendment for our manuscript, titled Efficacy of vitamin D supplementation on the severity of atopic dermatitis in children: A systematic review and meta-analysis (106957) and we are very happy about the amendment.

We hereby attach a revision of our manuscript, and we have tried to address the queries and improved it according to your suggestions.

Again, thank you very much for the advice, it was very helpful.

Best Regards,
Afif Nurul Hidayati,
Dermatologist, MD
Department of Dermatology and Venereology, Faculty of Medicine, Universitas Airlangga
Dr Soetomo Academic General Hospital
Universitas Airlangga Teaching Hospital
Surabaya, Indonesia
[Kutipan teks disembunyikan]

106957 Hidayati et al revised_ f1000research-null-null-v1 (1).docx
277K

F1000.Research <research@f1000.com> 4 Februari 2022 17.20
Kepada: "Dr. dr. Afif Nurul Hidayati, SpKK-K" <afif_nurulhidayati@fk.unair.ac.id>

Dear Afif Nurul Hidayati,

Hoping you are well.

Many thanks for your email and revisions. Please find attached the most recent version of your manuscript where I have added some additional comments and suggestions. In particular, for your uploaded PRISMA checklist we would recommend indicating in which section/table/figure each item has been addressed, rather than page number, as this is likely to change during revisions and typesetting. We kindly ask that you address the comments in the manuscript using the Track Changes function in Word, and return the revised manuscript in reply to this email.

If you have any questions, please don't hesitate to get in touch.

Thanks and best wishes,

Kitty Nolan (she/her)

Senior Assistant Editor

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240 Blackfriars Rd
London SE1 8BF

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From: Dr. dr. Afif Nurul Hidayati, SpKK-K <afif_nurulhidayati@fk.unair.ac.id>
Sent: 31 January 2022 09:30
To: F1000.Research.Editorial <editorial@F1000Research.com>
Subject: Re: Manuscript 106957 conditionally accepted for publication

Dear Mrs. Kitty Nolan

[Kutipan teks disembunyikan]

[Kutipan teks disembunyikan]

[Kutipan teks disembunyikan]

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Best wishes,

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264K

Dr. Afif Nurul Hidayati, dr., SpKK., FINSDV <afif_nurulhidayati@fk.unair.ac.id> 4 Februari 2022 18.47
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From: "F1000.Research" <research@f1000.com>
Date: 4 February 2022 17.20.42 GMT+7
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Subject: RE: Manuscript 106957 conditionally accepted for publication

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We hereby attach a revision of our manuscript, and we have tried to address the queries and improved it according to your suggestions.

Again, thank you very much for the advice, it was very helpful.

Best Regards,
Afif Nurul Hidayati,
Dermatologist, MD
Department of Dermatology and Venereology, Faculty of Medicine, Universitas Airlangga
Dr Soetomo Academic General Hospital

Universitas Airlangga Teaching Hospital
Surabaya, Indonesia

Pada tanggal Rab, 19 Jan 2022 pukul 22.50 <editorial@f1000research.com> menulis:

Dear Afif Nurul,

Efficacy of Vitamin D Supplementation on the Severity of Atopic Dermatitis in Children: Systematic Review and Meta-Analysis
Hidayati AN, Sawitri S, Sari DW, Prakoeswa CRS, Indramaya DM, Damayanti D, Zulkarnain I, Citrashanty I *et al.*

Thank you for your submission to F1000Research and apologies for the delay. We have noted a few issues with your manuscript (below) – once these are addressed we will be pleased to accept your article for publication.

Reporting guidelines: We endorse the **PRISMA** guidelines for reporting Systematic Reviews; we suggest that you ensure the article adheres to the checklist and add any details that are missing. The comments in the manuscript provide some queries relating to the checklist, but these are not exhaustive.

Content: There seems to be some missing information in your manuscript. Please bear in mind that reviewers and readers must be exactly able to recreate your study from the level of detail that you give. Track Changes provide comments in the manuscript, but these are not exhaustive.

Data availability: Thank you for uploading your data and PRISMA checklist to Figshare, however the DOIs in your manuscript appear to be incorrect. The existing project only appears to contain one data file, '01.140421 Daftar Isi Tesis Desiana_BARU.docx'. Please update the *data availability* statement with the correct DOIs.

Acknowledgements: Please confirm that you have obtained permission from the people you would like to acknowledge to be named in the manuscript.

Reviewers: Thank you for providing reviewer suggestions. We note that the majority of your suggested reviewers are affiliated in Indonesia. As mentioned in our reviewer criteria, we require reviewer suggestions to be affiliated at geographically-diverse institutions, to ensure that an international perspective can be gained on your article. Please ensure you are providing a global spread of reviewers when suggesting.

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We have also lightly copyedited your article - please download the document and check you are happy with the amendments and **then address the queries detailed above using track changes in Word. Please return your revised manuscript to the e-mail address above**. Please note that this is your final opportunity to make any changes to the content of your manuscript. Once the typeset PDF of your manuscript has been created, we will send you a final PDF proof for checking prior to publication.

Please respond to this email within two weeks addressing any issues raised. After two weeks, we will send you a reminder email to complete your revisions. If we do not hear from you within seven weeks your submission will be withdrawn. If you have any questions, please don't hesitate to ask.

Best wishes,

Kitty
The Editorial Team, F1000Research

3 lampiran

image001.png
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~WRD0000.jpg
1K

Compared - KN.docx
264K

Dr. dr. Afif Nurul Hidayati, SpKK-K <afif_nurulhidayati@fk.unair.ac.id> 13 Februari 2022 11.25
Kepada: editorial@f1000research.com

Dear Mrs. Kitty Nolan
F1000Research Senior Assistant Editor

We have received the most recent version of our manuscript, titled Efficacy of vitamin D supplementation on the severity of atopic dermatitis in children: A systematic review and meta-analysis (106957)

We hereby attach a revision of our manuscript, and we have tried to explain the comments and suggestions. We also had to re-upload the revised prisma checklist according to your suggestion.

Thanks in advance.

Best Regards,
Afif Nurul Hidayati,
Dermatologist, MD
Department of Dermatology and Venereology, Faculty of Medicine, Universitas Airlangga
Dr Soetomo Academic General Hospital
Universitas Airlangga Teaching Hospital
Surabaya, Indonesia

Pada tanggal Rab, 19 Jan 2022 pukul 22.50 <editorial@f1000research.com> menulis:
[Kutipan teks disembunyikan]

Hidayati et al revised ver 2.docx
267K

F1000.Research <research@f1000.com> 19 Februari 2022 01.07
Kepada: "Dr. dr. Afif Nurul Hidayati, SpKK-K" <afif_nurulhidayati@fk.unair.ac.id>

Dear Afif Nurul Hidayati,

Many thanks for your email and revisions, and sincerest apologies for the delayed reply. I will be in touch again early next week with a further update on your submission.

