PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

ARTICLE DETAILS

Title (Provisional)

Temporal changes in the burden of leukaemia and lymphoma in the Australasia and Oceania regions, 2010-2019: an analysis of the Global Burden of Disease Study 2019

Authors

Ho, Thi Quynh Anh; Lee, Peter; Gao, Lan

VERSION 1 - REVIEW

Reviewer	**1**
Name	**Bizuayehu, Habtamu**
Affiliation	**The University of Newcastle**
Date	**29-Apr-2024**
COI	**None**

Thank you for the opportunity to review the article “Temporal changes in the burden of leukaemia and lymphoma in the Australasia and Oceania regions, 2010-2019: an analysis of the Global Burden of Disease Study 2019". It was an honour to contribute my expertise to the peer review process and to engage with the innovative research presented in the manuscript. I have included some suggestions and comments below, and I believe they would improve the quality of the paper.

1. The study gap is not clear; has the topic not been addressed so far, and how could this study add to the existing knowledge should be addressed.

2. Case definition (page 5, lines 39-52): it might be good to define how the outcomes were measured and identified specific to this study e.g. the ICD-10 code used or other options of outcome measure (details could be linked by creating appendix material).

3. Discussion (paragraph 2, line 24-6): "age-specific leukaemia/lymphoma burden generally increased with increasing age." Did this result confound, and also would the analysis approach (linear regression appropriate) have given the outcomes are age-dependent (peak at young and

old age, as you have also noted in the discussion section)? I would suggest a sensitivity analysis for peak ages to check the generalisability of the study.

4. I suggest cutting the discussion a bit (longer) by focusing on pertinent outcomes and reducing the repetition of the result, i.e. already presented in the results section. This could include the areas that cause the difference in outcomes across countries. It is also good to include content about the strategies to prevent the disease.

5. Data quality variations (data source for outcomes and how they are measured, including cancer registries) between included countries should be discussed as a study limitation.

6. I am sure you are aware of the new data release on progress by GBD (it is not yet public, though). Hence, it is good to highlight the age of the data and its implications somewhere.

7. Did the author team have a cancer researcher if not, I would suggest including at least one to provide more insight and add value to the paper

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Reviewer	**2**
Name	**Godoy-Casasbuenas, Natalia**
Affiliation	**Pontificia Universidad Javeriana**
Date	**03-May-2024**
COI	**None to declare**

Peer Review

Article: "Temporal Changes in the Burden of Leukaemia and Lymphoma in the Australasia and Oceania Regions, 2010-2019: An Analysis of the Global Burden of Disease Study 2019"

Key Message of the Manuscript:

This epidemiological study aims to examine the burden of leukaemias/lymphomas and their temporal trends in Australasia and Oceania from 2010 to 2019. Overall, the manuscript is well-written, addressing the problem and research questions appropriately. The methodology is clearly described, and the statistical analysis appears to be appropriate.

I have some suggestions but no major comments.

Abstract and introduction:

In the abstract and introduction, it would be beneficial for the authors to specify the age groups considered in the analysis. As the disease behavior varies between children and adults, clarifying whether the study includes both age groups or only adults is important. While the

methods section briefly mentions analysis by sex and age group, it lacks clarity on the specific age groups examined. Additionally, in the results section of the abstract, including numerical data (e.g., age-standardized rates of incidence, prevalence, mortality) for different leukaemias and lymphomas would enhance understanding.

Methods:

The authors present key elements of the study design and adequately describe the data source, case definition, population, and outcomes.

Regarding the analysis, the authors derived age-standardized rates (ASRs) to account for age structure's impact on overall population prevalence, incidence, mortality, and DALYs. However, considering the distinct behavior of childhood leukemia/lymphoma compared to adults, it's important to address whether this may influence DALYs and mortality results.

Regarding trend analysis, the description of how the estimated percentage change was calculated is clear. Have you considered conducting a joinpoint regression analysis developed by the National Cancer Institute, which provides EAPC along with graphical representation?

(please refer to:
https://surveillance.cancer.gov/help/joinpoint#:~:text=The%20Joinpoint%20Regression%20Program%20is,in%20trend%20is%20statistically%20significant.)

The sensitivity analysis complements the main analysis and strengthens the findings.

Results:

The results are concise and clear, and the tables are well-presented. Although I was not able to see Figure 1, including graphics to illustrate leukaemias and lymphomas' trend in these regions would enhance visualization, as suggested by joinpoint regression analysis.

Discussion:

The discussion is well-written, and the findings are effectively compared to existing literature. The strengths and limitations section is also well described. For future implications, I suggest conducting age, period, cohort analysis to examine age, period, and birth cohort effects on leukaemia/lymphoma incidence risk in these regions.

VERSION 1 - AUTHOR RESPONSE

Reviewer 1: Dr. Habtamu Bizuayehu, The University of Newcastle

Thank you for the opportunity to review the article “Temporal changes in the burden of leukaemia and lymphoma in the Australasia and Oceania regions, 2010-2019: an analysis of the

Global Burden of Disease Study 2019". It was an honour to contribute my expertise to the peer review process and to engage with the innovative research presented in the manuscript. I have included some suggestions and comments below, and I believe they would improve the quality of the paper.

