

**Appendix Table 5. Studies Excluded from Key Question 2**

| Study Citation   | Reason for Exclusion               |
|--|------------------------------------|
| Adams PC, Kertesz AE, Valberg LS. Rate of iron reaccumulation following iron depletion in hereditary hemochromatosis. Implications for venesection therapy. <i>J Clin Gastroenterol.</i> 1993;16:207-10. [PMID: 8505491]   | Does not present relevant outcomes |
| Adams PC. Factors affecting the rate of iron mobilization during venesection therapy for genetic hemochromatosis. <i>Am J Hematol.</i> 1998;58:16-9. [PMID: 9590143]   | Does not present relevant outcomes |
| Askari AD, Muir WA, Rosner IA, Moskowitz RW, McLaren GD, Braun WE. Arthritis of hemochromatosis. Clinical spectrum, relation to histocompatibility antigens, and effectiveness of early phlebotomy. <i>Am J Med.</i> 1983;75:957-65. [PMID: 6650551]   | Quality                            |
| Barton JC, Bottomley SS. Iron deficiency due to excessive therapeutic phlebotomy in hemochromatosis. <i>Am J Hematol.</i> 2000;65:223-6. [PMID: 11074539]  | < 20 patients                      |
| Batey RG, Hussein S, Sherlock S, Hoffbrand AV. The role of serum ferritin in the management of idiopathic haemochromatosis. <i>Scand J Gastroenterol.</i> 1978;13:953-7. [PMID: 725519]  | Does not present relevant outcomes |
| Bodemann HH, Tanzi-Fetta RF, Schroter-Urban H, Volk BA, Keul J, Lohr GW. Ferritin in erythrocytes and plasma of patients with iron overload. <i>Blut.</i> 1985;51:25-31. [PMID: 3848335]   | Quality                            |
| Candell-Riera J, Lu L, Seres L, Gonzalez JB, Batlle J, Permanyer-Miralda G, et al. Cardiac hemochromatosis: beneficial effects of iron removal therapy. An echocardiographic study. <i>Am J Cardiol.</i> 1983;52:824-9. [PMID: 6624673]  | Quality                            |
| Cesana M, Mandelli C, Tiribelli C, Bianchi PA, Conte D. Concomitant primary hemochromatosis and beta-thalassemia trait: iron depletion by erythrocytapheresis and desferrioxamine. <i>Am J Gastroenterol.</i> 1989;84:150-2. [PMID: 2916524]   | < 20 patients                      |
| Chow LH, Frei JV, Hodzman AB, Valberg LS. Low serum 25-hydroxyvitamin D in hereditary hemochromatosis: relation to iron status. <i>Gastroenterology.</i> 1985;88:865-9. [PMID: 3838288]  | Quality                            |
| Cleton MI, de Bruijn WC, van Blokland WT, Marx JJ, Roelofs JM, Rademakers LH. Iron content and acid phosphatase activity in hepatic parenchymal lysosomes of patients with hemochromatosis before and after phlebotomy treatment. <i>Ultrastruct Pathol.</i> 1988;12:161-74. [PMID: 3363682] | < 20 patients                      |
| Cleton MI, Roelofs JM, Blok-Van Hoek CJ, De Bruijn WC. Integrated image and X-ray microanalysis of hepatic lysosomes in a patient with idiopathic hemosiderosis before and after treatment by phlebotomy. <i>Scan Electron Microsc.</i> 1986;999-1006. [PMID: 3798023]                       | < 20 patients                      |
| Conte D, Mandelli C, Cesana M, Ferrini R, Marconi M, Bianchi A. Effectiveness of erythrocytapheresis in idiopathic hemochromatosis. Report of 14 cases. <i>Int J Artif Organs.</i> 1989;12:59-62. [PMID: 2925263]  | Does not report relevant outcomes  |
| Conte D, Piperno A, Mandelli C, Fargion S, Cesana M, Brunelli L, et al. Clinical, biochemical and histological features of primary haemochromatosis: a report of 67 cases. <i>Liver.</i> 1986;6:310-5. [PMID: 3023781]   | Quality                            |
| Cundy T, Butler J, Bomford A, Williams R. Reversibility of hypogonadotropic hypogonadism associated with genetic haemochromatosis. <i>Clin Endocrinol (Oxf).</i> 1993;38:617-20. [PMID: 8334747]   | < 20 patients                      |
