Clinical and economic assessment of screening for HFE1 haemochromatosis in 2004

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Aim
To reassess the benefit of mass screening for haemochromatosis in France on the basis of data published since the ANAES 1999 report.

Results
(i) *Definition:* The type of iron overload of genetic origin for which a mass screening programme is discussed in this report is HFE1-haemochromatosis.
(ii) *Natural history:* The disease develops in 4 stages after the age of 30: (1) asymptomatic, (2) biochemical evidence, (3) symptomatic, (4) complications leading to higher mortality in affected individuals (insulin-dependent diabetes, cirrhosis, hepatocellular carcinoma and cardiomyopathy).
(iii) *Prevalence:* The frequency of the C282Y homozygous genotype in the French population (studies including ≥ 200 subjects) is in the range 0.2–0.8%. The unknown and incomplete penetrance by the genotype precludes a precise estimate of the number of affected individuals in France.
(iv) *Treatment:* The efficacy of phlebotomy on life expectancy has not been reassessed in 2004. Data published 15 years ago showed a return to a normal life expectancy .
(v) *Screening tests:* Measurement of blood ferritin and transferrin saturation coefficient detects iron overload; a test for C282Y homozygotes confirms HFE1-haemochromatosis.
(vi) *Benefits of screening*: No study has measured the anticipated clinical benefit of mass screening. Our economic models show that mass screening would identify 1 166-1 875 C282Y homozygotes out of 375 000 subjects tested, at a total cost of 3.6-19.5 million euros. Family screening would identify 198 homozygotes out of 1 496 subjects tested in the first year, at a total cost of 78 000 euros.
(vii) *Conditions for mass screening:* Unresolved questions are screening frequency, age range, strategy, threshold values for laboratory tests, problems of logistics, financing, regulation, raising awareness among professionals, reimbursement by Health Insurance.

Conclusions
(i) Clinical data and economic models are in favour of increasing family screening for the C282Y homozygous genotype. The question of mass screening for HFE1-haemochromatosis in France is still unresolved in 2004 in view of the total cost of the strategies involved and the lack of clinical data for long-term efficacy.
(ii) Pilot studies should be carried out in regions with an adequate infrastructure to answer unresolved questions and assess the feasibility of mass screening.

Methods
The data in the ANAES 1999 report were updated by searching several databases up to January 2004 (Medline, Embase, Pascal, Healthstar, PsycInfo, Cochrane library, National Guideline Clearinghouse, HTA Database, French Public Health data). Studies were selected according to their level of evidence and design quality. The critical literature analysis was validated by a multidisciplinary working group (n = 24). The benefit of screening was assessed according to the WHO criteria for mass screening programmes.

Looking ahead

(i) Encourage diagnosis of individuals; provide French practitioners with a decision algorithm - based on clinical, biochemical and genetic criteria - for managing patients;
(ii) Continue clinical and basic research to improve our knowledge of the disease, and carry out a study of penetrance of the mutation in France;
(iii) Assess current medical practice for prescribing genetic testing;
(iv) Assess how patients are managed, their expectations and quality of life, through surveys in hospitals and/or in independent practice;
(v) Determine mechanisms and procedures for family screening.

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