Thanks and best wishes,

Kitty Nolan (she/her)

Senior Assistant Editor

F1000

240 Blackfriars Rd
London SE1 8BF

www.f1000.com

F1000

From: Dr. dr. Afif Nurul Hidayati, SpKK-K <afif_nurulhidayati@fk.unair.ac.id>
Sent: 13 February 2022 04:26
To: F1000.Research.Editorial <editorial@F1000Research.com>

[Kutipan teks disembunyikan]

[Kutipan teks disembunyikan]
[Kutipan teks disembunyikan]

Dear Afif Nurul,

Efficacy of Vitamin D Supplementation on the Severity of Atopic Dermatitis in Children: Systematic Review and Meta-Analysis
Hidayati AN, Sawitri S, Sari DW, Prakoeswa CRS, Indramaya DM, Damayanti D, Zulkarnain I, Citrashanty I *et al.*

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We have also lightly copyedited your article - please download the document and check you are happy with the amendments and **then address the queries detailed above using track changes in Word. Please return your revised manuscript to the e-mail address above**. Please note that this is your final opportunity to make any changes to the content of your manuscript. Once the typeset PDF of your manuscript has been created, we will send you a final PDF proof for checking prior to publication.

Please respond to this email within two weeks addressing any issues raised. After two weeks, we will send you a reminder email to complete your revisions. If we do not hear from you within seven weeks your submission will be withdrawn. If you have any questions, please don't hesitate to ask.

Best wishes,

Kitty
The Editorial Team, F1000Research

Dr. Afif Nurul Hidayati, dr., SpKK., FINSDV <afif_nurulhidayati@fk.unair.ac.id> 19 Februari 2022 05.36
Kepada: desiana_ws@yahoo.co.id

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From: "F1000.Research" <research@f1000.com>
Date: 19 February 2022 01.07.21 GMT+7
To: "Dr. dr. Afif Nurul Hidayati, SpKK-K" <afif_nurulhidayati@fk.unair.ac.id>
Subject: RE: Manuscript 106957 conditionally accepted for publication

[Kutipan teks disembunyikan]

Dr. dr. Afif Nurul Hidayati, SpKK-K <afif_nurulhidayati@fk.unair.ac.id>

Your article 106957 is now accepted

4 pesan

editorial@f1000research.com <editorial@f1000research.com> 22 Februari 2022 00.55
Kepada: afif_nurulhidayati@fk.unair.ac.id

Dear Afif Nurul,

Efficacy of vitamin D supplementation on the severity of atopic dermatitis in children: A systematic review and meta-analysis Hidayati AN, Sawitri S, Sari DW, Prakoeswa CRS, Indramaya DM, Damayanti D, Zulkarnain I, Citrashanty I *et al.*

We have now accepted your article for publication in F1000Research. It will be sent to the typesetters and a member of the Production team will send you a proof in due course.

One of our editorial team will be assisting you with the peer review process of your article, and will be your main contact once the article is published.

Best wishes,

Kitty
The Editorial Team, F1000Research

Dr. Afif Nurul Hidayati, dr., SpKK., FINSDV <afif_nurulhidayati@fk.unair.ac.id> 22 Februari 2022 11.52
Kepada: desiana_ws@yahoo.co.id

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Begin forwarded message:

From: editorial@f1000research.com
Date: 22 February 2022 00.55.38 GMT+7
To: afif_nurulhidayati@fk.unair.ac.id
Subject: Your article 106957 is now accepted

Dear Afif Nurul,

Efficacy of vitamin D supplementation on the severity of atopic dermatitis in children: A systematic review and meta-analysis
Hidayati AN, Sawitri S, Sari DW, Prakoeswa CRS, Indramaya DM, Damayanti D, Zulkarnain I, Citrashanty I *et al.*

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Best wishes,

Kitty
The Editorial Team, F1000Research

Dr. dr. Afif Nurul Hidayati, SpKK-K <afif_nurulhidayati@fk.unair.ac.id> 22 Februari 2022 12.32
Kepada: editorial@f1000research.com

Dear Mrs. Kitty Nolan,
Senior Assistant Editor F1000Research

Thank you for accepting our manuscript, entitled Efficacy of vitamin D supplementation on the severity of atopic dermatitis in children: A systematic review and meta-analysis
We are very happy and grateful to have a chance to submit our manuscript at f1000Research and have received a lot of suggestions and comments regarding the improvement of our manuscript, and it was all very meaningful.
We are looking forward to receiving information from you on the next progress of our manuscript.
Again, thank you very much for your consideration for accepting our manuscript.

Best Regards,
Afif Nurul Hidayati,
Dermatologist, MD
Department of Dermatology and Venereology, Faculty of Medicine, Universitas Airlangga
Dr Soetomo Academic General Hospital
Universitas Airlangga Teaching Hospital
Surabaya, Indonesia
[Kutipan teks disembunyikan]

F1000.Research <research@f1000.com> 22 Februari 2022 16.57
Kepada: "Dr. dr. Afif Nurul Hidayati, SpKK-K" <afif_nurulhidayati@fk.unair.ac.id>

Dear Afif Nurul Hidayati,

Many thanks for your kind email, it was my pleasure. Best wishes for the peer review process going forward.

Thanks and kind regards,

Kitty Nolan (she/her)

Senior Assistant Editor

F1000

240 Blackfriars Rd
London SE1 8BF

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[Kutipan teks disembunyikan]
[Kutipan teks disembunyikan]

Dear Afif Nurul,

Efficacy of vitamin D supplementation on the severity of atopic dermatitis in children: A systematic review and meta-analysis
Hidayati AN, Sawitri S, Sari DW, Prakoeswa CRS, Indramaya DM, Damayanti D, Zulkarnain I, Citrashanty I *et al.*

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One of our editorial team will be assisting you with the peer review process of your article, and will be your main contact once the article is published.

Best wishes,

Kitty
The Editorial Team, F1000Research

Information Classification: General

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Dr. dr. Afif Nurul Hidayati, SpKK-K <afif_nurulhidayati@fk.unair.ac.id>

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Australia: +61 3 8842 2413

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Dr. Afif Nurul Hidayati, dr., SpKK., FINSDV <afif_nurulhidayati@fk.unair.ac.id> 25 Februari 2022 13.18
Kepada: desiana_ws@yahoo.co.id

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From: Customer Services Team <accounts@f1000.com>
Date: 25 February 2022 06.46.04 GMT+7
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Subject: Invoice-6686126129

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Payment ID: 3391577
Thank you.

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Afif Nurul Hidayati,
Dermatologist, MD

Department of Dermatology and Venereology, Faculty of Medicine, Universitas Airlangga
Dr. Soetomo Academic General Hospital
Universitas Airlangga Teaching Hospital
Surabaya, Indonesia

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Payment confirmation for invoice 6686126129

2 pesan

noreply@f1000.com <noreply@f1000.com> 26 Februari 2022 11.55
Kepada: afif_nurulhidayati@fk.unair.ac.id

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Payment ID: 3391577

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Date: 26 February 2022 11.55.07 GMT+7

To: afif_nurulhidayati@fk.unair.ac.id
Subject: Payment confirmation for invoice 6686126129

Dear Afif Nurul Hidayati,

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Kepada: "afif_nurulhidayati@fk.unair.ac.id" <afif_nurulhidayati@fk.unair.ac.id>

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Dear Afif Nurul Hidayati,

Thank you for your email regarding invoice 6686126129.

I am pleased to confirm that your payment has been received and your invoice is now showing as paid.

If you have any further questions, please do not hesitate to contact me.