| Dabestani A, Child JS, Henze E, Perloff JK, Schon H, Figueroa WG, et al. Primary hemochromatosis: anatomic and physiologic characteristics of the cardiac ventricles and their response to phlebotomy. <i>Am J Cardiol.</i> 1984;54:153-9. [PMID: 6741807]                                   | < 20 patients                      |
| Dymock IW, Cassar J, Pyke DA, Oakley WG, Williams R. Observations on the pathogenesis, complications and treatment of diabetes in 115 cases of haemochromatosis. <i>Am J Med.</i> 1972;52:203-10. [PMID: 5058506]  | Quality                            |
| Easley RM Jr, Schreiner BF Jr, Yu PN. Reversible cardiomyopathy associated with hemochromatosis. <i>N Engl J Med.</i> 1972;287:866-7. [PMID: 5071966]  | < 20 patients                      |
| Failla M, Giannattasio C, Piperno A, Vergani A, Grappiolo A, Gentile G, et al. Radial artery wall alterations in genetic hemochromatosis before and after iron depletion therapy. <i>Hepatology.</i> 2000;32:569-73. [PMID: 10960451]  | < 20 patients                      |
| Fargion S, Mandelli C, Piperno A, Cesana B, Fracanzani AL, Fraquelli M, et al. Survival and prognostic factors in 212 Italian patients with genetic hemochromatosis. <i>Hepatology.</i> 1992;15:655-9. [PMID: 1312985]   | Quality                            |
| Feely J, Counihan TB. Haemochromatosis presenting as angina and responding to venesection. <i>Br Med J.</i> 1977;2:681-2. [PMID: 902053]   | < 20 patients                      |
| Fellows IW, Stewart M, Jeffcoate WJ, Smith PG, Toghill PJ. Hepatocellular carcinoma in primary haemochromatosis in the absence of cirrhosis. <i>Gut.</i> 1988;29:1603-6. [PMID: 2850272]   | < 20 patients                      |
| Fracanzani AL, Fargion S, Romano R, Conte D, Piperno A, D'Alba R, et al. Portal hypertension and iron depletion in patients with genetic hemochromatosis. <i>Hepatology.</i> 1995;22:1127-31. [PMID: 7557861]  | Quality                            |
| Gama R, Smith MJ, Wright J, Marks V. Hypopituitarism in primary haemochromatosis; recovery after iron depletion. <i>Postgrad Med J.</i> 1995;71:297-8. [PMID: 7596937]   | < 20 patients                      |
| Goh J, Callagy G, McEntee G, O'Keane JC, Bomford A, Crowe J. Hepatocellular carcinoma arising in the absence of cirrhosis in genetic hemochromatosis: three case reports and review of literature. <i>Eur J Gastroenterol Hepatol.</i> 1999;11:915-9. [PMID: 10514128]                       | < 20 patients                      |
| Grima KM. Therapeutic apheresis in hematological and oncological diseases. <i>J Clin Apher.</i> 2000;15:28-52. [PMID: 10767050]  | Review article                     |
| Guillygomarc'h A, Mendler MH, Moirand R, Laine F, Quentin V, David V, et al. Venesection therapy of insulin resistance-associated hepatic iron overload. <i>J Hepatol.</i> 2001;35:344-9. [PMID: 11592595]   | Wrong population                   |
| Hash RB. Hereditary hemochromatosis. <i>J Am Board Fam Pract.</i> 2001;14:266-73. [PMID: 11458969]   | Review article                     |
| Hines C Jr, Davis WD Jr, Ferrante WA. Hepatoma developing in hemochromatosis in spite of adequate treatment by multiple phlebotomies. <i>Am J Dig Dis.</i> 1971;16:349-55. [PMID: 4324431]   | Case report                        |
| Hramiak IM, Finegood DT, Adams PC. Factors affecting glucose tolerance in hereditary hemochromatosis. <i>Clin Invest Med.</i> 1997;20:110-8. [PMID: 9088667]   | Quality                            |