Reviewer comments	Author responses/revisions
1. The study gap is not clear; has the topic not been addressed so far, and how could this study add to the existing knowledge should be addressed.	**Response** We have clarified the study gap in the Introduction (Pages 5 and 6). **Revision** *"Haematological malignancies, including leukaemias and lymphomas, arise from the uncontrolled proliferation of cells in the lymphatic or circulatory systems. Based on the Global Burden of Disease, Injuries and Risk Factors Study 2019 (GBD 2019), which provides the most comprehensive estimates of global disease and injury burden to date, haematological malignancies contribute to a considerable proportion of the global disease burden attributed to cancer* [1-3]. *Globally, leukaemias and lymphomas contributed to 11·7 million and 8·2 million disability-adjusted life years (DALYs) in 2019,* respectively [2]. *Studies exploring the temporal trend in haematological malignancies across countries using data from the GBD 2019 study have found that over a 30-year period, age-standardised mortality/DALYs have declined, against a background of increasing incident/prevalent burden. However, the distribution of disease burden and temporal trends in leukaemias/lymphomas varies across geographic regions and varying levels of socioeconomic* development [1 2 4 5]. Differences in disease burden across regions of high/low socioeconomic development were largely attributed to social and environmental factors including poverty, educational attainment, and access to health care [1 2 4]. *These large disparities in the health care system highlight the need for population-based epidemiological studies in both high and low- and middle-income countries (LMICs) to inform public health policy and healthcare delivery* planning [1 2 4 5]. Importantly, no studies have systematically explored trends in disease incidence/prevalence or burden of leukaemias/lymphomas for Australasia and Oceania [1 2]. *Epidemiological studies comparing these two Pacific regions are particularly beneficial given the considerable socioeconomic, cultural and ethnic differences between these regions* [3]. *As such, a comparison of*

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	contemporaneous leukaemia/lymphoma trends between Australasia and Oceania may facilitate the understanding of healthcare disparities, the impacts of sociodemographic factors on disease occurrence and outcomes, and the role of healthcare infrastructure in managing these cancers. Moreover, although data on leukaemia and lymphoma burden are often reported in regional cancer registry reports, and also publicly available in the GBD data set, research specifically focusing on trends in haematological malignancies in Australasia and Oceania are scarce [6-9]*. This gap in the literature underscores the importance of region-specific research to better understand these trends and inform policies tailored to these regions. Ultimately, such a study would inform future research, public healthcare planning strategies, and policies aimed at reducing the burden related to leukaemia/lymphoma in Australasia and Oceania – the two regions populated with Indigenous people, closely geographically located but varied sociodemographic factors.* *Hence, this study aims to (1) examine the prevalence, incidence, mortality, and DALYs attributed to leukaemias and lymphomas by sex and age groups and (2) explore the temporal trend in these metrics for leukaemias and lymphomas from 2010 to 2019 in Oceania and Australasia regions using GBD 2019 data."*
2. Case definition (page 5, lines 39-52): it might be good to define how the outcomes were measured and identified specific to this study e.g. the ICD-10 code used or other options of outcome measure (details could be linked by creating appendix material).	**Response** We have since included the ICD-10 codes mapped to the GBD cause list for leukaemias and lymphomas in the appendix A. **Revision** Changes in the manuscript [Page 6 Line 16-17] *"The definition of leukaemias and lymphomas used in the GBD 2019 study has been defined previously using International Clasisication of Diseases (ICD) codes (Appendix A)* [2 3]*", and:* A description of ICD codes in Appendix A: *"The International Classification of Diseases (ICD) definition of leukaemias and lymphomas used in the GBD 2019 study has been defined previously* [2 3]*. ICD codes mapped to the GBD cause list for leukaemia or lymphoma incidence data are as follows: AML (C92.0–C92.02, C92.3–C92.62, C93.0–C93.02, C94.0–C94.02, C94.2–C94.22), ALL (C91.0–C91.02), CML (C92.1–C92.12), CLL*

Reviewer comments	Author responses/revisions
	(C91.1–C91.12), HL (C81–C81.49, C81.7–C81.79, C81.9–C81.99, Z85.71–Z85.72), and NHL (C82–C85.29, C85.7–C86.6, C96–C96.9) [2 3]*. ICD codes mapped to the GBD cause list for leukaemia or lymphoma mortality data are as follows: AML (C92.0, C92.3–C92.6, C93.0, C94.0, C94.2, C94.4–C94.5), ALL (C91.0), CML (C92.1), CLL (C91.1), HL (C81–C81.9), and NHL (C82–C86.6, C96–C96.9)* [2 3]*.*
3. Discussion (paragraph 2, line 24-6): "age-specific leukaemia/lymphoma burden generally increased with increasing age." Did this result confound, and also would the analysis approach (linear regression appropriate) have given the outcomes are age-dependent (peak at young and old age, as you have also noted in the discussion section)? I would suggest a sensitivity analysis for peak ages to check the generalisability of the study.	**Response** We had acknowledged that potential confounders, such as environmental factors, lifestyles, or socioeconomic status) could influence the association between age and cancer burden. To clarify, results pertaining to disease burden for age (Figure 1 and Tables B1 and B2 of Appendix B) are purely exploratory. That is, exploring disease trends over time across age groups, as well as exploring the relationship between age and cancer burden and any potential confounding, is beyond the scope of this present study. We have since re-worded the statement for clarity (Page 11, Line 21-23), and highlighted the need for age-period-cohort effect analyses to explore the impact of age-specific risk-factors on disease trends (Page 11, Line 31-32). Moreover, we have updated Figure 1 to include the distribution of disease burden by age group for 2010 to facilitate the comparison between 2010 and 2019. Lastly, for the reviewers' reference, we have attached an analysis of trends across across five different age groups as part of the re-submission. The results of this trend analysis coincide with findings presented in Figure 1 and Appendix B. That is, upon stratification by age, the observed leukaemia/lymphoma burden was greater for older populations across both regions. **Revision** Page 11, Line 21-23 *"Upon stratification to explore the distribution of age (5-year age group) and sex (male/female) burden, the observed leukaemia/lymphoma burden was greater for older populations and males compared to younger people and females across both regions."*