Kind regards

Jo Newman
F1000 Accounts

---------- Original Message ----------
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Sent: 26/02/2022 05:22
To: accounts@f1000.com
Subject: Re: Invoice-6686126129

Dear The F1000 Research Global Customer Services team,

We would like to inform you that we have paid $1,350.00 for invoice 6686126129.

Payment ID: 3391577
Thank you.

Best regards,
Afif Nurul Hidayati,
Dermatologist, MD
Department of Dermatology and Venereology, Faculty of Medicine, Universitas Airlangga
Dr. Soetomo Academic General Hospital
Universitas Airlangga Teaching Hospital
Surabaya, Indonesia

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Singapore: +65 6508 2862

Australia: +61 3 8842 2413

ref:_00D0Y35lji._5007R3Cx8WX:ref

Dr. dr. Afif Nurul Hidayati, SpKK-K <afif_nurulhidayati@fk.unair.ac.id>

Tracked Articles alert - 29 Mar 2022

2 pesan

F1000Research <no-reply.research@f1000.com> 29 Maret 2022 08.00
Kepada: afif_nurulhidayati@fk.unair.ac.id

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F1000Research Tracking alert

Dear Afif Nurul,

This is your requested daily tracking alert - a note under each article indicates the new activity.

Systematic Review

Efficacy of vitamin D supplementation on the severity of atopic dermatitis in children: A systematic review and meta-analysis [version 1; peer review: 1 approved]

Afif Nurul Hidayati, Sawitri Sawitri, Desiana Widityaning Sari, Cita Rosita Sigit Prakoeswa ... Iskandar Zulkarnain, Irmadita Citrashanty, Yuri Widia, Sylvia Anggraeni

New activity: Author response

Dr. Afif Nurul Hidayati, dr., SpKK., FINSDV <afif_nurulhidayati@fk.unair.ac.id> 29 Maret 2022 16.59
Kepada: desiana_ws@yahoo.co.id

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From: F1000Research <no-reply.research@f1000.com>
Date: 29 March 2022 08.00.11 GMT+7
To: afif_nurulhidayati@fk.unair.ac.id
Subject: Tracked Articles alert - 29 Mar 2022

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2 pesan

production@f1000research.com <production@f1000research.com> 3 Maret 2022 23.29
Kepada: afif_nurulhidayati@fk.unair.ac.id

Dear Afif Nurul,

I'm pleased to let you know that your article: "Efficacy of vitamin D supplementation on the severity of atopic dermatitis in children: A systematic review and meta-analysis" has just been published on F1000Research.

The Peer Review Process

We are now inviting the reviewers you have suggested. As part of their reports, reviewers are asked to provide a recommendation of 'Approved', 'Approved with Reservations' or 'Not Approved', and their report will be published alongside the article with their full name and affiliation. You will be able to respond to any published reports with a comment and/or by publishing revisions as a new version of your article – we will send you instructions on how to proceed when you begin to receive reports.

It is important that authors do not contact the reviewers directly, as this could result in invalidating their report.

Please note that we will ask you for additional reviewer suggestions if the invited reviewers decline. In order to avoid any delays with the peer review of your article, please continue to check your Suggest Reviewers page for updates and respond to any email requests as soon as you can.

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Now that your article has been published and assigned a DOI (10.12688/f1000research.106957.1) we would strongly recommend that you include this DOI in the metadata of any published dataset associated with this article. If you would like assistance with this, please contact our editorial team.

Increasing Discoverability

Now that your article has been published, why not take advantage of the tools we provide to help maximize your article's reach and share your article using the Email and Share options on the article page.

Your article will be listed in ePMC shortly as a preprint, and then updated once it has passed peer review.

Regards

Zena Nyakoojo
Senior Managing Editor, F1000Research

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Dr. Afif Nurul Hidayati, dr., SpKK., FINSDV <afif_nurulhidayati@fk.unair.ac.id> 4 Maret 2022 00.54
Kepada: desiana_ws@yahoo.co.id

Sent from my iPhone

Begin forwarded message:

From: production@f1000research.com
Date: 3 March 2022 23.29.42 GMT+7
To: afif_nurulhidayati@fk.unair.ac.id
Subject: Your article is now published

Dear Afif Nurul,

I'm pleased to let you know that your article: "Efficacy of vitamin D supplementation on the severity of atopic dermatitis in children: A systematic review and meta-analysis" has just been published on F1000Research.

The Peer Review Process

We are now inviting the reviewers you have suggested. As part of their reports, reviewers are asked to provide a recommendation of 'Approved', 'Approved with Reservations' or 'Not Approved', and their report will be published alongside the article with their full name and affiliation. You will be able to respond to any published reports with a comment and/or by publishing revisions as a new version of your article – we will send you instructions on how to proceed when you begin to receive reports.

It is important that authors do not contact the reviewers directly, as this could result in invalidating their report.

Please note that we will ask you for additional reviewer suggestions if the invited reviewers decline. In order to avoid any delays with the peer review of your article, please continue to check your Suggest Reviewers page for updates and respond to any email requests as soon as you can.

Linking Your Data

Now that your article has been published and assigned a DOI (10.12688/f1000research.106957.1) we would strongly recommend that you include this DOI in the metadata of any published dataset associated with this article. If you would like assistance with this, please contact our editorial team.

Increasing Discoverability

Now that your article has been published, why not take advantage of the tools we provide to help maximize your article's reach and share your article using the Email and Share options on the article page.

Your article will be listed in ePMC shortly as a preprint, and then updated once it has passed peer review.

Regards

Zena Nyakoojo
Senior Managing Editor, F1000Research

Press releasing articles: Please avoid promoting articles in the media until the article has passed the open peer review process. Promotion on social media is encouraged once the article has been published; please ensure the full citation is included, as this contains the peer review status. F1000Research should be cited as the source of these articles with a link to the article.

Efficacy of vVitamin D sSupplementation on the sSeverity of aAtopic dDermatitis in cChildren: A sSystematic rReview and mMeta-aAnalysis

Afif Nurul Hidayati[1,2,*], Sawitri Sawitri[1], Desiana Widityaning Sari[1,*], Cita Rosita Sigit Prakoeswa[1], Diah Mira Indramaya[1], Damayanti Damayanti[1], Iskandar Zulkarnain[1], Irmadita Citrashanty[1], Yuri Widia[1], Sylvia Anggraeni[1]

[1]Department of Dermatology and Venereology, Faculty of Medicine, Universitas Airlangga/Dr. Soetomo General Academic Hospital, Surabaya, East Java, 60132, Indonesia
[2]Department of Dermatology and Venereology, Universitas Airlangga Hospital, Surabaya, East Java, 60115, Indonesia
***Corresponding author: Afif Nurul Hidayati, afif_nurulhidayati@fk.unair.ac.id; Desiana Widityaning Sari, desiana_ws@yahoo.co.id**

Abstract

Background: Atopic Dermatitis (AD) is a common dermatosis in children, that includes skin architecture defects, immune dysregulation, and changes of skin flora. Several new drugs have been found to reduce the severity of AD. Vitamin D is one of the new therapies that ~~its use~~ is still controversial. The purpose of this research is ~~**Purpose:** t~~To conclude the efficacy of Vitamin D on atopic dermatitis severity in children aged 0-18 years old.

