DYNAMIC MAINTENANCE TREATMENT OF CHILDREN WITH LEUKAEMIA

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Children with leukaemia are treated with chemotherapy for 2-2.5 years. During oral maintenance therapy the children receive two cytostatics (Methotrexate and 6-Mercaptopurine). Once a week a blood sample from the diseased child is analysed and the treating physician modifies the drug doses according to a specified strategy based on the test results and the previous doses.

To investigate a new dosing strategy a study of 538 children diagnosed with leukaemia was conducted in the Nordic countries in 1992-1996 (the NOPHO ALL-92 study). The children were randomly assigned to have their doses of cytostatics adjusted by blood counts only (standard treatment, control group) or by a combination of blood counts and drug levels (new treatment, pharmacology group). Quite surprisingly the new treatment strategy did not lead to improved results: The girls in the pharmacology group had an increased risk of relapse of 6.6 ($p=0.0003$) compared to the girls in the control group whereas the results for the boys were the same in the two treatment groups (Schmiegelow et al. (2003)). This demonstrates the need for an improved understanding of the treatment as well as the dosing strategies.

Dynamic treatment regimes has lately received much attention in the statistical literature. Much of the work is based on the framework set up by Robins (e.g. 1994). Several authors have focused on the estimation of optimal treatment strategies, including Murphy (2003), Robins (2004) and van der Laan et al. (2005). In general, these methods have been applied to data with a simple dynamic treatment (treat / do not treat) but the methods should also be suitable for more complex dynamic treatments involving doses on a continuous scale.
We have been studying the proposed methods in order to see whether they were useful in the search for a better treatment strategy for children with leukaemia. We have documented (in a simpler case, Rosthøj et al. (2006)) that some of the above methods will require significant elaboration in order to be useful for estimation of better dosing strategies. In the talk we will present the results we were able to obtain based on the above framework and will focus on the possibilities and limitations of these methods when applied to data as ours.

References:

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