Reviewer comments	Author responses/revisions
	And Page 11, Line 31-32: *"The greater burden observed in adults and older age groups also highlights the need for age-period-cohort effect analysis to explore the age-specific risk factors and examine the effects of age, time period, and birth cohort on leukaemia/lymphoma incidence and mortality in these regions."*
4. I suggest cutting the discussion a bit (longer) by focusing on pertinent outcomes and reducing the repetition of the result, i.e. already presented in the results section. This could include the areas that cause the difference in outcomes across countries. It is also good to include content about the strategies to prevent the disease.	**Response** We have updated the Discussion accordingly. **Revision** Page 13 (line 7-13): *"To effectively address the ongoing burden of leukaemias/lymphomas, especially among peak age groups and older populations, further research should prioritise exploring trends in disease burden and treatment outcomes across different age groups, with a focus on identifying and addressing the factors contributing to the observed disparities among these groups. Although causes of most leukaemias/lymphomas are unknown, general cancer prevention strategies can target lifestyle factors, such as avoiding tobacco, having a healthy diet, and reducing exposure to hazards such as radiation and toxic chemicals to reduce the risk of leukaemias/lymphomas [1]."*
5. Data quality variations (data source for outcomes and how they are measured, including cancer registries) between included countries should be discussed as a study limitation.	**Response** We have added the data quality variations among included countries as a study limitation (seeDiscussion, page 14, line 7-9). **Revision:** *"Moreover, data variation among the included countries in both regions, such as data quality, accuracy and the degree of missing data, might contribute to the deviation in the estimates, leading to discrepancies between regions [1]."*
6. I am sure you are aware of the new data release on progress by GBD (it is not yet public, though). Hence, it is good to highlight the age	**Response** We are aware of the latest version of GBD data and have acknowledged the age of the current data set as a limitation. **Revision:** Change to the manuscript: [Discussion, Page 13 Line 33-34]

Reviewer comments	Author responses/revisions
of the data and its implications somewhere.	*"First, this study used data from GBD 2019, which does not include data in 2020 and 2021 (which will be included in the updated GBD 2021). As a result, it may not capture the most recent trends in disease burden up to 2021."*
7. Did the author team have a cancer researcher if not, I would suggest including at least one to provide more insight and add value to the paper	**Response** The research team includes Lan Gao, who is a researcher specialising in cancer economics.

Reviewer 2: Dr. Natalia Godoy-Casasbuenas, Pontificia Universidad Javeriana

Key Message of the Manuscript:
This epidemiological study aims to examine the burden of leukaemias/lymphomas and their temporal trends in Australasia and Oceania from 2010 to 2019. Overall, the manuscript is well-written, addressing the problem and research questions appropriately. The methodology is clearly described, and the statistical analysis appears to be appropriate.

I have some suggestions but no major comments.

Reviewer comments	Author responses/revisions
Abstract and introduction: In the abstract and introduction, it would be beneficial for the authors to specify the age groups considered in the analysis. As the disease behavior varies between children and adults, clarifying whether the study includes both age groups or only adults is important. While the methods section briefly mentions analysis by sex and age group, it lacks clarity on the specific age groups examined.	**Response** We have clarified the age groups in the abstract as suggested. **Revision** Abstract [Page 2 Line 9-14] *"Data from the Global Burden of Disease (GBD) 2019 was used to examine the burden of leukaemia/lymphoma key subtypes (acute lymphocytic leukaemia (ALL), acute myeloid leukaemia (AML), chronic lymphocytic leukaemia (CLL), chronic myeloid leukaemia (CML), Hodgkin-lymphoma (HL), and non-Hodgkin lymphoma (NHL)) by sex and 5-year age groups (from <5yrs to 85yrs+), in terms of incidence, prevalence, disability-adjusted-life-years (DALYs), and deaths."*
Additionally, in the results section of the abstract, including numerical data (e.g., age-standardized rates of incidence, prevalence, mortality) for different leukaemias and lymphomas would enhance understanding.	**Response** We have added further results in response to the comment. **Revision** Results: [Page 2 Line 18-30] *"AML and NHL were the leading causes of leukaemia/lymphoma burden in both regions. Age-standardised rates (ASRs) for AML vs NHL in Australasia were: incidence 4.72 vs. 19.06, DALYs 89.01 vs. 161.68, and deaths 4.15 vs. 8.02 per 100 000 population. ASRs for AML vs. NHL in Oceania were: incidence 1.36 vs 1.08, DALYs 49.16 vs 38.3, and deaths 0.94 vs. 0.98 per 100 000 population. From 2010 to 2019, Australasia observed an increasing trend in*