Methods: A systematic search was conducted on the PubMed, Cochrane, Proquest, Google Scholar, Clinical Trial website, and university ~~repository~~ repositories including studies published ~~f~~from January 2010 through October 2020. We compared populations, intervention, study design, and outcomes., ~~and s~~Statistical analysis was done~~done~~ with Review Manager 5.4.1

Results: ~~.~~ Eight articles met eligibility and inclusion criteria, four~~4~~ articles provided complete data and were analysed. Not all studies demonstrated the efficacy of v~~V~~itamin D but a meta-analysis of four~~4~~ studies of v~~V~~itamin D supplementation vs placebo found a mean difference of -0.93 (95%CI -1.76, to -0.11, p<0.001) of patients outcome, but statistically, there was no difference in cure rate (relative risk 1.46 (95%CI 0.72, to 2.97, p=0.008) in vitamin D supplementation groups compared to placebo groups.

Conclusion: Vitamin D supplementation in paediatric atopic dermatitis patients could offer improvement of disease severity but the recommended dose and duration of administration cannot be concluded yet.

Keywords: atopic dermatitis, children, efficacy, vitamin D, human & health

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Introduction

Atopic Dermatitis (AD~~DA~~) is now ~~is~~ considered a complex multifactorial disease that includes defects in skin barrier structures, immune dysregulation, genetic susceptibility, and changes in skin flora which mostly occur in infancy and childhood. Based on the clinical features, AD~~DA~~ can be divided into 3 forms, namely AD in infants (2 months-2 years), children (2–12 years), and adolescents (over 12 years) [1]. Increasing prevalence of AD has been reported in areas including the Asia-~~-~~Pacific region, where it is ~~had been~~ reported that 88% of children with AD have either mild or moderate and 12% have severe AD. H~~h~~owever, Indonesia still has a lower prevalence in children between 6-7 years old when compared to

Thailand and Malaysia, ~~in children between 6-7 years old~~ and a lower prevalence in children aged 13-14 years when compared to Pakistan [2].

In addition to the reduction of skin inflammation, recently, AD treatment has focused more on the regulation of the immune response and enhancing the barrier function of the skin. [3]. Poor compliance with the use of topical drugs makes some researchers try to find other drugs that are not only safe, cheap, easy to use but also effective. Several recent studies have shown that vitamin D supplementation may be an option ~~choice~~, although the results of intervention trials are still conflicting [4].

In AD patients, defects in the skin barrier structure, as well as decreased functional integrity and reduced ability to regenerate have roles in inducing immune responses and specific inflammatory reactions [5]. In acute lesions, there will be a decrease in AMP (Antimicrobial Peptide) ~~-~~production, an increase in *S. aureus* colonization, and an effect on the severity of the disease and reduce the risk of infection. Vitamin D can increase barrier function, induce AMP and enhance monocyte and macrophage cell function [6]. Vitamin D has been known to have some effects on the innate and adaptive immune systems. Several mechanisms can modulate the progression of AD lesions, ~~through several mechanisms~~ such as increasing epidermal differentiation, increasing production of cathelicidin, decreasing Th2 cytokines, decreasing Ig E production, decreasing B cell proliferation, and upregulating of T cells [7].~~] an~~

A previous systematic review ~~-~~and meta-analysis in 2019 on vitamin D and AD had ~~been~~ reported a highly statistically significant reduction in SCORAD (Scoring of Atopic Dermatitis) on intervention with vitamin D, in the paediatric and adult population [8]. While a systematic review published by Huang on the paediatric AD population in 2018 concluded that 67% of the collected studies reported a significant improvement in AD severity with vitamin D supplementation, but this systematic review did not include a meta-analysis [9]. We conducted a meta-analysis with research published in last 10 years because there has been an increase in publications regarding vitamin D supplementation during this time [10].

~~Our study aimed~~We performed a systematic review and meta-analysis to provide an updated review of the interventional study of vitamin D in the paediatric AD population to investigate clinical outcomes from measuring scales.~~, especially in the last 10 years because in the last 10 years there has been an increase in publications regarding vitamin D supplementation during this time [5] [6] and [7].~~

Methods

Search p~~P~~rocedures

We conducted a systematic search of the literature on several databases, namely PubMed, Cochrane Library, ProQuest, and a clinical trial website, ClinicalTrials with keywords showed in T~~t~~able 1. We also did manual hand searching on Google Scholar and searched for ~~kinds of~~ grey literature on the repository (January 1st 2010 to October 31st 2020, last searched was 2nd November 2020). The search procedure was based on Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA). This search of titles and abstracts was limited to articles that were human-focused and published in English and

Bahasa Indonesia. Statistical analysis was carried out with Review Manager **(RevMan, Cochrane, London, UK) version 5.4.1** with standardized mean difference and risk ratio as a measure of the effect of therapy.

In studies that include children and adults as participants, we contacted the author to obtained separate data that contained child ren subjects only. The ethical clearance of this study has been published from the Ethical Committee of Dr. Soetomo General Academic Hospital Surabaya number 0206/LOE/301.4.2/XI/2020. We did not register the protocol.

Table 1. Database search strategy

Database	Keywords
Cochrane Library	eczema OR atopic in Title Abstract Keyword AND therap* OR treatment in Title Abstract Keyword AND vitamin D in Title Abstract AND children OR child OR paediatrics OR paediatrics AND Clinical trials AND SCORAD
PubMed	(((((eczema [MeSH Terms]) OR eczema [Title/Abstract]) OR dermatitis[Title/Abstract]))) AND ((Vitamin D [MeSH Terms]) OR Vitamin D [Title/Abstract])) AND (((treatment [Title/Abstract]) OR therap* [Title/Abstract]) OR therapeutics [MeSH Terms])
ProQuest	(ti(eczema* OR dermatitis OR atop*) OR ab(eczema* OR dermatitis OR atop*)) AND ti (children OR paediatrics OR pediatri) OR ab(children OR paediatrics OR pediatri) AND ti (therapy OR treatment) AND(ti(vitamin D) OR ab(vitamin D)).
www.clinicaltrials.gov	*vitamin D* AND *Interventional Studies* AND *Atopic Dermatitis* AND *SCORAD* AND *Child*

Eligibility cCriteria for iInclusion and eExclusion

Intervention studies including Randomized Control Trials and Prospective Cohort studies with clinical outcomes measured on a scale in both groups, before and after the intervention were assessed. . Inclusion criteria were as follows: (1) studies with aAge group 0-18 years old and diagnosed as mild, moderate, or severe aAtopic dDermatitis in both females and males;. (2) NThere was no limit restriction to the duration of intervention, type of vitamin D, doses used, frequency and route of administration, and clinical outcome measuring scale: SCORAD, EASI (Eczema Area and Severity Index), IGA (Investigator Global Assessment). (3) studies that provided complete data for clinical outcomes. with SCORAD, EASI, or another scale were also calculated in each study. Exclusion criteria were articles that did not provide full text.

Outcomes of the study

1. Evaluating the outcome of the disease (changes in SCORAD or EASI) in the Vitamin D supplementation groups compared to placebo groups.
2.
3. Calculating the clinical importance of both groups so that the CER (Control Event Rate), EER (Experimental Event Rate) and NNT (Number Needed to Threat) values can be obtained.

