

PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Profile and treatment outcomes among young tuberculosis patients aged 15-24 years in Faridabad district of Haryana, India
AUTHORS	Kamble, Bhushan; Malhotra, Sumit

VERSION 1 – REVIEW

REVIEWER	Ejeta, Eyasu Jimma University, Medical Laboratory Sciences
REVIEW RETURNED	14-Feb-2022

GENERAL COMMENTS	<p>I wonder your original work try to present the profile and treatment outcome of TB patients among youth in the Faridabad District of Haryana State in high burden country India.</p> <p>Here below find my recommendations for area need major revision and points need clarity for the readers</p> <p>Areas need major revision</p> <ol style="list-style-type: none"> 1. The title of the manuscript written on hard to locate where the study was done, hence need to include the study state and country in the title of the study. 2. The multivariate analysis needs correction; the multivariate analysis should only include variables what have association on bivariate analysis to control for confounding factors. 3. The discussion part about factors associated with successful treatment outcome deems revision by using related studies done on the different part of the world and its implication for future programme in control and prevention of TB <p>Question for clarity</p> <ol style="list-style-type: none"> 1. What is the difference between the current study and your published work entitled with Profile of pediatric TB patients registered under Faridabad District TB center of Haryana (Indian J Tuberc 2022 Jan;69(1):35-41.) 2. Is your study have large sample size to be generalize? Explain 3. What data are missed due to poor record keeping in the study facilities and how do you managed the missed data?
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REVIEWER	Hoddinott, Graeme Stellenbosch University Faculty of Medicine and Health Sciences, Desmond Tutu TB Centre
REVIEW RETURNED	28-Feb-2022

GENERAL COMMENTS	<p>Well done to the co-authors on presenting these important data. Below some suggested revisions.</p> <p>Major revisions:</p>
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	<p>Line 130 - do you have continuous data on age available? Rather than 15-19- vs 20-24-year-old categories. Socially, many people transition at age 18, not at age 20, meaning 19 and 20-year-olds may be more similar to 21-24-year-olds rather than 15-17-year-olds. If treatment outcomes are generally good for young people, it might be useful to disaggregate as much as possible to identify the sub-groups of young people who have the least good outcomes. E.g., perhaps outcomes are excellent for young people in school, and really good again once they have found their feet as independent adults in their early 20s, but that young people transitioning from their parental home toward independence post school might have only 'average' outcomes. We might be able to see this if the age bands were single years. Further, perhaps this effect is gendered. E.g., perhaps young women typically do not transition (they stay living with their parents until marriage), but young men have to head out into the world and seek work post school. Then a dip in TB outcomes might be pronounced for the young men. All my statements are hypothetical, but worth investigating if the data allows - the overall sample is large. See also lines 148-150.</p> <p>Overall - the manuscript may benefit from some language editing.</p> <p>Minor revisions:</p> <p>Lines 4-6 - Consider dropping this first sentence. There is no reference, and it adds no substantive information to the paragraph not covered by subsequent sentences. The style is also not especially scientific - quite emotive. If you wish to make the point that TB is associated with poverty or socio-economic status, just do that and provide a reference, don't evoke with words like 'malady'.</p> <p>Line 8 - 'developed TB disease' rather than 'fell ill'.</p> <p>Lines 13-14 - This suggests that 'Young People' should therefore be 10-24-years-old, but you have reported on young people as 15-24-years-old. Explain here or in the section on study population.</p> <p>Lines 20-22 - This language is quite blaming of young people. I suggest instead: 'Prevention of onward transmission requires reaching people with TB disease who spend a lot of time untreated and around other people who might acquire TB infection – and young people are both.'</p> <p>Lines 24-31 - Could be shortened.</p> <p>Line 34 - Remove 'It was', rather: 'A secondary analysis ...'</p> <p>Line 46 - reports, not report</p> <p>Lines 51-52 - Font changes?</p> <p>Line 52 - 'every quarter', or 'quarterly' not 'every quarterly'</p> <p>Line 56 - Data 'were', not data 'was', data are plural</p> <p>Line 56 - up 'until', not 'up till'</p> <p>Line 59 - if the age band of 15-24 is already specified earlier, no need to repeat this here</p> <p>Line 60 - 'were', not 'was', see above</p> <p>Line 66 - Remove repetition of this information</p> <p>Lines 67-101 - This seems unnecessary detail and information that will be obvious in the findings section. Suggest significant shortening and only include definitions where these differ from standard practice / WHO guidelines</p> <p>Line 109 - 'Data analysis', no longer a 'plan' after it is implemented</p> <p>Lines 123-125 - are these descriptors (year of registration and TU) relevant to the core analysis?</p> <p>Lines 127-128 - rather '48% of patients were 15-19-years-old and 52% were 20-24-years-old'</p> <p>Table 1 - I do not understand what the p-values here reflect. Suggest removing this column altogether as the point of the table</p>
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	<p>is to describe the sample, not present tests of statistical significance</p> <p>Line 138-140 - suggest instead reporting the % of patients 15-19-years-old and 20-24-years-old who had a past history of TB (i.e., numerator = number 15-19-year-olds with prior TB, denominator = total number of 15-19-year-olds) rather than the proportion of patients with prior TB who were in either age category</p> <p>Lines 142-145 - several grammar and formatting errors</p> <p>Line 147 - rather, ' ... most (93.2%) had successful treatment outcomes ...', leave out the 'of them', and 'outcomes', not 'outcome'</p> <p>Line 148-149 - please report the % with successful treatment outcome for each of these age categories</p> <p>Table 2 - the denominator for the columns in the two age group columns should be the number of 15-19-olds or 20-24-year-olds. What is interesting is the relative cure rate, treatment completion rate etc. by age, not the proportion of people with each outcome by age (as currently reported) - this will always just sum to 100%.</p> <p>Line 164 - 'lower' rather than 'lesser'</p> <p>Lines 217-218 - consider removing the sentence 'The present study ... and policy making', unless you revise it to state what those planning and policy recommendations are this sentence adds nothing.</p> <p>Line 237 - please make the language less informal</p> <p>Line 239 - 'Limitations to extrapolation from the study are because (a) it was a retrospective record review and there had been poor ...' There are a few recent publications on TB and adolescents that the authors may consider including in the discussion, e.g., https://doi.org/10.1542/peds.2020-032490; https://doi.org/10.3390/pathogens10121591; https://doi.org/10.1002/jia2.25671; https://link.springer.com/article/10.1186/1471-2334-11-156; https://doi.org/10.1183/23120541.00308-2020</p>
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VERSION 1 – AUTHOR RESPONSE

