

Title:	Polymerase chain reaction in the diagnosis and monitoring of patients with BCR-ABL gene rearrangement in chronic myeloid leukaemia, 2004
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Aim

To assess the safety, effectiveness and cost effectiveness of PCR testing for these indications and the circumstances under which public funding should be supported for them.

Conclusions and results

Safety. The PCR assays discussed in this review have no additional safety concerns. The required quantity of blood or marrow is minimal and would usually be collected concurrently with other routine blood or marrow tests.

Effectiveness

Diagnostic accuracy in CML diagnosis. PCR testing detected BCR-ABL in 100 per cent (95% CI 99-100) of patients cytogenetic positive for t(9;22) and was also positive in 79 per cent (95% CI 49-95) of CML patients who were t(9;22) negative on cytogenetic testing. PCR was estimated to have a specificity of 100 per cent (95% CI 91-100).

Diagnostic accuracy in CML monitoring. PCR was evaluated for its ability to predict subsequent cytogenetic and haematological relapse in the monitoring studies. In the 10 studies examining quantitative PCR where validity of the test could be estimated, the pooled sensitivity was 83 per cent (95% CI 76-89) and specificity was 80 per cent (95% CI 76-84). In the 25 studies examining qualitative PCR, the pooled sensitivity was estimated to be 94 per cent (95% CI 90-97) and specificity to be 72 per cent (95% CI 70-75).

Change in management. Accurate identification of CML associated with the fusion transcript BCR-ABL at diagnosis is useful for defining appropriate therapeutic strategies such as imatinib mesylate. Detection of molecular relapse post-transplant (through PCR monitoring) allows the early institution of salvage therapy in this group.

Effect of additional PCR testing on patient outcome. Patients with BCR-ABL CML are preferentially treated with transplantation, interferon or imatinib and these forms of treatment are associated with improved outcomes compared with alternative therapies. The improved detection of BCR-ABL with PCR could be expected to produce improved health outcomes. The early prediction of relapse in monitoring with PCR, combined with limited data on the effectiveness of early therapy, suggests improved health outcomes that are unlikely to be explained by lead time bias.

Cost-effectiveness

Diagnosis. The economic analysis evaluating the use of PCR in the diagnosis of CML found the incremental cost per life year saved was \$60,650 for cytogenetic and PCR testing compared with cytogenetic testing alone.

Monitoring. The incremental cost per life year saved for PCR monitoring was \$2,145 for monitoring with cytogenetic plus PCR testing combined compared with cytogenetic testing alone.

Recommendations

MSAC recommended that public funding should be supported for PCR testing in the diagnosis and monitoring of CML.

Method

A systematic review of the PCR in diagnosis and monitoring of BCR-ABL CML was conducted. The literature was searched up to October 2002 using Medline, Embase, Current Contents, Cancerlit, Cochrane Library, NHS Centre for Reviews and Dissemination databases and various website sources. Study selection criteria were stipulated and standard checklists were used to appraise study quality.

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