I.12 Methotrexate and monitoring for hepatotoxicity

Chalmers R, Kirby B, Smith A et al. Replacement of routine liver biopsy by procollagen III aminopeptide for monitoring patients with psoriasis receiving long-term methotrexate: a multicentre audit and health economic analysis. Br J Dermatol. 2005; 152(3):444-450. Ref ID: CHALMERS2005

Study details	Population & interventions	Costs	Health outcomes	Cost effectiveness
Economic analysis: Cost consequence analysis **Study design:** Multicentre prospective audit in four centres in the UK and Ireland. Health care costs and outcomes of two intervention groups from centres where serial PIIINP measurement was employed were compared to those of two control groups from centres in which liver biopsy was used for monitoring patients at risk of methotrexate-induced hepatotoxicity.	**Population:** Patients established on methotrexate for psoriasis; similar duration of psoriasis between groups (24-27 years) **Group 1:** Serial PIIINP only (Manchester) n=138 Mean age = 38.3 years Mean duration of MTX therapy = 72 months **Group 2:** Serial PIIINP (London) + baseline liver biopsy (note that no patient actually underwent baseline liver biopsy) n=28 Mean age = 35.6 years Mean duration of MTX therapy = 66.3 months	**Unit cost of monitoring tests:** PIIINP measurement: £22.50 Liver Biopsy: Group 1: £577.00 Group 2: £451.72 Group 3: NR Group 4: £270.00 **Total costs (mean per patient):** Group 1: £113 Group 2: £99 Group 3 & 4: £76 **Currency & cost year:** 2001 UK pounds **Cost components incorporated:** Direct medical costs related to different monitoring methods (e.g. hospitalisation, biopsy, histopathology, PIIINP	**Primary outcome measure:** **Mean biopsies per patient per year:** **Group 1: 0.04** (19 patient qualified for, but only 10 underwent liver biopsy; 8/10 had minor histology findings and did not change treatment, two had mild portal fibrosis for which change in treatment was considered) **Group 2: 0.02** (1 liver biopsy was performed and showed inflammation with portal fibrosis, thus the patient discontinued MTX) **Group 3: 0.26** (26 liver biopsies were peformed; 9/26 were normal and 16/26 had minor	The total costs of different strategies are highly dependent on the unit cost of performing a liver biopsy. When the unit cost of liver biopsy was low (e.g. £270 as quoted for group 3), then a strategy of only routine liver biopsy was less costly than routine PIIINP. However, when the unit cost of liver biopsy was higher (e.g. £641 as quoted in 2000 NHS reference costs), then serial PIIINP with occasional liver biopsy was cost-saving.

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Approach to analysis: Within study analysis **Perspective:** UK NHS **Time horizon:** **Treatment effect duration:** 2 yrs **Discounting:** NA	**Group 3:** Liver biopsy only (Essex) n=43 Mean age = 44.6 years Mean duration of MTX therapy = 73.2 months **Group 4:** Liver biopsy only (Dublin) n= 44 Mean age = 42.4 years Mean duration of MTX therapy = 87.9 months	analysis)	abnormalities and 1/26 had Roenigk grade 3a changes and discontinued MTX) **Group 4: 0.30** (21 liver biopsies were performed; 5/21 were normal and 14/21 had minor abnormalities and 2/21 had Roenigk grade 3a changes and discontinued MTX) Mean liver biopsy rate from Essex and Dublin combined was 0.28 biopsies per patient per year. 54% of control patients (Essex and Dublin) underwent liver biopsy during 2 year study period, but in only 3 did the results change management. Thus, 15.7 biopsies were required to detect each abnormality of sufficient severity to influence management.	
Data sources				
Health outcomes: Within study analysis **Quality-of-life weights:** NA **Cost sources:** Local NHS costs; 2000 NHS reference costs				

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Comments
Source of funding: Northwest Regional Research and Development Fund **Limitations:** Given that treatment with methotrexate may continue for more than 2 years, time horizon may be insufficient. Does not report incidence of adverse events/ complications associated with liver biopsy and any effect on costs. Within trial analysis and so does not incorporate all available evidence on differences between monitoring methods but results appear consistent with results of clinical review. QALYs not used (cost consequence analysis). **Other:**
Overall applicability*: Partially applicable **Overall quality**:** Very serious limitations