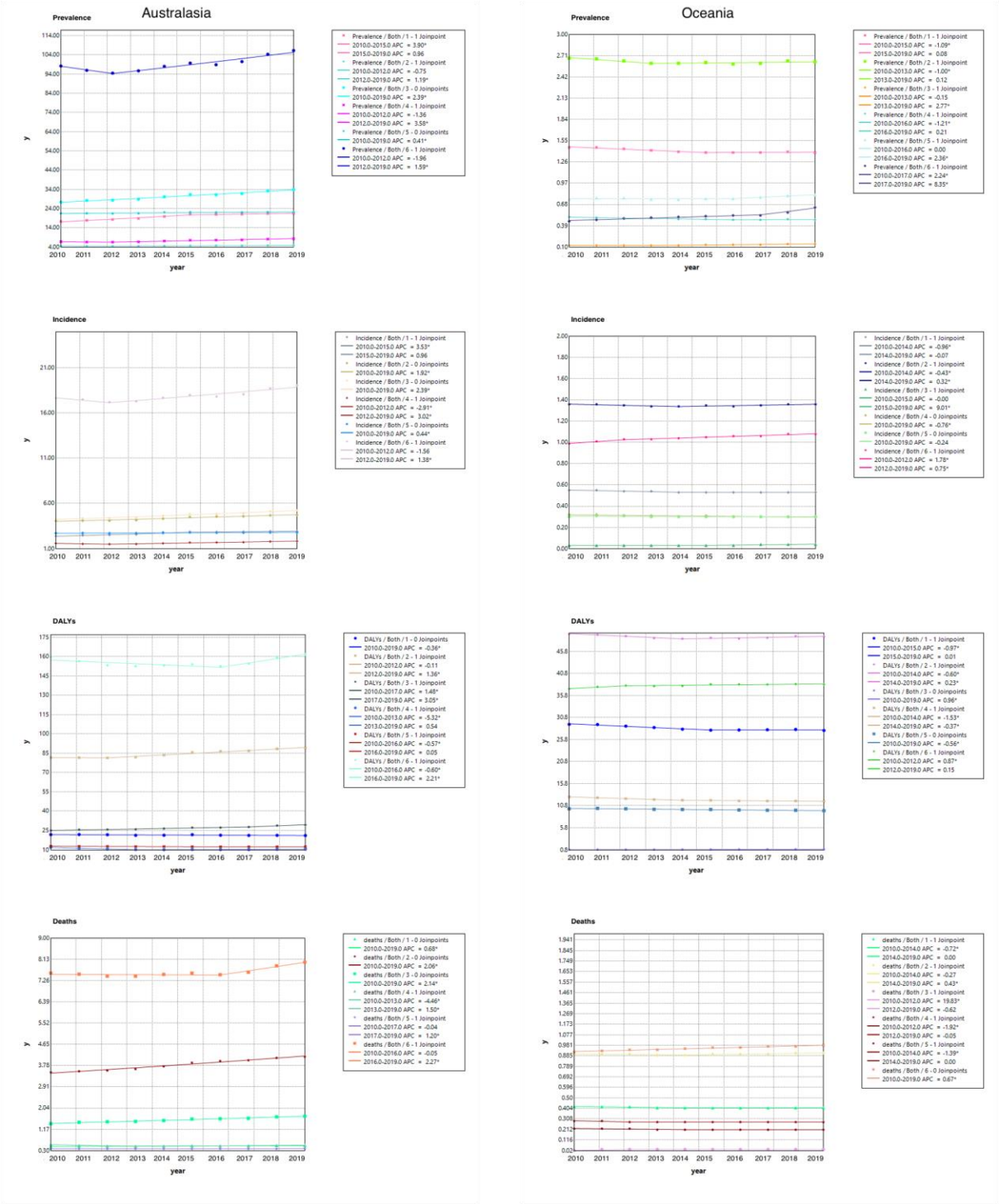
Reviewer comments	Author responses/revisions
	incidence/prevalence/deaths across most leukaemias/lymphomas and increasing/stable trend in DALYs for AML/CLL/NHL, while Oceania observed increasing trends in incidence/prevalence/DALYs for CLL/NHL and stable trends in all outcomes (except for prevalence (stable)) for AML. Contrasting mortality trends for ALL/CML/HL were observed between the two regions (increasing/stable in Australasia and decreasing in Oceania). Statistically significant differences were observed in disease burden trends between sexes, with males experiencing a greater increase (or smaller decrease) in the burden for AML in both regions."
Methods: The authors present key elements of the study design and adequately describe the data source, case definition, population, and outcomes.	**Response** We thank the Reviewer for this positive comment.
Regarding the analysis, the authors derived age-standardized rates (ASRs) to account for age structure's impact on overall population prevalence, incidence, mortality, and DALYs. However, considering the distinct behavior of childhood leukemia/lymphoma compared to adults, it's important to address whether this may influence DALYs and mortality results.	**Response** Age-standardised rates (ASRs) are commonly used to compare disease rates among populations and groups with different age structures. Age-standardised measures are useful in comparing disease burden across populations of different sizes, through adjusting for differences in age distribution (Zhang et al., 2023). However, ASRs have recognised limitations, as they are weighted sums of age-specific rates and may not accurately capture actual rates where behaviors vary across age groups (Thurber et al. 2022) . Aggregating all age groups into a single statistic can lead to less accurate estimates and obscure differences between children and adults. ASRs may also overestimate DALYs and mortality rates in groups with higher rates. As a result, we acknowledge this as a limitation of our study and suggest future research should explore burden trends within specific cohorts, particularly those experiencing the greatest disease burden. For the reviewers' reference, an additional analysis to explore the trend across young children (<5yrs), children and adolescents (5-14 years), young and middle age adults (15-49 years), older adults (50-