Data eExtraction and qQuality aAnalysis

This analysis included all articles that qualified for selection criteria. Two author, ANH and S extracted data from each included study including author, country, publication year, study population, AD severity, supplementation dose, frequency, route of administration, duration and outcome scale. The clinical outcome was measured by scale: SCORAD, EASI or IGA. We defined the clinical outcomes as follows:

(1) SCORAD: A clinical measurement tool used to calculate the severity of Atopic Dermatitis patients. The lesion area was calculated based on the rule of nine with a value of 0-100. Intensity was measured in a representative area by looking at the form of skin abnormalities that were erythema, edema, oozing or crusts, excoriations, lichenification, and dry skin, and each was assigned a value of 0 if there was no lesion, 1 if the lesion was mild, and 2 if the lesion was moderate and 3 if the lesion was severe, then the scores were summed to get B (0-18). Subjective symptoms were measured by Visual Analog Scale (VAS), calculated on average for every 3 night whether there were symptoms of itching and sleep disturbances, with a score of 0 if there was no itching or sleep disturbances, and 10 for the most severe itching or sleep disturbances. These numbers are summed to give C (0-20). The results of the three parameters were submitted into the formula A5+7B/2+C, then grouped into mild AD (<25), moderate AD(25-50) and severe AD(>50) categories [11].

(2) EASI: an instrument used by examiners (doctors, dermatologists) to quantify lesion progression and severity of AD patients, by assessing the extent of the disease at four body sites (head/neck, trunk including genitalia, superior and inferior extremities) and measures four clinical signs: (1) erythema, (2) induration/papulation, (3)excoriation, and (4) lichenification each on a scale of 0 to 3. The score can then be divided into 0 (clean), 0.1-1.0 (nearly clean), 1.1-7 (mild), 7.1-21 (moderate), 21.1-50 (severe), 50 ,1-72.0 (very severe). EASI confers a maximum score of 72 [11].

(3) IGA: an instrument used to assess overall disease severity at one given time point, and it consists of a 6-point severity scale from clear to very severe disease (0 = clear, 1 = almost clear, 2 = mild disease,3 = moderate disease, 4 = severe disease and 5 = very severe disease). IGA uses clinical characteristics of erythema, infiltration, papulation, oozing and crusting as guidelines for the overall severity assessment [12].

The quality of each study was assessed by three authors (ANH, S and DWS) independently by using the RCT (Randomized Control Trial) worksheet. Another author resolved any disagreement between them (CRSP, DMI, and D). Quality analysis of the interventional studies had showed three studies scoring randomized double-blind clinical trials with adequate randomization and blinding. These were [13] [14] and [15]. The other study, Earlia did not mention randomization but confirmed the blinding of both participants and researchers [16].

The risk of bias in RCT studies was assessed with The Cochrane Collaboration's tool for assessing risk of bias [17] by ANH, S and DWS, then we discussed the outcome until we were in agreement.~~to agree.~~ The assessment results were categorized as “yes” for low-risk bias, “unclear”, and “no” for high-risk bias (table 5). Cohort studies was assessed with

Newcastle-Ottawa Scale (NOS) [18] and comprised several items including: comparability of the groups (2 points), and ascertainment of exposure (3 points). Each study was interpreted to be low quality (scores <4), moderate quality (scores of 5–6), or high quality (scores ≥7) that was shown in table 4.

Table 2. Critical appraisal of included interventional studies in systematic review using RCT Worksheet

		Camargo, 2014 [14]	**Galli, 2015 [19]**	**Lara-Corrales, 2018 [13]**	**Sanchez-Armendariz, 2018 [15]**	**Earlia, 2020 [16]**	**Mansour, 2020 [20]**
Recruitment	*Randomization*	*Yes*	*Unclear*	*Yes*	*Yes*	*Unclear*	*Yes*
	Similarity	*Yes*	*Yes*	*Yes*	*Yes*	*Yes*	*Yes*
Allocation	*Treated equally*	*Yes*	*Yes*	*Yes*	*Yes*	*Yes*	*Yes*
	Minimum loss to follow up	*Yes*	*Yes*	*Yes*	*Yes*	*Yes*	*Yes*
Measurement Blinding Outcome		*Yes*	*Yes*	*Yes*	*Yes*	*Yes*	*Yes*
Importance	*Clinical*	+	-	-	+	+	-
	Statistical	*p=0,04*	*P =0,5*	*p=0,07*	*p=0,02*	*P<0,001*	*p= 0,039*
Applicability		*Yes*	*Yes*	*Yes*	*Yes*	*Yes*	*Yes*

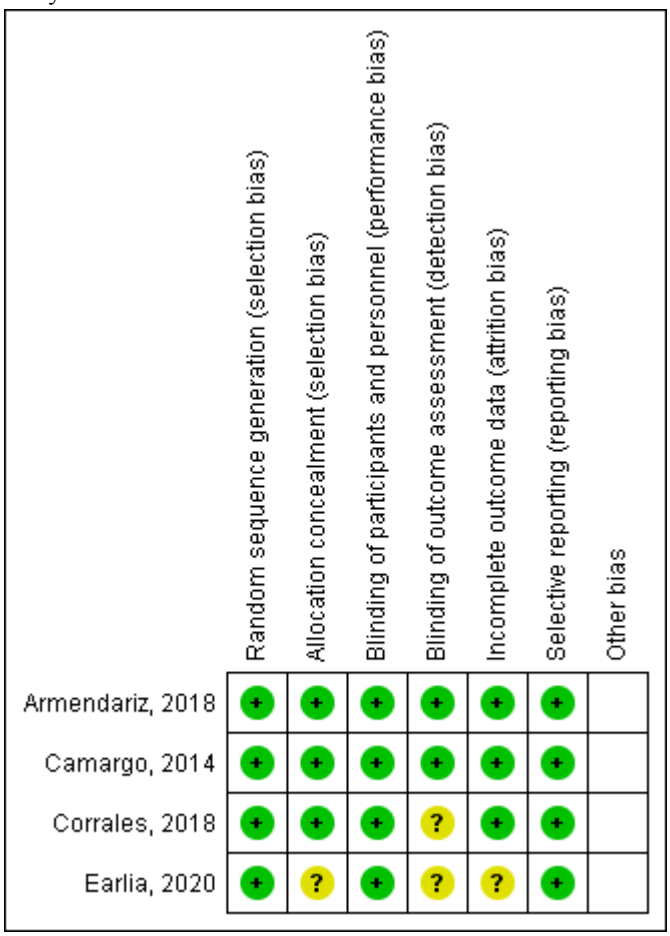
Table 3. Critical appraisal of included cohort studies in systematic review

	Filippo, 2015 [21]	**Raj 2020 [22]**
Representative of the population	*Yes*	*Yes*
Methods for exposure objective and consistent	*Yes*	*Yes*
Subjects / outcome accessor blinded	*Unclear*	*Unclear*
Sufficiency of follow up	*Unclear*	*Yes*
Overcoming confounding factor	*Yes*	*No*
Importance	*Yes*	*Yes*
Applicability	*Yes*	*Yes*

Table 4. Quality analysis of included studies using Newcastle Ottawa Quality Assessment Form for Cohort Studies.