| Hultcrantz R, Angelin B, Bjorn-Rasmussen E, Ewerth S, Einarsson K. Biliary excretion of iron and ferritin in idiopathic hemochromatosis. <i>Gastroenterology.</i> 1989;96:1539-45. [PMID: 2714579]   | Quality                            |
| Jakeman A, Thompson T, McHattie J, Lehotay DC. Sensitive method for nontransferrin-bound iron quantification by graphite furnace atomic absorption spectrometry. <i>Clin Biochem.</i> 2001;34:43-7. [PMID: 11239514]   | < 20 patients                      |
| Kaltwasser JP, Werner E, Schalk K, Hansen C, Gottschalk R, Seidl C. Clinical trial on the effect of regular tea drinking on iron accumulation in genetic haemochromatosis. <i>Gut.</i> 1998;43:699-704. [PMID: 9824354]  | Quality                            |
| Kelly TM, Edwards CQ, Meikle AW, Kushner JP. Hypogonadism in hemochromatosis: reversal with iron depletion. <i>Ann Intern Med.</i> 1984;101:629-32. [PMID: 6435491]  | Does not present relevant outcomes |
| Kohan A, Niborski R, Daruich J, Rey J, Bastos F, Amerise G, et al. Erythrocytapheresis with recombinant human erythropoietin in hereditary hemochromatosis therapy: a new alternative. <i>Vox Sang.</i> 2000;79:40-5. [PMID: 10971213]   | < 20 patients                      |

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Appendix Table 5—Continued

| Study Citation   | Reason for Exclusion               |
|--|------------------------------------|
| Leitman SF, Browning JN, Yau YY, Mason G, Klein HG, Conry-Cantilena C, et al. Hemochromatosis subjects as allogeneic blood donors: a prospective study. <i>Transfusion</i> . 2003;43:1538-44. [PMID: 14617312]   | Does not report relevant outcomes  |
| Limdi JK, Crampton JR. Hereditary haemochromatosis. <i>QJM</i> . 2004;97:315-24. [PMID: 15152104]  | Review article                     |
| Lombard M, Bomford A, Hynes M, Naoumov NV, Roberts S, Crowe J, et al. Regulation of the hepatic transferrin receptor in hereditary hemochromatosis. <i>Hepatology</i> . 1989;9:1-5. [PMID: 2642288]  | Does not present relevant outcomes |
| Lufkin EG, Baldus WP, Bergstralh EJ, Kao PC. Influence of phlebotomy treatment on abnormal hypothalamic-pituitary function in genetic hemochromatosis. <i>Mayo Clin Proc</i> . 1987;62:473-9. [PMID: 3106726]  | Quality                            |
| Mainous AG 3rd, Wells B, Carek PJ, Gill JM, Geesey ME. The mortality risk of elevated serum transferrin saturation and consumption of dietary iron. <i>Ann Fam Med</i> . 2004;2:139-44. [PMID: 15083854]   | No phlebotomy treatment            |
| Mandelli C, Cesarini L, Piperno A, Fargion S, Fracanzani AL, Barisani D, et al. Saturability of hepatic iron deposits in genetic hemochromatosis. <i>Hepatology</i> . 1992;16:956-9. [PMID: 1398502]   | Does not present relevant outcomes |
| McDonnell SM, Witte DL, Cogswell ME, McIntyre R. Strategies to increase detection of hemochromatosis. <i>Ann Intern Med</i> . 1998;129:987-92. [PMID: 9867752]   | Review article                     |
| Milman N, Pedersen P, A; Steig T, Byg KE, Graudal N, Fenger K. Clinically overt hereditary hemochromatosis in Denmark 1948-1985: epidemiology, factors of significance for long-term survival, and causes of death in 179 patients. <i>Ann Hematol</i> . 2001;80:737-44. [PMID: 11797115]                      | Quality                            |
| Milman N. Hereditary haemochromatosis in Denmark 1950-1985. Clinical, biochemical and histological features in 179 patients and 13 preclinical cases. <i>Dan Med Bull</i> . 1991;38:385-93. [PMID: 1914539]  | Does not report relevant outcomes  |
| Moirand R, Adams PC, Bicheler V, Brissot P, Deugnier Y. Clinical features of genetic hemochromatosis in women compared with men. <i>Ann Intern Med</i> . 1997;127:105-10. [PMID: 9229998]  | Does not report relevant outcomes  |