Reviewer comments	Author responses/revisions
	74years), and elderly (75yrs+) was performed. As discussed above, the results of this trend analysis coincide with findings presented in Figure 1 and Appendix B. That is, upon stratification by age, the observed leukaemia/lymphoma burden was greater for older populations across both regions. Reference: Thurber KA, Thandrayen J, Maddox R, et al. Reflection on modern methods: statistical, policy and ethical implications of using age-standardized health indicators to quantify inequities. Int J Epidemiol 2022;51(1):324-33. doi: 10.1093/ije/dyab132 Zhang N, Wu J, Wang Q, et al. Global burden of hematologic malignancies and evolution patterns over the past 30 years. Blood Cancer J 2023;13(1):82. doi: 10.1038/s41408-023-00853-3 [published Online First: 20230517] **Revision** [Discussion: Page 14 Line 20-23]: *"Moreover, trends of leukaemia/lymphoma burden were predicted based on a single measure, age-standardised rate, across age groups. This is likely to overlook the differences in trends between children/adolescents and adult population, who might have distinct characteristics and exposures to leukaemias/lymphomas."*
Regarding trend analysis, the description of how the estimated percentage change was calculated is clear. Have you considered conducting a joinpoint regression analysis developed by the National Cancer Institute, which provides EAPC along with	**Response:** We acknowledge that joinpoint regression can be used to explore cancer burden trends and has been utilized in previous cancer research. However, our study focused on a short 10-year period, thus there would be maximum one joinpoint for the data of leukaemia/lymphoma incidence/prevalence/DALy/death rates (see Supplementary material 1). While the joinpoint regression model might provide a more robust prediction of temporal trends, previous research also shows that joinpoint regression could be more effective when there is a significant change in growth rate (e.g., >10%) as noted by Gillis (2019) . Additionally, log-linear regression has been employed in several studies to explore trends

Reviewer comments	Author responses/revisions
graphical representation?	for longer periods, such as Ren et al. (2020) and Yang et al. (2024) investigating trends over 28-30 year period. Given the relatively small changes in trend observed in our study (most EAPC < 3%) and the underlying regression to identify trends in the joinpoint regression can also be a loglinear model, we believe that log-linear regression is also appropriate for such a short timeframe. Nonetheless, we discussed using log-linear regression as a limitation due to its assumption of a linear trend and its potential to overlook any potential changes in trends within the 10-year period. Although joinpoint regression is not our primary method, for the review purposes and to address the reviewer's concern regarding the use of joinpoint regression, we have included additional information about the basic joinpoint regression results based on point estimtes of EAPCs, which visualize the trend over time. Visually, the trend was the same. The most obvious change identified in the joinpoint regression is consistent with what was observed with our current method in Figure 2. Regardless of which method used (either loglinear model or joinpoint regression), our main findings would not change. Having said that, we are happy to run the joinpoint regression properly with 95% confidence intervals. Change in manuscript: [line 18-20 page 14] *"Additionally, our EAPC model was limited to detect constant linear trends during the 10-year period. Future research could consider capturing nonlinear trends during this explored period."* Gillis, D., & Edwards, B. P. M. (2019). The utility of joinpoint regression for estimating population parameters given changes in population structure. *Heliyon*, *5*(11), e02515. https://doi.org/https://doi.org/10.1016/j.heliyon.2019.e02515 Ren, Z.-H., Hu, C.-Y., He, H.-R., Li, Y.-J., & Lyu, J. (2020). Global and regional burdens of oral cancer from 1990 to 2017: Results from the global burden of disease study. *Cancer Communications*, *40*(2-3), 81-92. https://doi.org/https://doi.org/10.1002/cac2.12009

Reviewer comments	Author responses/revisions
	Yang, F., Zhang, B., Lodder, P., & Guo, J. (2024). The burden of acute lymphoid leukemia among adolescents and young adults in the Western Pacific Region: evidence from Global Burden Disease 2019. *Cancer Causes & Control*, *35*(5), 839-848. https://doi.org/10.1007/s10552-023-01843-3
The sensitivity analysis complements the main analysis and strengthens the findings.	**Response** We thank the Reviewer for this comment.
Results: The results are concise and clear, and the tables are well-presented. Although I was not able to see Figure 1, including graphics to illustrate leukaemias and lymphomas' trend in these regions would enhance visualization, as suggested by joinpoint regression analysis.	As discussed above, a log linear model is appropriate for our study to explore trends of cancer burden in a short timeframe with relatively small EAPCs. We have since presented a graphical representation of leukaemia/lymphoma trends (Figure 2). For the reviewer's reference, Supplementary Figure R1 based on joinpoint regression analysis has been provided. Notably, the results from log-linear regression modelling are comparable with results from the joinpoint analysis.
Discussion: The discussion is well-written, and the findings are effectively compared to existing literature. The strengths and limitations section is also well described. For future implications, I suggest conducting age, period, cohort analysis to examine age, period, and birth cohort effects on leukaemia/lymphoma incidence risk in these regions.	**Response** We have added the future implication for age-period-cohort effect analysis in Page 11. **Revision** Change in manuscript: [Page 11 Line 31-32 and Page 12 Line 1-2] *"The greater burden observed in older age groups also highlights the need for age-period-cohort effect analysis to explore the age-specific risk factors and examine the effects of age, time period, and birth cohort on leukaemia/lymphoma incidence and mortality in these regions* [10]*."*

