Reviewer's report

Title: New epidemiological data on hereditary hemochromatosis

Version: 1 Date: 14 February 2005

Reviewer: Robert Britton

Reviewer's report:

General

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Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

The goal of this study was to assess the impact of HFE genetic testing on the epidemiology of hereditary hemochromatosis. The impact of the study is decreased because the authors did not perform a population screening study using HFE genetic testing, but rather studied individuals who were referred to a phlebotomy program with transferrin saturations of > 45%. Large population studies have shown that a substantial proportion of C282Y homozygotes have transferrin saturations of less than 45% (ref 39, Adams et al, Gastroenterology 122:A634, 2002) and thus would be missed using the current study design. Therefore, the current study overestimates the impact of C282Y homozygosity on laboratory values, and clinical signs and symptoms. The authors should temper the interpretation of their findings, and it is suggested that the title of the manuscript be changed to "Impact of HFE genetic testing on clinical presentation of hereditary hemochromatosis".

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Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

p 2, line 5: change "phlebotomies program" to "phlebotomy program" throughout the manuscript
p 2, line 8: change "development of" to "implementation of"

p 2, line 13: change "made in front of" to "made before" throughout the manuscript
p 4, line 5: change "mutation" to "mutations"

p 4, line 8: change "suspicions" to "suspicion"

p 7, line 19: change to "This study included only C282Y homozygous patients"

p 8, line 18: change "overloads" to "overload"

p 11: In the section describing the study population, please state the last date of patient entry for inclusion in this study. Was HFE genetic testing performed on any individual by the referring physician before referral to the phlebotomy program?

p 11: In the section describing the clinical questionnaire, is the "age of onset" the "age of diagnosis" or the "age of entry" into the phlebotomy program? The term "age of onset" should be changed throughout the manuscript. How were the clinical signs determined for the questionnaire: was a clinical exam performed at the phlebotomy center, or was a clinical exam performed by each referring physician?

p 11, line 22: change to "Recently, another technique was adopted for this analysis"

p 13: change to "odds-ratio", "Authors"

Ref 38: change "increase" to "increases" and provide the volume and page numbers
Discretionary Revisions (which the author can choose to ignore)

p 2, line 16: change to "Detection of HFE-related HH in its presymptomatic.."
p 3, line 6: change to "for transferrin receptor 2"
p 4, line 3: change to "most common mutations of the HFE gene..


What next?: Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

Level of interest: An article of limited interest

Quality of written English: Needs some language corrections before being published

Statistical review: No

Declaration of competing interests:

I declare that I have no competing interests.