



Screening for Hereditary Hemochromatosis: A Focused Evidence Review: Evidence Synthesis Number 43

U. S. Department of Health and Human Services, Agency for Healthcare Research and Quality

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Screening for Hereditary Hemochromatosis is a topic that has not been previously considered by the United States Preventive Services Task Force (USPSTF) for a possible recommendation as a clinical preventive service for primary care clinicians. This product is a pilot approach to systematically review the sufficiency of evidence for a focused (as opposed to comprehensive) set of key questions related to two main USPSTF screening criteria: the burden of suffering and the potential effectiveness of a preventive intervention, therapeutic phlebotomy. The USPSTF considers conditions of major significance that are relatively common in the U.S. to be candidates for preventive interventions, such as screening. Also, for a condition to be a candidate for a USPSTF screening recommendation, there must be evidence that persons with the condition detected early have a better clinical outcome than those detected without screening. Key questions for this review were limited to what the USPSTF judged to be critical evidence gaps in establishing these requirements. Key questions were constructed and applied using strict and consistent definitions of disease, which are described in more detail below. The resulting report is intended to demonstrate evidence sufficiency or insufficiency as its primary aim, and thus does not have the usual breadth associated with a USPSTF systematic evidence review. Hemochromatosis (HC) was originally thought to be a rare idiopathic disorder characterized by end-stage disease (cirrhosis, diabetes, and bronzed skin), but is now recognized as often having a hereditary component due to an autosomal recessive inherited disorder of iron metabolism. In HC, body iron accumulates and can lead to iron overload. In iron overload, excess iron is deposited in the liver, pancreas, heart, joints, and endocrine glands, resulting in tissue damage that may lead to one or more disease conditions (e.g., cirrhosis, diabetes, increased skin pigmentation, heart failure, arthropathy, and impotence). Iron overload can be primary (as in hereditary hemochromatosis) or secondary (e.g., due to anemias with inefficient erythropoiesis or repeated blood transfusions). Key questions addressed include: Key Question 1. Among those with a homozygous C282Y genotype, what is the risk of developing clinical hemochromatosis? Key Question 2. Does earlier therapeutic phlebotomy of individuals with primary iron overload due to HH reduce morbidity and mortality compared with treatment after diagnosis in routine clinical care? Key Question 3. Are there group(s) at increased risk for developing HH that can be readily identified prior to genetic screening?

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