

Resolving Issues with the simple Continual Reassessment Method

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The simple Continual Reassessment Method (CRM) has been available for over 20 years and there is evidence that it is an improvement over the traditional 3+3 design, but it has not yet become the predominant methodology (Rogatko et al, J Clin Oncol 2007; 25:4982-4986). Why? Fundamentally because there have been a number of criticisms of the approach. First, it has been criticised for over-accelerating the dose escalation so that there is a high chance of patients suffering dose-limiting toxicities. Approaches based on over-dose have been proposed to overcome this (Babb et al, Stats in Med 1998; 17: 1103-1120) and it has also been suggested that a two-parameter model can reduce the issue (Neuschwander et al, Stats in Med 2008; 27:2420–2439). Second recent research has suggested the the CRM can react too quickly to an early event and the influence of this will continue for a large number of future patients irrespective of response (Resche-Rigon et al, Clin Trials 2008; 5: 595-606). In this talk I look at an aspect of Bayesian estimation that can negatively impact on these issues.