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Leiden  
The Netherlands

## **Analysis of sarcoma and non-sarcoma clinical data with statistical methods and machine learning techniques**

Kantidakis, G.

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# Stellingen

behorend bij het proefschrift getiteld

*“Analysis of sarcoma and non-sarcoma clinical data with statistical methods and machine learning techniques”*

1. There is a need to raise the bar of thresholds for the commonest soft-tissue sarcoma (STS) types in future histology-tailored phase II trials in order to achieve higher success rates in new prospective confirmatory phase III trials (this thesis).
2. A metastatic profile in the bone is detrimental, although not statistically significant, for both overall and progression-free survival of STS patients of any line receiving palliative systemic therapy. Stratification is not justified in randomised studies with this population (this thesis).
3. STS show tremendous heterogeneity both in clinical and genomic settings and thus should be treated separately (Du *et al.*, *Frontiers in Oncology*, 2020).
4. Anthracycline-based therapy remains the most important systemic treatment for advanced STS. The selection of optimal systemic therapy after anthracycline-containing regimens remains a challenge, with few agents showing survival benefit (Smrke *et al.*, *Current Oncology*, 2020).
5. In rare cancers such as STS, flexibility and out-of-the-box thinking are required to advance research. Strong collaborations between clinicians and statisticians are key to bring new project ideas into maturity.
6. A review and critical appraisal of survival neural networks using prognostic factors for clinical prediction indicates poor reporting as well as inaccurate model development/validation with these methods (this thesis).
7. Machine learning (ML) techniques can be a useful tool versus statistical models (SM) for both prediction and interpretation of complex time-to-event data (this thesis).
8. For non-complex survival data, ML methods should only be applied complementary to SM as exploratory tools of model's performance. More attention to calibration is urgently needed (this thesis).
9. There is a strong need that ML techniques adhere to established methodological standards already defined in prediction model research. Fair and neutral evaluations and comparisons against existing prediction model approaches must be done (Collins & Moons, *The Lancet*, 2019).
10. We must ask ourselves whether a difference in predictive performance of a novel model is clinically meaningful, and whether it is worth all the added complexity (Leisman *et al.*, *Critical Care Medicine*, 2020).
11. Existing or new methods should address unmet needs such as research, benchmarking, or bedside application.