Study	*Criterion Score*		
	Selection	*Comparability*	*Exposure*
Filippo, 2015 [21]	★★★	★★	★★
Raj, 2020 [22]	★★★	★★	★★

Table 5: Risk of bias summary: review authors' judgements about each risk of bias item for each included study.



Statistical aAnalysis

We performed the data with Review Manager (RevMan, Cochrane, London, UK) version 5.4.1. Three authors, DWS, IC, and SA conducted statistical analysis and presented the result in a forest plot and funnel plot. Statistical analysis Itwas done by calculating the standardized mean differences (SMDs), with 95% CIs, of *pre*- and *post*-intervention in both groups, also and the standard deviation of each study, and was also calculating risk ratio (RR), with 95% CIs, by counting the number of event in each group with a dichotomy table (table 6). Significance of RRs was determined using the Z test ($p<0.05$ was considered statistically significant). We assessed the heterogeneity among the studies using I^2 (considered heterogeneity existed if $I^2 > 25\%$), then Random Effect Model was adopted. For publication bias, we used funnel plot and it can be seen that the four studies are distributed symmetrically, that is, the distribution of research is balanced on the left and right of the

centre line boundary. This means that there is no potential for publication bias regarding the conclusions.
(https://doi.org/10.6084/m9.figshare.19091474.v1)

Table 6. ~~:~~ Dichotomy table of studies that provide every subject's outcome that measured in a scale, before and after supplementation in both groups.

	Vitamin D			Placebo		
	Not cure	Cure	Total	Not cure	Cure	Total
Camargo, 2014 [14]	25	32	57	27	20	47
Sanchez-Armendariz, 2018 [15]	3	16	19	6	18	24
Earlia, 2020 [16]	2	13	15	15	0	15

Results

570 articles were initially retrieved, and the results of the evaluation of duplicate articles by title showed 157 articles with similar titles and were subsequently excluded from this study. The next evaluation was carried out by reviewing the title of each piece of literature that had been searched based on keywords, ~~,~~ T~~t~~here was 11 literature by excluding 402 literature that was irrelevant with the study design. We did further evaluation of 11 kinds of literature based on eligibility criteria, critical appraisal, and quality assessment, and excluded two articles with subject included aged > 18 years old and one article with non-AD subjects as a comparison group. Qualitative synthesis then resulted two studies that could not be included in the meta-analysis due the fact that~~to~~ no standard deviation was reported [19] and [20]. A further~~,~~ two studies were also excluded due to the study design which was single~~one~~-arm cohort [21] and [22] so that the final results were four articles which were~~ill~~ then ~~be~~analysed in this study.

Four articles were included in meta-analysis, as described in F~~f~~igure 1. The years of publication for all studies were ranging from January 2010 to October 2020**.** Three studies were conducted with paediatric participants only [13] [14] and [16] and one study was conducted with adult and paediatric participants [15]. There were different doses and durations in supplementing vitamin D among studies. One study reported that vitamin D supplementation did not significantly improve the severity of the disease [13], but ~~another~~ the other three studies reported otherwise. This study only included AD participants with deficiency or insufficiency status of serum vitamin D. We summarized all studies including

population, sample size, intervention, and mean difference outcome of both groups (Vitamin D and placebo groups)**.** All outcomes listed as positive ($p<0.05$) or negative ($p>0.05$) are~~that was~~ shown~~ed~~ in T~~t~~able 8.

Table 7. Characteristics and outcome of included studies

Author	Country	Dose, frequency and duration	Study Design	Mean age (years)	Outcome scale	AD Severity	Supplementation Giving method	Study population	Result
Camargo *et al., 2014* [14]	Mongolia	Vitamin D_3 1000 IU/ day for 1 month	*RCT*	9	EASI	Mild, moderate, severe	orally	Paediatric patients with winter-associated AD, EASI between 10-72, based on randomization with a random number generator.	Vitamin D supplementation showed clinical improvement
Lara-Corrales *et al., 2018* [13]	Canada	Vitamin D 2000 IU/ day for 3 months	*RCT*	7.4	SCORAD	Mild, moderate, severe	orally	Paediatric patients with AD, with vitamin D deficiency or insufficiency status	Vitamin D supplementation did not significantly improve severity
Sanchez-Armendariz *et al., 2018* [15]	Mexico	Vitamin D_3 5000 IU/ day for 3 months	*RCT*	12.6	SCORAD	Mild, moderate, severe	orally	Paediatric and adult patients with AD according to the criteria of Hanifin Rajka, which were randomized (simple randomization) with a software.	Vitamin D3 can be considered as adjuvant therapy in AD
Earlia *et al., 2020* [16]	Indonesia	Vitamin D 600 IU / day for 1 month	*RCT*	5	SCORAD	Mild, moderate, severe	orally	Paediatric patients with AD who seek for treatment at the Dermatology Clinic for a certain period	Vitamin D supplementation for 1 month was more effective in reducing the severity of AD in children than standard therapy.

Table 8. Summary of the included studies

Author	n- (experimental group)	n- (control group)	Mean difference of intervention group (pre and post Vitamin D supplementation) ; standard deviation	Mean difference of intervention group (pre and post placebo supplementation) ; standard deviation	Duration	*p value*	Other outcomes	Adverse effect
Camargo *et al., 2014* [14]	57	47	-6,5 (8,8)	-3,3 (7,6)	1 month	0,04	IGA Score in the experimental group was smaller than the placebo group	None
Lara-Corrales *et al., 2018* [13]	21	24	-15,35 (9,71)	-15,13 (8,97)	3 months	0,07	Patients with severe AD have low 25(OH)D levels	None
Sanchez-Armendariz *et al., 2018* [15]	19	24	-22,84 (11,43)	-13,45 (11,04)	3 months	0,02	Serum vitamin D levels in all experimental groups reached >30ng/ml at the end of the study.	Not reported
Earlia *et al., 2020* [16]	15	15	-16 (6,64)	-3,31 (2,47)	1 month	<0,001	None	Not reported

Note: n, Number of subject; IGA, Investigator Global Assessment; AD, Atopic Dermatitis; 25(OH)D, 25-hydroxy vitamin D