| Morcos M, Dubois S, Bralet MP, Belghiti J, Degott C, Terris B. Primary liver carcinoma in genetic hemochromatosis reveals a broad histologic spectrum. <i>Am J Clin Pathol</i> . 2001;116:738-43. [PMID: 11710692]   | Does not report relevant outcomes  |
| Muncunill J, Vaquer P, Galmes A, Obrador A, Parera M, Bargay J, et al. In hereditary hemochromatosis, red cell apheresis removes excess iron twice as fast as manual whole blood phlebotomy. <i>J Clin Apher</i> . 2002;17:88-92. [PMID: 12210712]   | < 20 patients                      |
| Muting D, Kalk JF, Fischer R, Wiewel D. Spontaneous regression of oesophageal varices after long-term conservative treatment. Retrospective study in 20 patients with alcoholic liver cirrhosis, posthepatic cirrhosis and haemochromatosis with cirrhosis. <i>J Hepatol</i> . 1990;10:158-62. [PMID: 2332585] | Not phlebotomy treatment           |
| Niederau C, Stremmel W, Strohmeyer GW. Clinical spectrum and management of haemochromatosis. <i>Baillieres Clin Haematol</i> . 1994;7:881-901. [PMID: 7881158]   | Review article                     |
| Niederau C, Strohmeyer G, Stremmel W. Epidemiology, clinical spectrum and prognosis of hemochromatosis. <i>Adv Exp Med Biol</i> . 1994;356:293-302. [PMID: 7887234]  | Review article                     |
| Olsson KS, Ritter B, Lundin PM. Liver affection in iron overload studied with serum ferritin and serum aminotransferases. <i>Acta Med Scand</i> . 1985;217:79-84. [PMID: 3976436]  | Quality                            |
| Piperno A, Vergani A, Salvioni A, Trombini P, Vigano M, Riva A, et al. Effects of venesections and restricted diet in patients with the insulin-resistance hepatic iron overload syndrome. <i>Liver Int</i> . 2004;24:471-6. [PMID: 15482345]  | Does not report relevant outcomes  |
| Propper R, Nathan D. Clinical removal of iron. <i>Annu Rev Med</i> . 1982;33:509-19. [PMID: 6282184]   | Clinical review article            |
| Prunescu CC, Prunescu P, Vilcu AL. Ultrastructure of the liver in idiopathic haemosiderosis and results of a treatment by repeated bleedings. <i>Morphol Embryol (Bucur)</i> . 1987;33:133-6. [PMID: 2956507]  | Case report                        |
| Riquelme A, Soza A, Nazal L, Martinez G, Kolbach M, Patillo A, et al. Histological resolution of steatohepatitis after iron depletion. <i>Dig Dis Sci</i> . 2004;49:1012-5. [PMID: 15309893]   | Case report                        |
| Sargent T, Saito H, Winchell HS. Iron absorption in hemochromatosis before and after phlebotomy therapy. <i>J Nucl Med</i> . 1971;12:660-7. [PMID: 5000107]  | Does not report relevant outcomes  |
| Seamark CJ, Hutchinson M. Controversy in primary care: Should asymptomatic haemochromatosis be treated? <i>BMJ</i> . 2000;320:1314-7. [PMID: 10807626]   | Case report                        |
| Sigal SH, Fleischner GM, Weiner FR. Hypogonadal-induced anemia in genetic hemochromatosis: implications for phlebotomy therapy. <i>Am J Gastroenterol</i> . 1995;90:152-3. [PMID: 7801923]   | Case report                        |
| Spellberg MA. Treatment of hemochromatosis. <i>Am J Gastroenterol</i> . 1969;51:516-22. [PMID: 4894612]  | Review article                     |
| Tiniakos G, Williams R. Cirrhotic process, liver cell carcinoma and extrahepatic malignant tumors in idiopathic haemochromatosis. Study of 71 patients treated with venesection therapy. <i>Appl Pathol</i> . 1988;6:128-38. [PMID: 2839215]   | Quality                            |
| Weintraub LR, Conrad ME, Crosby WH. The treatment of hemochromatosis by phlebotomy. <i>Med Clin North Am</i> . 1966;50:1579-90. [PMID: 5339192]  | < 20 patients                      |