Supplementary figure R1: Trend of disease burden based on ASR in Australasia and Oceania by leukaemia and lymphoma subtypes using a joinpoint model



1: ALL = acute lymphocytic leukaemia; 2: AML = acute myeloid leukaemia; 3: CLL = chronic lymphocytic leukaemia; 4: CML = chronic myeloid leukaemia; 5: HL = Hodgkin lymphoma; 6: NHL = non-Hodgkin lymphoma

Supplemental Table 1

EAPCs and the 95% confidence intervals across leukaemia and lymphoma subtypes in 2010 and 2019 by age groups

Region	Measure	Age					
		<5 years	5-14 years	15-49 years	50-74 years	75+ years	All ages[#]
Australasia	**Incidence**						
	ALL	*-0.48 (-0.89 to -0.06)*	*-1.97 (-2.98 to -0.96)*	*-2.33 (-3.32 to -1.33)*	-1.1 (-3.83 to 1.7)	*-3.97 (-7.31 to -0.51)*	**2.37 (1.96 to 2.78)**
	AML	-0.54 (-1.17 to 0.09)	0.5 (-0.06 to 1.06)	**2.39 (1.87 to 2.91)**	**7.03 (2.81 to 11.43)**	**4.52 (2.32 to 9.27)**	**1.93 (1.69 to 2.17)**
	CLL	0 (0 to 0)	0 (0 to 0)	*-3.54 (-4.65 to -2.43)*	0.35 (-2.62 to 3.41)	-1.1 (-3.43 to 2.32)	**2.4 (2.23 to 2.57)**
	CML	*-0.9 (-1.69 to -0.11)*	*-2.4 (-3.16 to -1.63)*	*-2.28 (-2.95 to -1.6)*	0.09 (-2.93 to 3.21)	*-4.64 (-7.93 to -1.09)*	**2.16 (1.35 to 2.97)**
	HL	*-13.15 (-16.12 to -10.07)*	*-9.09 (-11.17 to -6.95)*	*-3.02 (-4.19 to -1.84)*	1.7 (-1.48 to 4.98)	-1.61 (-5.2 to 2.32)	**0.44 (0.34 to 0.54)**
	NHL	*-7.47 (-9.31 to -5.6)*	*-6.02 (-7.29 to -4.72)*	*-1.36 (-2.15 to -0.56)*	1.82 (-1.3 to 5.04)	-0.06 (-3.32 to 2.69)	**0.95 (0.49 to 1.41)**
	Prevalence						
	ALL	*-0.44 (-0.86 to -0.02)*	*-1.9 (-2.93 to -0.85)*	*-2.71 (-3.51 to -1.92)*	-0.59 (-3.74 to 2.66)	*-4.1 (-7.47 to -0.61)*	**2.57 (2.09 to 3.05)**
	AML	*-5.72 (-6.46 to -4.97)*	*-4.8 (-5.53 to -4.06)*	*-4.04 (-4.92 to -3.14)*	**5.85 (1.82 to 10.04)**	**4.29 (1.89 to 7.27)**	**0.9 (0.66 to 1.13)**
	CLL	0 (0 to 0)	0 (0 to 0)	*-3.47 (-4.47 to -2.46)*	1.15 (-2.5 to 4.93)	-1.15 (-4.58 to 2.3)	**2.4 (2.23 to 2.56)**
	CML	-0.58 (-1.36 to 0.19)	*-1.95 (-2.73 to -1.16)*	*-1.72 (-2.3 to -1.15)*	-3.56 (-7.87 to 0.96)	-2.06 (-5.34 to 0.52)	**2.87 (2.19 to 3.56)**
	HL	*-13.12 (-16.09 to -10.04)*	*-9.06 (-11.15 to -6.93)*	*-2.9 (-4 to -1.78)*	1.94 (-1.31 to 5.3)	-1.21 (-4.62 to 2.31)	**0.4 (0.29 to 0.52)**
	NHL	*-7.48 (-9.32 to -5.6)*	*-6.05 (-7.34 to -4.74)*	*-1.63 (-2.14 to -1.12)*	0.23 (-5.29 to 6.06)	-0.02 (-2.97 to 3.03)	**1.07 (0.52 to 1.63)**
	DALYs						