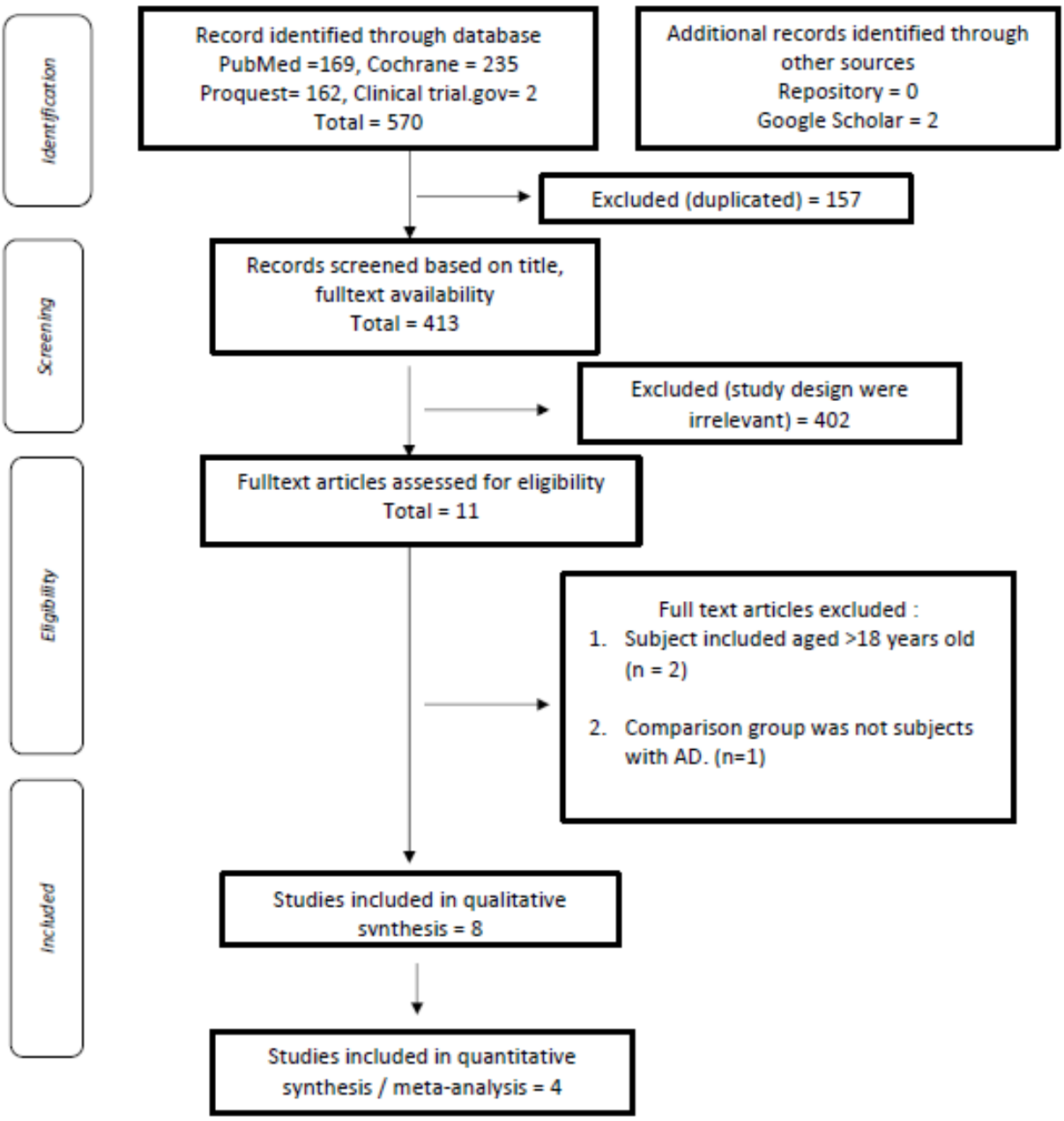


Figure 1. PRISMA flow diagram to show results of the search process and inclusions/exclusion

Effect of vVitamin D sSupplementation in pPaediatric AD pPatients

Four randomized controlled trials assessed the efficacy of vitamin D supplementation. The characteristics of the included studies are summarized in Table 7. Three studies measured the SCORAD indexes, whereas only one of the included studies assessed the efficacy of vitamin D supplementation by using EASI. One study used both adults and children as a participant, so that we contacted the author and to obtain the used separated data associated with only forthe children only. A meta-analysis of four trials showed that the SCORAD index and EASI score decreased significantly after vitamin D supplementation (standardized mean difference = -0.93, 95% CI = -1.76 to -0.11). We observed statistical heterogeneity among the studies (I^2 > 25%; Figure 2). We also assessed the potency of the publication bias in those included studies with funnel plot and the result was symmetrical indicated that there was no potency of the publication bias in the four included studies.

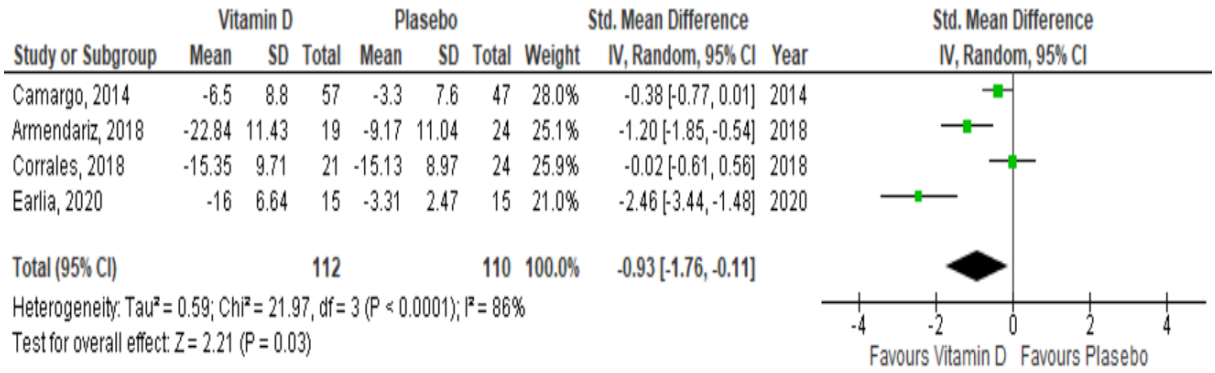


Figure 2. Forest plot for meta-analysis of role of Vitamin D supplementation in ~~AD~~ Atopic Dermatitis severity.

Risk ratio of vVitamin D sSupplementation gGroup

We used three studies that provide raw data so that the risk ratio of those studies could be measured. The forest plot showed that statistically, there was no difference risk ratio between vitamin D group and placebo group (risk ratio = -0.93, 95% CI = 1.46 to 2.97). We observed statistical heterogeneity among the studies (I^2 > 25%; Figure 3) so Random Effect Model was adopted.

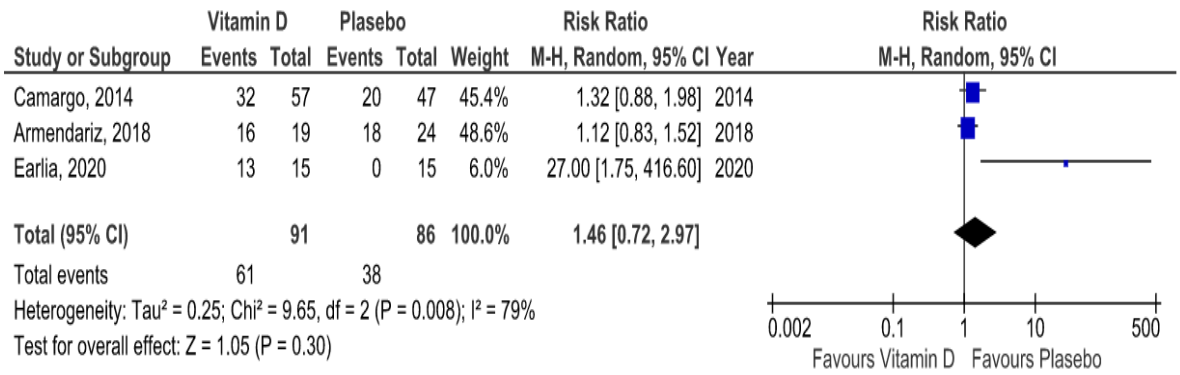


Figure 3. Forest plot for meta-analysis of role of Vitamin D supplementation in resulting risk ratio.