Reviewer Number	Original comments of the reviewer	Reply by the author(s)	Changes done on page number and line number
Reviewer 1 Major Revision	The title of the manuscript written on hard to locate where the study was done, hence need to include the study state and country in the title of the study.	We have included state and country name in the title	Page No. 1 Line no.2
	The multivariate analysis needs correction; the multivariate analysis should only include variables what have association on bivariate analysis to control for confounding factors.	We have removed the age variable during multivariable analysis.	Page No.10 Table no.4
	The discussion part about factors associated with successful treatment outcome deems revision by using related studies done on the different part of the world and its implication for	Few studies available on adolescent and youth population have been added in the discussion.	Page No. 13, Lines 215-220

	future programme in control and prevention of TB		
	Overall - the manuscript may benefit from some language editing.	We have done extensive language editing to revise the paper	Page 14, lines 229-239
Reviewer 1 Question for clarity	1. What is the difference between the current study and your published work entitled with Profile of pediatric TB patients registered under Faridabad District TB center of Haryana (Indian J Tuberc 2022 Jan;69(1):35-41.)	Our published article on pediatric TB include data on pediatric age group i.e. 0-14 years as Indian National TB Programme Guideline consider pediatric age group for TB programme as 0-14 years. This age group is not included in the current paper. We have now explained this explicitly in the paper under study population section.	Page 4 lines 72-74.
	2. Is your study have large sample size to be generalize? Explain	We have modified now the limitations section and explicitly mentioned generalizability of the findings would be limited to similar settings in northern part of India.	Page 2, line 26
	3. What data are missed due to poor record keeping in the study facilities and how do you managed the missed data?	We have now included this information and explained in the limitations section of the paper. Some data was missing for variables like weight of TB cases, sputum result at end of treatment, site of extrapulmonary TB, we have included information on the variables where information was available. Data on weight of the TB patient was missing in 4364(83%) patients out of 5257 patients, sputum result at end of intensive phase and continuation phase was	Page 15, lines 245-248

		missing in 817(29.6%) patients out of 2762 pulmonary TB patients. Extra-pulmonary site: out of 2137 extra-pulmonary TB patients, 1846 (86%) patient's site of extra-pulmonary TB was missing. We will publish missing data separately in different paper.	
Reviewer 2 Major Revision	Line 130 - do you have continuous data on age available? Rather than 15-19- vs 20-24-year-old categories. Socially, many people transition at age 18, not at age 20, meaning 19 and 20-year-olds may be more similar to 21-24-year-olds rather than 15-17-year-olds. If treatment outcomes are generally good for young people, it might be useful to disaggregate as much as possible to identify the sub-groups of young people who have the least good outcomes	As per reviewer's suggestion, we have analysed data taking age as continuous variable and presented separately in supplemental material table 2 to study the reviewer's hypothesis. We did not find any major differences except a slight increase in 1% proportion of unfavourable outcomes (failure/default/death/shift to category IV/transfer) in age band 17-22years. We have included this information as part of the paper now, as per suggestion.	Page 8, lines 149-153.
Reviewer 2 Minor Revisions	Lines 4-6 - Consider dropping this first sentence. There is no reference, and it adds no substantive information to the paragraph not covered by subsequent sentences. The style is also not especially scientific - quite emotive. If you wish to make the point that TB is associated with poverty or socio-economic status, just do that and provide a reference, don't evoke with words like 'malady'.	We have dropped the first sentence.	Page No.2 Lines 29-31
	Line 8 - 'developed TB disease' rather than 'fell ill'.	We have modified this in the manuscript	Page No. 2 Line no. 30
	Lines 13-14 - This suggests that 'Young People' should therefore be 10-24-years-old, but you have reported on young people as 15-24-years-old. Explain here or in the section on study population.	We have explained the rationale of inclusion of 15-24 years in view of covering paediatric population in different paper cited now and	Page 4, lines 72-74.