	ALL	*-1.88 (-2.36 to -1.4)*	*-2.66 (-3.52 to -1.78)*	*-3.63 (-4.31 to -2.95)*	-1.2 (-3.91 to 1.59)	-3.05 (-6.14 to 0.42)	*-0.36 (-0.45 to -0.27)*
	AML	*-1.14 (-1.68 to -0.6)*	0.15 (-0.42 to 0.73)	**1.3 (0.59 to 2.02)**	**7.52 (4.12 to 11.04)**	**4.05 (1.17 to 7.02)**	**1.14 (0.95 to 1.34)**
	CLL	0 (0 to 0)	0 (0 to 0)	*-4.84 (-6 to -3.67)*	-1.39 (-3.59 to 0.87)	0.46 (-1.75 to 1.94)	**1.74 (1.5 to 1.98)**
	CML	*-1.78 (-2.64 to -0.91)*	*-3.37 (-4.07 to -2.67)*	*-3.51 (-4.24 to -2.77)*	-3.08 (-6.32 to 0.27)	*-3.08 (-5.93 to -0.14)*	*-1.22 (-2.39 to -0.04)*
	HL	*-13.17 (-16.14 to -10.1)*	*-9.99 (-12.4 to -7.53)*	*-4.02 (-5.24 to -2.78)*	0.71 (-2.31 to 3.83)	-1.54 (-3.13 to 0.15)	*-0.4 (-0.5 to -0.3)*
	NHL	*-8.71 (-10.48 to -6.91)*	*-7.24 (-8.56 to -5.9)*	*-1.73 (-2.87 to -0.59)*	-4.61 (-10.41 to 1.56)	*-1.08 (-1.62 to -0.55)*	0.18 (-0.39 to 0.75)
	Deaths						
	ALL	*-2.18 (-2.66 to -1.7)*	*-2.7 (-3.55 to -1.84)*	*-3.43 (-4.1 to -2.77)*	-0.89 (-3.56 to 1.87)	-2 (-5.74 to 1.06)	**0.75 (0.61 to 0.88)**
	AML	*-1.1 (-1.64 to -0.56)*	0.28 (-0.22 to 0.79)	**1.68 (0.96 to 2.41)**	**7.28 (2.93 to 11.82)**	**3.66 (0.82 to 6.58)**	**2.07 (1.9 to 2.25)**
	CLL	0 (0 to 0)	0 (0 to 0)	*-4.88 (-6.02 to -3.72)*	-0.29 (-3.15 to 2.65)	-1.05 (-4.35 to 2.26)	**2.11 (1.94 to 2.29)**
	CML	*-1.75 (-2.62 to -0.88)*	*-3.51 (-4.21 to -2.81)*	*-3.28 (-3.87 to -2.69)*	*-2.55 (-4.47 to -0.58)*	-2.71 (-5.56 to 0.23)	-0.27 (-1.35 to 0.83)
	HL	*-13.17 (-16.14 to -10.1)*	*-10.44 (-12.65 to -8.17)*	*-3.82 (-4.9 to -2.72)*	0.84 (-2.19 to 3.98)	-3.28 (-6.69 to 0.26)	0.05 (-0.06 to 0.16)
	NHL	*-8.82 (-10.59 to -7.01)*	*-7.35 (-8.67 to -6.02)*	*-2.09 (-2.94 to -1.23)*	0.9 (-2.54 to 4.47)	*-2.43 (-4.48 to -0.32)*	**0.61 (0.17 to 1.05)**
Oceania							
	Incidence						
	ALL	*-2.03 (-2.41 to -1.65)*	*-1.76 (-3.14 to -0.36)*	-0.99 (-6.9 to 5.3)	*-12.65 (-20.04 to -4.57)*	*-8.09 (-15.85 to -1.58)*	*-0.45 (-0.62 to -0.29)*
	AML	*-0.59 (-0.91 to -0.26)*	-0.95 (-2.27 to 0.39)	3.31 (-3.12 to 10.16)	*-8.35 (-15.87 to -0.16)*	*-8.13 (-15.7 to -1.19)*	-0.02 (-0.17 to 0.14)