Discussion

Vitamin D can modulate the innate immune system and also increases the phagocytic ability of immune cells and strengthens the barrier function of epithelial cells [6].
An *in vitro* study reported that cathelicidin and defensin (which are antimicrobial-like peptides) increased after vitamin D supplementation [23]. Another clinical trial also demonstrated that cathelicidin production could be increased and LL-37 expression could be induced by vitamin D supplementation. Thus, vitamin D could increase antimicrobial activity and external tolerability against pathogens [24].

Vitamin D stimulates the production and regulation of skin antimicrobial peptides, such as cathelicidins which exert direct antimicrobial activity and induce host cellular responses to produce cytokine release, inflammation, and angiogenesis, thus, based on the above theory, vitamin D deficiency may predispose to secondary infection in AD patients [25]. This is following what was reported by Haridas, Udompataikul *et al*. who found a reduction in *S. aureus* colonization in a paediatric population, as well as Rahmawati *et al*, who have reported that there was a significant difference in the reduction of *S. aureus* colonization after vitamin D3 supplementation in children with AD [26] and [27].

This theory is following the results of the meta-analysis of our forest plot. Our findings showed a statistically significant difference between the vitamin D supplementation group and the placebo group. In our study, we found high heterogeneity and we assumed that it was caused by variation of the doses and duration. The meta-analysis published by Kim in 2016 [28] reported the same results but for the paediatric and adult population, as well as the meta-analysis reported by Haridas in 2018. To our knowledge, our study is the first one that reported vitamin D supplementation efficacy only in children population with AD as the meta-analysis.

The outcome of cure rate is one of the relative risks, wherein this study the relative risk calculated is the comparison of the probability of recovered participant between vitamin D and placebo. In the forest plot with relative risk output, three squares were obtained, each represented 3 studies, with a weight of 45.4%; 48.6%, and 6%. All of these studies have heterogeneity above 50% and p-value <0.05 so that the forest plot used the Random Effect Model as seen from the heterogeneity test results and with the *eyeball test*. Diamond, the result of all studies is on the left side, with a pooled result of 1.46 (CI between 0.72 to 2.97) and touched the vertical line, which means that statistically, there was no difference in cure rate in the vitamin D group and the placebo group. Previously, there were no published meta-analysis with a forest plot with relative risk outcomes so to our knowledge, our finding is the first meta-analysis with the relative risk outcome, by point of interest “cure rate” in the experimental group compared to placebo.

In this study, the clinical significance could only be calculated from 3 studies that provided data on the proportion of subjects who recovered and did not recover or had persistent symptoms from the start of the study to the end. As a determination of the criteria for recovery, we had referred to a journal that mentioned MCID (Minimal Clinically Important Difference) in AD, MCID could be described as a clinical improvement that

significantly along with reduction of SCORAD of 9 points and EASI by 6 points and IGA score reduced by 1 point [29]. From the Ttable 5, it can be calculated that the CER or incidence in the control group (placebo) was 38/86, which is 44%, means that 44% of cases were cured in the group of subjects who were given placebo and EER or the incidence in the experimental group was 61/91, which is equal to 67%, which means that 67% of cases of cure were found in the vitamin D group. Absolute risk reduction or absolute risk reduction in both groups was enabled by reducing CER and EER by 23%, and NNT (number needed to treat) was the amount subjects who must be treated at one time to prevent 1 adverse outcome. In these studies, NNT = 4.34 or required 5 subjects to be treated to prevent 1 unwanted event.

If toxicity occurs, there will be an increase in 25(OH)D levels which can trigger hypercalcemia by increasing calcium absorption and bone resorption. Hypercalcemia can lead to hypercalciuria, and persistently elevated calcium levels can lead to polyuria and dehydration [30]. Vitamin D toxicity is caused by hypercalcemia, which is described by the appearance of symptoms in several organs that can be involved, such as the central nervous system (lethargy, apathy, depression to coma), heart and blood vessels (hypertension, heart rhythm disturbances), gastrointestinal (vomiting), recurrent abdominal pain, anorexia, constipation, and weight loss), and kidney (hypercalciuria is an early symptom, polyuria, polydipsia, nephrocalcinosis, up to life-threatening symptoms such as dehydration and kidney failure requiring haemodialysis) [31]. The diagnosis of vitamin D toxicity was established based on a detailed examination and history of taking medication, as well as supporting examinations. Laboratory tests show suppression of parathyroid hormone, which results in increased levels of 1,25(OH)2D [32].

Limitations: dose and duration among studies are not similar, and not all studies have observed vitamin D levels before and after supplementation so it has not been seen whether there is an increase in vitamin D levels that exceeds the limit, which could potentially cause signs of vitamin D toxicity in several organs.

The limitation of our study were that we did not perform sub-group analysis outcome according to the measuring scale and the severity of AD due to the limitations of the studies included, so that the result of our study should be used carefully.

Suggestion: Further trials with vitamin D3 with the same dose and duration, followed by observation of serum vitamin D levels as an evaluation of the occurrence of side effects.

Conclusion

Our study had showed that statistically, vitamin D supplementation can improve the outcome of atopic dermatitis in children as assessed by SCORAD, EASI or IGA Score and clinically, vitamin D supplementation can increase the cure rate in AD patients. Observation of side effects and monitoring of 25(OH)D levels in AD patients are required as the toxicity can lead into morbidity. The recommendation of the proper dose of Vitamin D supplementation cannot be determined yet because there were no studies with the same dose and duration of administration of the vitamin D supplementation.

Data availability

Underlying data

Figshare: Data for Efficacy of Vitamin D Supplementation on the Severity of Atopic Dermatitis in Children: Systematic Review and Meta-Analysis. https://doi.org/10.6084/m9.figshare.19091474.v1

~~https://doi.org/10.6084/m9.figshare.17104547.~~

This project contains the following underlying data:

- Data untuk forest plot.xlsx

Extended data

Figshare: Data for Efficacy of Vitamin D Supplementation on the Severity of Atopic Dermatitis in Children: Systematic Review and Meta-Analysis.

https://doi.org/10.6084/m9.figshare.19091474.v1

This project contains the following extended data:

- Cochrane, Pubmed and ProQuest search strategies (in JPEG format).

Reporting g~~G~~uidelines

Figshare: PRISMA checklist for Efficacy of vitamin D supplementation on the severity of atopic dermatitis in children: A systematic review and meta-analysis.

https://doi.org/10.6084/m9.figshare.19091474.v1

~~Data for Efficacy of Vitamin D Supplementation on the Severity of Atopic Dermatitis in Children_Systematic Review and Meta-Analysis. https://doi.org/10.6084/m9.figshare.17104547. This project contains the following reporting guidelines: PRISMA checklist for Efficacy of Vitamin D Supplementation on the Severity of Atopic Dermatitis in Children_Systematic Review and Meta-Analysis.~~

Competing interests

No competing interests were disclosed.

Grant information

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Author contributions

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