		explained in the manuscript.	
	Lines 20-22 - This language is quite blaming of young people. I suggest instead: 'Prevention of onward transmission requires reaching people with TB disease who spend a lot of time untreated and around other people who might acquire TB infection – and young people are both.'	We have modified this in the manuscript	Page No. 2-3 Lines 42-44
	Lines 24-31 - Could be shortened.	We have incorporated the suggestion	Page No. 3, Line No.45-49
	Line 34 - Remove 'It was', rather: 'A secondary analysis.	We have incorporated the suggestion	Page No. 3 Line No. 52.
	Line 46 - reports, not report	We have incorporated the suggestion	Page No. 3 Line No. 64
	Lines 51-52 - Font changes?	We have incorporated the suggestion	Page No. 4 Line No. 67-70
	Line 52 - 'every quarter', or 'quarterly' not 'every quarterly'	We have incorporated the suggestion	Page No. 4 Line No. 69
	Line 56 - Data 'were', not data 'was', data are plural	We have modified this in the manuscript	Page No. 4 Line No. 75
	Line 56 - up 'until', not 'up till'	We have incorporated the suggestion	Page No. 4 Line No. 75
	Line 59 - if the age band of 15-24 is already specified earlier, no need to repeat this here	We have incorporated this suggestion	Page No. 4 Line No. 78
	Line 60 - 'were', not 'was', see above	We have modified this in the manuscript	Page No. 4 Line No. 80
	Line 66 - Remove repetition of this information	We have incorporated this suggestion	Page no.4
	Lines 67-101 - This seems unnecessary detail and information that will be obvious in the findings section. Suggest significant shortening and only include definitions where these differ from standard practice / WHO guidelines	We have removed standard definitions and kept only operational definitions	Page No. 4&5 Line No. 85-96
	Line 109 - 'Data analysis', no longer a 'plan' after it is implemented	We have incorporated this suggestion	Page No. 5 Line No. 107
	Lines 123-125 - are these descriptors (year of registration and TU) relevant to the core analysis?	These descriptors are not related to core analysis but depict distributions of study participants	

	Lines 127-128 - rather '48% of patients were 15-19-years-old and 52% were 20-24-years-old'	We have incorporated this suggestion	Page No. 6 Lines 123-124
	Table 1 - I do not understand what the p-values here reflect. Suggest removing this column altogether as the point of the table is to describe the sample, not present tests of statistical significance.	We have incorporated this suggestion	Page No. 7 Table 1
	Line 138-140 - suggest instead reporting the % of patients 15-19-years-old and 20-24-years-old who had a past history of TB (i.e., numerator = number 15-19-year-olds with prior TB, denominator = total number of 15-19-year-olds) rather than the proportion of patients with prior TB who were in either age category	We have modified this in the manuscript	Page No. 6 Lines no. 128-131
	Lines 142-145 - several grammar and formatting errors	We have reframed the sentences and corrected the formatting errors.	Page No. 6 Line no. 131-136
	Line 147 - rather, '... most (93.2%) had successful treatment outcomes ...', leave out the 'of them', and 'outcomes', not 'outcome'	We have incorporated this suggestion	Page No. 7-8 Line no. 144-145
	Line 148-149 - please report the % with successful treatment outcome for each of these age categories	We have incorporated this suggestion	Page no. 8, Lines 145-146
	Table 2 - the denominator for the columns in the two age group columns should be the number of 15-19-olds or 20-24-year-olds. What is interesting is the relative cure rate, treatment completion rate etc. by age, not the proportion of people with each outcome by age (as currently reported) - this will always just sum to 100%.	We have made changes in the table 2 to show the relative treatment outcomes rate in both age groups.	Page no.8, 9 Table. No.2
	Line 164 - 'lower' rather than 'lesser'	We have incorporated this suggestion	Page no. 10, Line no. 165
	Lines 217-218 - consider removing the sentence 'The present study ... and policy making', unless you revise it to state what those planning and policy recommendations are this sentence adds nothing.	We have removed this line	Page No. 13
	Line 237 - please make the language less informal	We have incorporated this suggestion	Page No. 14 Line no. 241 & 244.

	Line 239 - 'Limitations to extrapolation from the study are because (a) it was a retrospective record review and there had been poor ...'	We have modified this in the manuscript	Page No. 15 Line no. 245 to 249
	There are a few recent publications on TB and adolescents that the authors may consider including in the discussion	We have added suggested studies in the discussion part of the manuscript.	Reference nos. 14, 15, 21,22,23

VERSION 2 – REVIEW

REVIEWER	Hoddinott, Graeme Stellenbosch University Faculty of Medicine and Health Sciences, Desmond Tutu TB Centre
REVIEW RETURNED	23-Jun-2022
GENERAL COMMENTS	Thank you for addressing comments. Congratulations on the revised manuscript. Important work on a neglected population.