	CLL	0 (0 to 0)	0 (0 to 0)	0.43 (-5.63 to 6.88)	*-11.92* *(-18.73 to -4.54)*	-6.57 (-12.32 to 2.87)	**1.38** **(1.19 to 1.57)**
	CML	*-2.68* *(-3.15 to -2.21)*	-0.84 (-2.4 to 0.75)	6.67 (1.92 to 11.64)	*-11.04* *(-18.03 to -3.45)*	*-11.63* *(-18.38 to -4.31)*	*-0.58* *(-0.81 to -0.35)*
	HL	*-1.93* *(-2.51 to -1.35)*	-0.59 (-1.71 to 0.55)	2.67 (-3.53 to 9.27)	*-12.25* *(-19.47 to -4.38)*	*-4.47* *(-7.06 to -3.35)*	-0.05 (-0.18 to 0.07)
	NHL	-0.23 (-0.8 to 0.35)	0.27 (-1.36 to 1.92)	4.59 (-1.43 to 10.98)	*-9.66* *(-16.12 to -2.72)*	*-3.99* *(-7.07 to -1.75)*	**0.92** **(0.79 to 1.06)**
	Prevalence						
	ALL	*-1.41* *(-1.81 to -1.02)*	*-1.71* *(-3.09 to -0.32)*	1.74 (-4.48 to 8.37)	*-8.91* *(-16.49 to -0.64)*	*-3.97* *(-6.1 to -1.88)*	*-0.56* *(-0.74 to -0.37)*
	AML	*-0.5* *(-0.83 to -0.17)*	-0.84 (-2.17 to 0.49)	4.94 (-0.78 to 11)	-6 (-13.71 to 2.39)	*-4.11* *(-4.87 to -3.61)*	*-0.21* *(-0.39 to -0.02)*
	CLL	0 (0 to 0)	0 (0 to 0)	-1.34 (-6.8 to 4.44)	*-11.25* *(-18.43 to -3.43)*	*-9.38* *(-16.56 to -2.23)*	**1.99** **(1.72 to 2.25)**
	CML	*-2.54* *(-3.03 to -2.04)*	-0.46 (-1.97 to 1.09)	7.11 (0.91 to 13.69)	*-9.64* *(-15.32 to -3.57)*	-3.91 (-8.32 to 6.53)	*-0.76* *(-1 to -0.53)*
	HL	*-1.54* *(-2.19 to -0.88)*	0 (-1.07 to 1.08)	3.46 (-2.72 to 10.04)	*-15.37* *(-19.78 to -10.72)*	*-9.59* *(-16.47 to -2.35)*	**0.68** **(0.29 to 1.07)**
	NHL	-0.11 (-0.69 to 0.48)	0.64 (-1 to 2.31)	4.45 (-1.84 to 11.14)	*-13.56* *(-17.51 to -9.41)*	*-8.89* *(-15.76 to -1.45)*	**3.24** **(2.11 to 4.38)**
	DALYs						
	ALL	*-2.32* *(-2.69 to -1.96)*	*-1.78* *(-3.15 to -0.39)*	1.79 (-4.43 to 8.4)	*-12.25* *(-19.15 to -4.78)*	*-11.01* *(-17.16 to -6.54)*	*-0.56* *(-0.71 to -0.41)*
	AML	*-0.6* *(-0.93 to -0.28)*	-0.95 (-2.26 to 0.38)	3.29 (-3.31 to 10.35)	*-10.53* *(-17.53 to -2.95)*	*-8.84* *(-15.81 to -1.29)*	-0.12 (-0.27 to 0.03)
	CLL	0 (0 to 0)	0 (0 to 0)	1.38 (-4.5 to 7.62)	*-13.64* *(-21.74 to -4.69)*	*-16.13* *(-16.94 to -2.76)*	**0.92** **(0.79 to 1.05)**
	CML	*-2.76* *(-3.25 to -2.27)*	-0.87 (-2.4 to 0.69)	5.44 (0.51 to 10.61)	*-11.09* *(-18.07 to -3.53)*	*-11.75* *(-18.53 to -4.4)*	*-0.88* *(-1.1 to -0.66)*
	HL	*-2.64* *(-3.02 to -2.27)*	*-1.59* *(-2.6 to -0.57)*	0.79 (-4.94 to 6.87)	-7.99 (-17.6 to 2.75)	*-11.62* *(-17.18 to -3.54)*	*-0.55* *(-0.66 to -0.45)*

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	NHL	*-1* *(-1.43 to -0.56)*	-0.79 (-2.3 to 0.74)	**3.42** **(-2.96 to 10.22)**	-7.99 (-20.29 to 6.21)	*-7.9* *(-14.46 to -0.83)*	**0.26** **(0.14 to 0.38)**
	Deaths						
	ALL	*-2.32* *(-2.69 to -1.96)*	*-1.8* *(-3.18 to -0.4)*	3.16 (-2.14 to 8.74)	*-12.3* *(-19.18 to -4.83)*	*-8.78* *(-9.66 to -1.35)*	*-0.39* *(-0.53 to -0.24)*
	AML	*-0.6* *(-0.92 to -0.27)*	-0.97 (-2.28 to 0.37)	1.72 (-4.53 to 8.39)	1.21 (-9.2 to 12.81)	-0.45 (-2.21 to 0.82)	0.08 (-0.06 to 0.22)
	CLL	0 (0 to 0)	0 (0 to 0)	1.16 (-5.05 to 7.79)	*-12.93* *(-19.91 to -5.35)*	*-4.22* *(-6.25 to -2.03)*	**0.99** **(0.85 to 1.12)**
	CML	*-2.77* *(-3.26 to -2.28)*	*-1.67* *(-2.34 to -0.99)*	1.83 (-4.05 to 8.07)	*-11.12* *(-18.11 to -3.54)*	*-7.85* *(-9.17 to -5.85)*	*-0.48* *(-0.7 to -0.26)*
	HL	*-2.65* *(-3.02 to -2.28)*	*-1.63* *(-2.64 to -0.6)*	1.42 (-4.14 to 7.31)	*-9.32* *(-15.78 to -2.36)*	*-6.58* *(-7.12 to -3.51)*	*-0.35* *(-0.44 to -0.25)*
	NHL	*-1.01* *(-1.44 to -0.58)*	-0.62 (-1.96 to 0.75)	4.54 (-2.84 to 12.49)	*-10.28* *(-17.3 to -2.67)*	*-3.73* *(-4.39 to -2.7)*	**0.65** **(0.52 to 0.79)**

#: Trends estimated using age-standardised rate; ALL = acute lymphocytic leukaemia; AML = acute myeloid leukaemia; ASR = age-standardised rate; CLL = chronic lymphocytic leukaemia; CML = chronic myeloid leukaemia; DALY = disability-adjusted life year; EAPC = estimated annual percentage change; HL = Hodgkin lymphoma; NHL = non-Hodgkin lymphoma

Italics = decreasing trend; non-Italicised = stable; **Bold = increasing trend**

VERSION 2 - REVIEW

Reviewer	**2**
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COI	

I would like to thank the authors for incorporating the suggested adjustments into the manuscript. The revisions address the comments thoroughly, and I have no further suggestions. The manuscript is now suitable for publication.