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Common genetic disorder linked to more disease than previously thought

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The most common genetic disorder in people from northern Europe is associated with substantially higher levels of disease than previously thought, despite being easy to detect and treat, finds a study published in *The BMJ* today.

The findings show that a larger proportion than previously thought of people with two copies of a faulty gene (HFE C282Y) develop haemochromatosis (a build up of iron in the body that can damage vital organs such as the liver and heart). The study also found that the faulty genes often lead to serious health problems, including in later life.

Haemochromatosis can be prevented if spotted early, and is easily treated by regular removal of iron-rich blood (phlebotomy), but typical symptoms such as extreme tiredness and joint pain are often mistaken for normal signs of ageing.

Previous studies also suggest that very few people with the faulty gene develop haemochromatosis, and therefore health problems are rare.

So to better understand the impact of this disorder, researchers led by Professor David Melzer at the University of Exeter compared levels of illness and death among those with and without the gene mutations.

They analysed data for 2,890 people aged 40 to 70 years (average age 63) with HFE C282Y mutations from the UK Biobank, a large database of more than half a million British men and women recruited between

2006 and 2010.

Participants were monitored for an average of seven years, and hospital records were used to identify diagnosed conditions and deaths during that time.

After taking account of age and other genetic factors, haemochromatosis was diagnosed in 21.7% of men and 9.8% of women with HFEC282Y mutations by the end of the follow-up period—substantially higher than previous estimates suggest.

What's more, at the end of the follow-up period, when their sample had an average age of 63, one in five more men and one in 10 more women with HFE C282Y mutations had developed liver disease, diabetes, osteoarthritis or rheumatoid arthritis, compared with people with no HFE C282Y mutations.

More disease developed at older ages, and there was also a nominally significant increase in mortality in the HFE C282Y mutations group overall, including 14 deaths from liver cancer.

To show the impact of these additional diseases on health services, the researchers estimate that 1.6% of all hip replacements and nearly 6% of all liver cancers in men in their sample occurred in those with HFE C282Y mutations.

This is an observational study, and as such, can't establish cause, and the researchers point to limitations that may have influenced their findings. Nevertheless, they say this is the largest study of its kind and findings were similar after additional analyses to test the strength of the results.

In light of this evidence, and as treatment is safe and effective if started early, they say issues involved in offering screening and improving early

detection of HFE C282Y mutations need re-examining to help prevent unnecessary disease, including at older ages.

More information: Common conditions associated with hereditary haemochromatosis genetic variants: cohort study in UK Biobank , *BMJ* (2019). DOI: 10.1136/bmj.k5222 , www.bmj.com/content/364/bmj.k5222

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