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LETTER TO THE EDITOR

Need to minimize bias when surveying patient attitudes to stopping CML treatment

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Sanford *et al.* reported results from an interview-assisted survey of chronic myeloid leukemia (CML) patients, which indicated that neither treatment compliance nor the occurrence of side effects significantly affected patient willingness to stop tyrosine kinase inhibitor treatment[1]. This conclusion is surprising, and we suggest that the study may have failed to identify an association between these variables because of limitations in the methodology.

First, we do not believe the sample is representative of the CML patient group who might be eligible to stop treatment. Sustained deep molecular response (Bcr-Abl $\leq$ 0.0032% or undetectable Bcr-Abl) for at least 2 years has been used as the key eligibility criterion for treatment cessation[2]; however, patients in this study appear to have been included irrespective of the level and duration of molecular response. While the authors acknowledge this limitation, we believe that this inclusion criterion is vital if the conclusions are to be applied to the population of interest. Secondly, it is unclear whether every CML patient attending the clinic was invited to take part. If some selection criteria were applied, the characteristics of the patients not included in the survey should be taken into account. Finally, the single-centre nature of the study may have allowed for the opinion or influence of a small number of clinicians to have a significant impact on patient responses; a multicentre study would yield a more representative sample.

With respect to the measurement tool, we contend that there are flaws in many of the measures used, which may undermine the validity of the results. Importantly, the first two measures of patient preferences for relapse rates are confounded with willingness to stop treatment. These items reveal assumptions that all patients are willing to stop treatment, and that risk acceptability is the most important indicator of this willingness, overriding all other concerns. These items were measured using visual analogue scales which ranged from 0 to 100, where a zero chance of relapse (the desirable outcome) was labelled the *worst* imaginable health state and accompanied by a "sad face" image, and a 100% chance of relapse (the undesirable outcome) was labelled the *best* imaginable health state and accompanied by a "happy face" image. Assuming patients were presented with these scales, the results are difficult to interpret.

The response options for the first item on treatment compliance are double-barrelled: that is, they comprise more than one issue or concept. They reveal an underlying assumption that the reasons for compliance are dichotomous: taking medication is either "simple and easy" (which is combined with 100% compliance) or a "nuisance" (combined with less than 50% compliance). These response options oversimplify treatment compliance; in fact, studies on compliance in CML have shown a much more complex array of behaviours and choices[3]. Moreover, these response options do not make a distinction between unintentional and deliberate noncompliance[3]. Self-reported measures of compliance are notoriously unreliable, and evidence suggests that patients are more likely to misrepresent their treatment adherence in clinical settings[4]. Also, only a single-item measure was used to investigate the role of side effects, described in days per month and percentages. We query whether this is a meaningful representation of the patients' experience of toxicity, as it is not clear how these responses can be interpreted (that is, what was considered for high, medium, and low toxicity). Validated measures for patient-reported outcomes of compliance and toxicity specific to CML exist and are likely to have provided superior estimates[4,5].

Sanford *et al.* acknowledge that interviewer factors potentially biased responses, and we agree that this is a notable limitation of the study. The interviewers were said to have "rephrase[d] and clarif[ied] questions as needed"[1]. It is unclear which questions were rephrased, how, and with what frequency. This

method of addressing clarity introduces a significant amount of both interviewer and social desirability bias and a large degree of inconsistency in the responses, making the results difficult to interpret. Cognitive interviewing is a set of techniques for systematically developing and refining survey questions based on investigation of the thought processes of individuals presented with those inquiries. Use of cognitive interviewing techniques to refine the items is likely to have improved the clarity and comprehension of the questionnaire.

Because of limitations in the methodology, we query the conclusion that treatment compliance and side effects are not associated with willingness to stop treatment. While we agree with the authors' assertion that a prescriptive approach to stopping treatment would not be suitable for this patient group, further research is required to elucidate these issues.

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CONFLICT OF INTEREST DISCLOSURES

The authors have no financial conflicts of interest to declare.

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