Author's response to reviews

Title: The incidence of and mortality from leukaemias in the UK: A general population-based study

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Author's response to reviews: see over
Dear Editor

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The incidence of and mortality from leukaemias in the UK: A general population-based study

Thank you for reviewing our paper. We have addressed all of the issues raised by the reviewers and attached a revised manuscript. Below is a point-by-point response to the comments and concerns of both reviewers.

Response to reviewer: Alois Gratwohl

(1) Regarding the handling of MDS:
- MDS cases were excluded from the analysis and this has now been clarified within the text of the manuscript.

(2) With regard to the association between ALL incidence and social class:
- Although there was an apparent decrease in incidence with lower socio-economic class (i.e. higher Townsend Score), it is worth noting that the test-for-trend did not reach statistical significance (p=0.15).
- As regards the trend in specific age groups, 116 of the 182 ALL cases analysed were diagnosed under the age of 20 years. In this age category the trend was similar to the trend for all age groups together. The other age groups could not be meaningfully analysed due to the small number of remaining cases (which would result in even smaller case numbers in each of the other age categories).

(3) With regard to AML:
- The higher death rate in AML reflects the nature of the disease, which is known to have a poor prognosis.
- The incidence of AML among different social classes is not significantly different and there is no statistically significant trend in incidence across the social classes. Reasons for the significant difference in mortality across social class include possible differences in co-morbidity and/or a class bias in the treatment offered or undertaken, as alluded to in the discussion. We are currently investigating this hypothesis using other data sources, in addition to ‘THIN’ data. While such a bias may apply equally to other leukaemia sub-types, the reason it is apparent in AML may be due to the aggressive nature of AML and its poor prognosis.
(4) Minor comment re: using WHO terminology: this has now been corrected in the manuscript.

Response to reviewer: Elaine Gluckman

(1) With regard to the description of the population studied:

- This has been revised in the manuscript to include the geographic information requested. Unfortunately, ‘THIN’ does not hold data on occupation, but the dataset does represent the general population of the UK as has now been described (and referenced) in the revised manuscript.

(2) As regards to assessment of mortality:

- All mortality analyses have been mutually adjusted for age at diagnosis, Townsend Score, year of diagnosis and gender.
  - The impact of age, and the physical environment have thus been taken into account.
  - The type of leukaemia is an important predictor of mortality and it is for this reason that sub-type analyses have been done and presented.
  - The time period of analysis has been taken into account by adjusting for year of diagnosis, which will reflect changes in treatment protocols over time. More detail regarding the time period from which the data are drawn is provided in the revised manuscript.

- As regards access to healthcare, we believe this to be equal, in principle, across socio-economic classes due to the nature of the NHS in the UK. Furthermore, similar incidence rates across the spectrum of social class for each of the leukaemia sub-types studied here, suggest equal access to and uptake of healthcare in this population.

- We are currently investigating the hypothesis that worsening AML mortality with poorer socio-economic class may be explained by greater co-morbidity in poorer social classes and/or the existence of a class bias in the treatment offered or undertaken in these groups.

(2) Minor revision re: Townsend definition:

- The Townsend Score has been explained in better detail in the revised manuscript.

We hope this revision and our responses to the reviewers meet with your requirements.

Thank you.

Best Wishes

Dr. Fatima Bhayat